Is paracetamol being prescribed and used at the correct therapeutic dose in the children population in South Africa?

Award: Fulfilment of the award of M.Sc. in Pharmacy Administration and Pharmacy Policy specialising in regulatory sciences.

Author: Aadila Patel

Institution: Western Cape University, South African and Hibernia College, Ireland

Date of completion: 12 May 2014

Submitted in partial fulfilment of the requirements for the award of M.Sc. in Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences.

Is paracetamol being prescribed and used at the correct therapeutic dose in the children population in South Africa?

Table of Contents

List of tables

Declaration

I, Aadila Patel, declare that this thesis that I now submit for assessment on the programme of study leading to the award of Master of Science Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences has not been submitted as an exercise for a degree at this or any other college. It is entirely my own work and has not been taken from the work of others, save the extent that such work has been cited and acknowledged within the text of my work.

I agree to deposit this thesis in Hibernia College's institutional repository or allow the library to do so on my behalf, subject to Irish Copyright Legislation and Hibernia College Library conditions of use and acknowledgement.

Signed…… Dated……..

Abstract

Introduction: When used at the recommended and approved therapeutic dose, paracetamol is effective. Paracetamol is available in various forms and easily accessible from general dealers and pharmacies. The liquid form is the preferred form given with a device to children. *Hypothesis:* Paracetamol is effective within a defined therapeutic range; however, are prescribers and caregivers using paracetamol as authorised by regulators? *Method*: A qualitative review of product specific labelling and the department of health recommendations was conducted and evaluated by means of arithmetic means differences to the regulator requirements. Surveys of healthcare professionals and caregivers determined the quantity administered and to establish if a device was used. *Results*: The dosing information from product specific labelling, the department of health and the regulator source were reviewed for recommended dose, frequency of administration, maximum daily dose and recommendations for overdose treatment. There are similarities and differences with the null hypothesis being proven. *Conclusions:* Product labelling and department of health recommendations do not conform to the regulator accepted therapeutic dose. There was no unambiguous legislative medicine guideline on the age of a child with children between six and twelve being underdosed with liquid paracetamol in terms of volume and strength.

Keywords: paracetamol, therapeutic dose, children, labelling requirements.

Disclaimers

Terminology Drug and medicine

The preferred terminology for a drug is medicine by the South African regulator. Every effort has been made to use the international standard of drug in this research project.

Product Reference Source

Monthly Index of Medical Specialities (MIMS) May 2012 was used as the initial source to determine paracetamol mono-component products available on the market. A verification was performed against MIMS August 2013. This reference was accessible to the researcher and author of this research project and based on experience that not many companies invest in the registration of a mono-component paracetamol preparation.

MCC Reference source

The Medicines Control Council referred to the accepted standard references as Goodman and Gilman and the Martindale. Theses references are The Pharmacological Basis of Therapeutics and The Complete Drug Reference respectively.

Records

1) Individual completed surveys will be retained until the research project has been finalised and data cannot be used without the permission of the respondents.

2) Photographic observations were used to record the experiment of medical devices. They were not included in the appendix due to file size limitation and are available upon request.

3) Product information labelling is available upon request and not included due to file size

4) Agency guideline has not been included as appendices. These have been reflected in the reference list. Should a copy be required, they can be supplied electronically.

Acknowledgements

I would like to thank Hibernia College for investing in the development of continuing education in South Africa. There is certainly a need for this specialist masters degree.

It has been an awesome, enriching and fulfilling experience to me. I felt a sense of accomplishment when I was told that it has been observed that I had learnt a lot over the last two years by a family member.

I would like to thank Prof Beekie for her role, guidance and moral support throughout the last six months. An appreciation goes to Dr Johann Kruger for expanding my knowledge on South African legislation. A special thanks goes to Miriam O'Donoghue for her guidance and endless patience.

To my family, I thank you for your patience and the sacrifices that have you made alongside me over the last two years.

To all the children, love you all...this is for you!

Gabiebodien, I appreciate the encouragement to further my education, the moral support when it all seemed too much for me to handle and holding my hand every step of the way.

May the Almighty continue to grant us the ability and willingness to seek knowledge!

List of Abbreviations (if relevant)

Abbreviation	***Full text***
AAPS	American Academy of Paediatrics
AHFS	American Society of Health-System Pharmacists
ASA	Advertising Standards Authority (South Africa)
BNFC	British National Formulary for children
CDRH	Center for Devices and Radiological Health
DoH	Department of Health South Africa
eMC	Electronic Medicines Compendium, United Kingdom
EMEA/EMA	European Medicines Evaluation Agency
EML	Essential Medicines List (South Africa)
EU	European Union
FDA	Food and Drugs Administration (United States of America)
g	gram
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
kg	kilogram
MA	Marketing authorisation
MCA	Marketing Code Authority (South Africa)
MCC	Medicines Control Council (South Africa)
MHRA	Medicines and Healthcare Products Regulatory Authority (United Kingdom)
mg	milligram
ml	millilitre
NAC	N-acetylcysteine
OTC	Over-the-counter
PI	Package insert (South Africa) and Package Information Leaflet (European equivalent)
PIL	Patient Information Leaflet

Abbreviation	***Full text***
SAMF	South African Medicines Formulary
SAPC	South African Pharmacy Council
SmPC	Summary of product characteristics
UK	United Kingdom
US / USA	United States of America
WHO	World Health Organisation
ZA	South Africa

1. Introduction

Paracetamol (South Africa. Medicines and Related Substances Act 101, Schedules) is approved by regulatory authorities as a medicine (South Africa. Medicines and Related Substances Act 101, S1, medicine) for the treatment of pain and fever in children and adults (South Africa. Medicines and Related Substances Act 101, schedules and Bertolini et al, 2006) but yet its exact mechanism of action is unknown (Bertolini et al, 2006).

Paracetamol only containing products are available in a variety of pharmaceutical dosage forms (MIMS 2012) and can be purchased by a consumer from a general dealer store or from pharmacy or can be administered in hospital (South Africa. Medicines and Related Substances Act 101, Schedules), in South Africa. It is one of two substances that are available without prescription, the other being aspirin (South Africa. Medicines and Related Substances Act 101, Schedules).

Orally administered dosage forms are capsules, tablets or syrups (solutions) (MIMS, May 2012).The quantity of paracetamol is either 500 mg for the capsule and tablet (conventional, effervescent or meltab) or 125 mg meltab. Paracetamol syrup forms are available as 60 mg per 0,6 ml or 120 mg per 5 ml.
Rectal preparations contain either 125 mg or 250 mg of paracetamol per suppository (MIMS, May 2012).
Paracetamol injection contain either 1 g per 100 ml (100 ml vial) or 10 mg per 1 ml (50 ml vial) which are administered in hospital (MIMS, May 2012).

The different pharmaceutical dosage forms with different quantities of paracetamol could result in an over use of paracetamol leading to toxicity with severe liver

damage (Bradfield (ed), Paracetamol 2013). Although paracetamol is reported to have few side effects which are usually tolerated by the user, ovedosage can be common because of the narrow margin between therapeutic dose and toxic dose (South Africa. Department of Health, Essential Medicines List, 2008).

Orally administered paracetamol is less irritant on the gastrointestinal tract (Bertolini, 2006)) when compared to other non-steroidal anti-inflammatory agents and was therefore used as first line treatment especially in children (Bradfield (ed), Paracetamol 2013).

The focus of this research was to evaluate whether paracetamol was administered to children at therapeutic doses by caregivers. This involved reviews of various pieces of South African legislation and comparing them with international legislation, the review of packaging information of South African products and determination if medical devices were used to give paracetamol to children.

The Children's Act (South Africa. Department of Social Development, Act 38 of 2005) defines the legal age for a child as an individual under the age of 18 years while the Medicines and Related Substances Act (Act 101 of 1965) did not provide age clarity on age breakdown for dose administration.

The reason for the emphasis on children was concern of protecting children as they are vulnerable especially when administered medication by their caregivers. Furthermore, the revised dosing for liquid preparations by the United Kingdom's Medicines and Healthcare Products Regulatory Authority in 2011 (United Kingdom, Medicines and Healthcare Products Regulatory Authority, 2011) had highlighted the need to be vigilant (Jones, 2012)) when medication is given to children especially

when these medicines were easily accessible to the public via general dealers (South Africa. Medicines and Related Substances Act 101, section 22A). Unless published in public media, neither the general dealer nor the consumer would be aware of legislation changes which could affect the manner in which they sale or use paracetamol medication as legislative changes are only published in government gazettes in South Africa.

2. Literature Review

2.1 Introduction

Paracetamol is widely used internationally for the treatment of pain and fever in all age groups with recent focus on the intravenous dosage form (Gazarain, Drew and Bennett, 2014) and its associated overdose as a result of administration errors. Consequently recent research focussed on the treatment of paracetamol overdose and not its efficacy . Paracetamol is used on its own or combined with other active ingredients.

As paracetamol preparations are widely available to the public via general dealers or could either be recommended or prescribed by healthcare professionals, a review of the available paracetamol containing preparations literature and standard treatment guidelines should support the South African regulator approved recommended therapeutic doses for children.

South African national legislation provided a starting point (South Africa. Medicines and Related Substances Act 101) with the review extending to international legislation in the United Kingdom and the United States of America.

2.2 Legislative control of medicines

The principal legislation for governing medicines, or drugs, is the Medicines and Related Substances Control Act, Act 101 of 1965, with the short title being the Medicines and Related Substances Act ,1965. The national health regulator authority in South Africa is known as the Medicines Control Council (MCC).

The Medicines and Related Substances Act (South Africa. Medicines and Related Substances Act, 1965) provides for the registration, or authorisation, of drugs including the assessment of quality, safety and efficacy of drugs, how the drug could be sold and to whom it could be sold and where it could be sold.

The drug is further classified according to its pharmacological action, where paracetamol as a single component falls under the category antipyretics or antipyretics and anti-inflammatory analgesics (South Africa. Medicines and Related Substances Act 101, regulation 25).

In terms of safely and efficacy, a medicines must reflect details informing all stakeholders of the benefits or commonly referred to as indications, and the risks or adverse effects associated with the use of a drug. Information structure for the healthcare professional is defined under regulations 8 and 9 (South Africa. Medicines and Related Substances Act 101) and expanded under the regulator issued guidelines package inserts for human use and package inserts for human medicines standardised texts (South Africa. Medicines Control Council, 2014). Similarly, product information for the consumer is defined under regulations 8 and 10 and expanded in the guideline patient information leaflets (PILs) (South Africa. Medicines Control Council, 2014).

The National Health Act 2003 (South Africa. National Health Act 61, 2003) is the primary act relating to healthcare providers and health services delivery in South Africa. The national department of health had published a consolidated medicine list in February 2014 which confirmed that paracetamol is used across all levels of health care delivery (South Africa. Department of Health, essential medicines program, 2014).

The National Health Act 61 provides for the establishment of national guidelines addressing health care needs in ZA.

2.3 Legislated paracetamol effective dose

2.3.1 Paracetamol therapeutic dose

It is the responsibility of the applicant or marketing authorisation holder to provide supportive evidence to establish the safe and effective dose for any ingredient to the South African regulator, the MCC, before the product could be authorised for sale (South Africa. Medicines and Related Substances Act 101, section 15).

With paracetamol, the MCC had made a ruling whereby paracetamol safety was of primary concern and hence the MCC applied certain pack size restrictions based on paracetamol strengths in preparations in line with international trends (South Africa. Medicines and Related Substance Act 101, Schedules).

Legislation (South Africa. Medicines and Related Substances Act 101, Schedules) refers to formulations containing paracetamol as a single drug (or mono-component products) in strengths of 500 mg in tablets or capsules, 1 000 mg in individually wrapped powders or sachets in pack sizes not exceeding 12,5 grams. For liquids the prescribed paracetamol content should be 120 mg per 5 ml syrup or less with a maximum pack size of 100 ml. Other pharmaceutical dosage forms are suppositories, modified release formulations, and injections (South Africa. Medicines and Related Substances Act 101, Schedules).

The regulator standard accepted references (South Africa. Medicines Control Council, 2014), namely, the Goodman and Gilman and the Martindale, were reviewed to obtain paracetamol’s accepted therapeutic dose.

There was no documented evidence that paracetamol is not effective for the treatment of pain and fever within the defined therapeutic range when used as first line treatment for pain and fever.

2.3.2 Paracetamol overdose

Overdose with paracetamol has been defined as a medical emergency (Heard, 2008) internationally including South Africa (Rossiter, 2012). Appendix 8 reflects a list of products that were available in South Africa.

Treatment of paracetamol overdose (or poisoning), especially due to the potential of liver failure, requires that the healthcare professional be cognisant of the narrow therapeutic index of paracetamol and the treatment regimen for overdose.

Package inserts for human medicines standardised texts (South Africa, Medicines Control Council, standardised text, 2010) reflected that overdose in a child as an acute ingestion of 140 mg/kg within 4 hours. Treatment was emesis or lavage and a single dose of 50 g activated charcoal. Then followed up with N-acetylcysteine (NAC) within the first eight to thirty six hours. The recommended NAC intravenous dose was firstly 150 mg/kg in 200 ml of dextrose injection administered over 15 minutes, secondly 50 mg/kg in 500 ml dextrose injection over 4 hours, and lastly 100 mg/kg in 1 000 ml of dextrose injection over 16 hours. “The volume of intravenous fluid should be modified for children” (South Africa. Medicines Control Council, standardised text, 2010) is the only specific reference to overdose treatment in children.

NAC oral treatment was not recommended as first line overdose treatment; however, when used, the loading dose was 140 mg/kg dissolved in water followed by 70 mg/kg every 4 hours for 17 doses (or three days).

This treatment period coincided with the recommendation that patients be monitored for at least ninety six hours.

2.4 Medical device

Simultaneously with the review of effective therapeutic dose was the review of the use of an appropriate medical device to administer paracetamol oral liquid preparations. This was to determine if current legislation or practice addressed the safe use, or administration, of paracetamol preparations to children.

2.5 Paracetamol preparations

The Medicines and Related Substances Act 101 (South Africa. Medicines and Related Substance Act 101, Schedules), indicated that paracetamol was available as over the counter medicines directly to the consumer as schedule 0 at a specific strength in tablets, capsules, powders or sachets and syrup in limited pack sizes, while larger pack sizes were available from pharmacies as schedule 1 products. Rectal preparations and modified release formulations were available at pharmacies as schedule 2 preparations and could be supplied without a prescription, or as pharmacist initiated therapy; while, the injection form was only available via prescription as schedule 3 (South Africa. Medicines and Related Substances Act 101, Schedules).

The schedule determined to whom and how a medicines could be sold (South Africa. Medicines and Related Substances Act, Section 22A).

A review was conducted of marketed products available on the South African market (MIMS, May 2012) as consolidated in Appendix 7.

2.6 Marketing and advertising of drugs

The private healthcare sector had agreed that they would abide by rules to be self regulated (South Africa, Marketing Code Authority, 2013). This was either in terms of the Advertising Standards Authority code (South Africa. Advertising Standards Authority, 2014) for OTC medicines marketed directly to the consumers or the Marketing Codes Authority for prescribed drugs or those advertised to pharmacists, holders of a dispensing licence or prescribers .

The Medicines and Related Substances Act 101, under regulation 45 (South Africa. Medicines and Related Substances Act 101, Advertising of medicines), depicted that all drugs classified as schedule 0 and 1 can be advertised to the public whilst drugs classified as schedule 2 to 6 can be advertised to the healthcare professional only. Section 22A of the Medicines and Related Substances Act 1965 (South Africa. Medicines and Related Substances Act 101, Control of medicines and schedule substances) indicated that Schedule 0 drugs can be sold in an open shop or by a general dealer whereas schedule 1 to 6 medicines can be sold in pharmacy or by designated healthcare professionals within their scope of practice.

2.7 Clarification of child and administration of medicines

Children are dependent on guidance from adults in all respects. It is important that there is no ambiguity into the firstly the definition of a child and secondly the obligations and roles of caregivers and healthcare professionals in the effective administration of medicines as per the principles of clinical ethics (Ashcroft, 2007 and International Conference on Harmonisation. Guidelines for Good Clinical Practice, 1996).

The metabolism of paracetamol is different in children to that of adults (United Kingdom. Medicines and Healthcare Products Regulatory Authority, Public

assessment report, 2011). Coupled with the narrow therapeutic index of paracetamol (Brayfield, Paracetamol, 2014), it is important that the effect therapeutic dose be administered to children.

The alcohol content of orally administered preparations reflecting various children age groups (South Africa. Medicines Control Council, Alcohol content of medicines, 2003) must be taken into consideration when paracetamol liquid preparations are given to children. This information must be reflected on the labelling (South Africa. Medicines and Related Substances Act 101, regulations 8, 9 and 10).

As detailed in the MHRA Public Assessment report (United Kingdom. Medicines Regulatory and Healthcare Products Regulatory Authority, Public Assessment Report, Liquid Paracetamol, 2011), the route of metabolism is sulphation in children and glucoronidation in adults. Further the drug clearance is considered to be lower in children than adults with factors such as body weight and rate of metabolism influencing the metabolism.

Paracetamol has the highest reported overdose prevalence specifically in children under the age of 13 in South Africa (Veale, Wium and Müller, 2013); which corresponded to the increase of overdose reports in Australia (Gazarain, Drew and Bennett, 2014) as a result of the availability of the intravenous form of paracetamol. The common recorded paracetamol overdose symptoms are pallor, nausea, vomiting, anorexia and possibly abdominal pain. (South Africa. Medicines Control Council, Standardised text, 2010). Mild symptoms has the potential to mask the seriousness of liver damage (South Africa. Medicines Control Council, Standardised text, 2010).

2.8 Hypothesis

The aim of the research project was to determine whether the authorised therapeutic dose of paracetamol preparations that were available on the South African market conformed to legislation. Furthermore, to determine if the South African authorised therapeutic dose correlated to internationally approved therapeutic doses in children.

The objective was to determine if South African preparations were in agreement with the therapeutic dose for children and to determine if South African legislation, private sector and public sector, was in line with international recommendations by established regulatory health authorities.

The sources for review on paracetamol focussed on governmental policy for administration to children. No published references were freely available to indicate if prior research focussed on the evaluation of the accepted therapeutic dose of paracetamol used in children in South Africa. Recent international publications had centred on the determination of mechanism of action and treatment of overdose of paracetamol but not comparison of the therapeutic dose (Gazarain, Drew and Bennett, 2014). Some international data was available to review the restriction of packs sizes (United Kingdom. Medicines and Healthcare Products Regulatory Authority; and, the United States of America. Food and Drugs Administration).

The main intent of the research was to determine if paracetamol was being prescribed and used at the correct therapeutic dose in the children population in South Africa.

Paracetamol is effective within a defined therapeutic range; however, are prescribers and caregivers using paracetamol as authorised by regulators is the hypothesis of this research project.

For the testing of the hypothesis, the dependent variable was South African legislation based on international practice compared to the actual use or prescribing information appearing on the South African product specific labelling as the independent variable.

3. Methodology

The mixed methods approach was used to collect information for analysis on paracetamol mono-component products.

The rationale for the focus on mono-component products was ease of availability of paracetamol from either a general dealer or pharmacy. Analgesic and antipyretic preparations could be single or multiple active component products (MIMS, May 2012).

Paracetamol combination products generally contain either other analgesics such as aspirin, antihistamines such as diphenhydramine or other active components placing them in schedule 2 or higher schedules (South Africa. Medicines and Related Substances Act 101, Schedules), and therefore, only available from pharmacies as pharmacist initiated therapy or on prescription.

3.1 Legislation overview of effective dosing, medical devices and children

Legislation directs the control and sale of drugs for therapeutic purposes.

Paracetamol specific legislative requirements were reviewed in this research project to capture the accepted therapeutic dose in South Africa and that recommended by other established international regulatory authorities. This section was a qualitative analysis based on recordings and observations.

In general, the legislative requirements were comprehensive for medicines which focussed not only on quality, safety and efficacy in respect of dosing; but addressed marketing and advertising for the safe use of drugs.

The merit of this method of data collection was the extensive availability of data via the internet with the challenge being in the interpretation of information based on South African national legislation.

3.1.1 Therapeutic dose

A survey was conducted of current legislative requirements relating to paracetamol preparations in South Africa and those as recommended internationally via qualitative analysis. Details were recorded on a spreadsheet to consolidate the data gathered.

MCC's accepted references were compared to international recommended therapeutic doses to determine if the ZA authorised recommended doses were in line with international recommendations.

The merit was that paracetamol is regarded as a safe drug when used within the recommended "therapeutic dose with few side effects" (Cranswick and Coglan, 2000).

3.1.2 Medical Device

A method was devised (appendix 9) and observations (appendix 12) recorded to capture the volume determination of the various medical devices that are available. These observations were to determine if marketed oral paracetamol liquid preparations contained a medical device to ensure accurate dosing by administration of the correct volume or medicine measure. The observations were carried out at general dealers stores, a corporate pharmacy group and independently owned pharmacies.

The next step was to determine by experimentation and recording of results to establish if the available medical devices of medicine measures, syringes and household items provided an accurate dose measure as indicated on the product labelling or package insert. The experiment was conducted using only one liquid form

to ensure consistency of product characteristics thus minimising differences in formulation between products. Four different volumes of 2,5 ml, 5 ml, 7,5 ml and 10 ml were measured based on the medical device calibration and volume limitation.

Solid dosage forms did not require a medical device as administration is orally with a liquid preferably water.

Medical devices were not required for rectal preparations as suppositories are inserted into the anus by caregivers.

Injections are not for self administration but rather administered by healthcare professionals in a clinical setting. In this research project it was assumed that the syringe was appropriately marked and calibrated to allow for the correct volume to be extracted for administration.

The challenge was establishing a device that would be used as the calibrated equipment to verify volume delivery readings when compared to other medical devices as the research was not conducted at a university, laboratory or pharmaceutical company. However, this was overcome by comparison of a reading from one device to another. Visuals were recorded for verification purposes.

3.1.3. Children

The definition from a South African perspective and that used internationally were reviewed to determine if there is consistency in age groups categories.

The hurdle was determining which specific South African legislation would provide an unambiguous “child” definition as the Medicines and Related Substances Act 1965

(South Africa. Medicines and Related Substances Act 101) does not contain a definition for a child or children.

The merit was gaining familiarity with other legislation that impact on health decisions but which are not frequently encountered and thus not referenced in daily practice.

3.1.4 Public sector guidelines

The different documentation issued by the South African department of Health was reviewed to correlate government policy to ensure that information was consistent across treatment guidelines. Furthermore, a comparative analysis was performed to determine if the South African government documents had been updated with international recommendations including the World Health Organisation recommendations.

The weakness was that information and decisions made by government were not effectively or efficiently communicated to all healthcare stakeholders. As an example, the pharmaceutical healthcare sector is not made aware of revision via its statutory body the South African Pharmacy Council. The information is rather disseminated via interested groups or via professional associations or gained from personal review of documentation. The Standard Treatment Guidelines and essential medicines list for South Africa, Hospital level Paediatrics 2013 is an example of a document (South Africa. Department of Health, Standard treatment Guidelines and essential medicines List for South Africa, Hospital level Paediatrics, 2013).

3.2 Paracetamol preparation overview

A survey was conducted of products available via the private market and via the public sector documentation. Sources used were the Monthly Index of Medical Specialities (MIMS, May 2012 and MIMS August 2013) and online access to the Generics Dictionary (South Africa. Generics Dictionary) and government of health pricing and tender documents (South Africa. Department of Health). Verification of

information recorded was made comparing data sourced directly from International Marketing Survey Health (IMS) for the private sector.

Details recorded and summarised focussed on an overview of dosing and overdose captured on the product **labelling** reflected on the package insert. The package inserts were sourced from either purchasing the product, approaching a pharmacy, the internet via the South African package insert website (Intekom) or via specific company website, if available.

The results from the product labelling review were coded. Code 0 was not meeting the South African legislative requirements and Code 1 meant that the product labelling met legislative requirements.

Statistical analysis was then performed to determine arithmetic means and reflected as a percentage compared to the product total evaluated.

The challenge was determining the starting point for sourcing product labelling information. Reliability of the most recent information was based on procurement of products from pharmacy or general dealer as products must be sold that are still within the manufacturer's recommended shelf life. Established resources accessed via the internet were used to confirm product availability.
The positive step was cognisance of the reliability of source information.

3.3 Restriction of sale

Marketing and advertising were confined to observation of pack size availability at general dealers. No observations were noted as there were no contraventions noted at the general dealer stores.

Observations were not conducted in pharmacy as there are no pack size restrictions for paracetamol mono-component products sold in a pharmacy.

3.4 Surveys

Quantitative data was generated by conducting surveys in the private sector. Sample size of five pharmacists and ten caregivers were determined to obtain an overview of practice within the time limitation of the research project. Ethics approval was granted at the end of February 2014 by the Ethics Committee of the University of the Western Cape.

Sampling of pharmacies were chosen at random with the intent to survey pharmacies located within different social settings. Data was generated and collected by the researcher conducting face-to-face surveys at four independently owned pharmacies and one corporate pharmacy. Two of the pharmacies serviced low income groups, two were based in middle income areas and the corporate pharmacy was in a shopping centre.

The survey design was based on semi-structured interviews to obtain specific information with consideration of the respondent's available time and the opportunity for further discussion where acceptable by the respondent. The intent of an audio recording was not realised as the audio device malfunctioned prior to survey initiation. The survey of both the pharmacist, and healthcare professional, and the caregiver were conducted in the five pharmacies.

The design of the survey for the professional was aimed at investigating the prescribing data including the availability of a medical device; while the survey of the

caregiver was to investigate the appropriate use, administration of paracetamol and to ascertain if a medical device was used.

The limitation of the surveys were that most general dealer outlet stores are of corporate origin that required approval from head office for activity that is not initiated by head office. Due to the research project time constraint, these general dealer stores were not approached.

Small community based general dealers were not included as they could purchase the originator product in tablet form either in dispensers (42 x 2 tablets) or display cards (48 x 2 tablets). The consumer would only purchase on demand for once-off use thus there was minimal risk of a child being given more than the therapeutic dose.

Face validity confirmed data reliability as the researcher conducted the surveys at the pharmacy. Participant Information leaflets including a copy of a blank consent form was handed to each possible respondent upon introduction. In addition, the respondents were requested to sign the consent form after completion of the survey.

Survey results were analysed quantitatively, Completed surveys records were treated anonymously and available for review solely for the purposes of verification toward the attainment of the degree.

The merit of direct interaction with the consumer and professionals was that it provided an opportunity to initiate discussions about paracetamol.
The challenges were finding the time and identify pharmacists that would be open to participate in the survey within their pharmacies. The advantage of conducting the

survey in pharmacy only was that the purpose of the survey was received well by respondents willing to participate and not withdrawing their participation and responses were addressed in an open manner by the respondents to share their knowledge and information with the researcher..

3.5 Testing of hypothesis

Data collection was designed to test if paracetamol products on the market conform to legislative requirements by determining the number of products meeting the legislative requirements, those addressing specific dosing in all children age groups and whether data on overdose has been updated on product labelling.

The merit of selecting paracetamol was the ease of access to paracetamol preparations.

The challenge was determining if paracetamol was used within the prescribed therapeutic dose.

Thus the null hypothesis is that paracetamol is not used or prescribed within the therapeutic dose range in ZA.

4. Findings and Analysis

4.1 Legislation

The review of the Medicines and Related Substances Act 101 (South Africa. Medicines and Related Substances Act 101) focussed on the regulation of paracetamol and its restrictions, the use of medicines in children and labelling requirements. Legislative and the effective dose for paracetamol were evaluated concurrently.

4.2 Effective dose

4.2.1 Therapeutic effective dose: South Africa

The approved therapeutic dose for paracetamol ranges from 30 mg/kg to 1 g per single dose with no more than 4 doses per day or within a 24 hour period for children from 1 month to adults for oral, rectal and injection administration as captured below in tables 1 to 3 respectively.

Table 1: Paracetamol ORAL therapeutic dose

A summary of the recommended single oral dose, the frequency of administration and maximum daily dose for different age groups from MCC accepted sources.

Age group	*Dose(mg)*	*Frequency (hours)*	*Maximum daily dose*	*MCC Source*
Not defined	325–650 mg	4-6	4 g 2 g (alcoholics)	Goodman & Gilman
"Usual" - assumption adult was implied	500-1000	4-6	4 g	Martindale
***Children**: UK licensed dose*		4-6	4 doses	
12-16 years	480-750			
10-12 years	480-500			
8-10 years	360-375			
6-8 years	240-250			
4-6 years	240			
2-4 years	180			
6-24 months	120			
3-6 months	60			
1-3 months	30-60	8, if necessary	none	BNFC
Neonates >32 weeks	20 mg/kg, then 10-15 mg/kg	6-8	60 mg/kg daily	
Neonates 28-32 weeks	20 mg/kg, then 10-15 mg/kg	8-12	30 mg/kg daily	

Table 2: Paracetamol RECTAL therapeutic dose

A summary of the recommended single rectal dose, the frequency of administration and maximum daily dose for different age groups from MCC accepted sources.

Age group	*Dose(mg)*	*Frequency (hours)*	*Maximum daily dose (times daily)*	*MCC Source*
Not defined	500-1000	4-6	4	Martindale
5-12 years	250-500	4-6	4	
1-5 years	125-250	4-6	4	
3-12 months	60-125	4-6	4	
1-3 months	30-60	8	None specified	BNFC
Neonates >32 weeks	30 mg/kg, then 20 mg/kg	8	60 mg/kg	
Neonates 28-32 weeks	20 mg/kg, then 15 mg/kg	12	30 mg/kg	

Table 3: Paracetamol INTRAVENOUS therapeutic dose

A summary of the recommended single dose administered intravenously, the frequency of administration and maximum daily dose for different age groups from MCC accepted sources.

Age group	*Dose*	*Frequency (hours or more*	*Maximum daily dose*	*MCC Source*
Over 50 kg	1 g	4	4 g	Martindale
• Between 33-50 kg • Chronic alcoholism/malnutri-tion, dehydration	15 mg/kg	4	3 g (60 mg/kg)	
Children over 50 kg	Adult dose: 1g	4	4 g	
Children 33- 50 kg	15 mg/kg	4	3 g (60 mg/kg)	
Children 10- 33 kg	15 mg/kg	4	2 g (60 mg/kg)	
Full term neonates and children <10 kg	7,5 mg/kg	4	30 mg/kg	
	10 mg/kg	4-6	30 mg/kg	BNFC
Premature neonates (>32 weeks postmenstrual age)	7,5 mg/kg	8	25 mg/kg	

The treatment of post immunisation pyrexia is an indication listed in the MCC accepted reference source of Martindale (Brayfield (ed.), Paracetamol, 2014); however this is not included in any of the package inserts in South Africa and is therefore considered an “off label” claim or use of paracetamol.

The only requirement specified by the MCC for dosage is that the wording “DO NOT EXCEED THE RECOMMENDED DOSE” should be reflected in bold (South Africa. Medicines Control Council, Standardised text, 2010) on the package insert. Other specific wording was “CONTAINS PARACETAMOL – READ THE PACKAGE INSERT” on the OTC pack (South Africa. Medicines and Related Substances Act 101, Schedules) with the said legislation ambiguous on compulsory wording on other pack sizes sold in pharmacy or dispensed by an authorised prescriber.

4.2.2 Effective therapeutic dose: International

4.2.2.1 World Health Organisation

In terms of international evaluation, decisions made by the World Health Organisation (WHO) (United Nations. World Health Organisation), the MHRA (United Kingdom. Medicines and Healthcare Products Regulatory Authority) and the FDA (United States of America. Food and Drugs Administration) were reviewed.

The WHO in its publications of Model list of essential medicines for children (WHO. WHO Model List of Essential Medicines for Children, 2013) and model formulary for children (Bidgood et al (ed.), 2010) provided recommendations of paracetamol strengths for three pharmaceutical preparations. The two oral forms were liquid in the strength of 25 mg per 1 ml (or 125 mg per 5 ml), and, tablets with varying strengths of 100 to 500 mg per tablet.

The rectal preparation strength was 100 mg paracetamol per suppository. Administration from the rectal route was erratic and was therefore not a recommended route (Bidgood et al (ed.), 2010).

The WHO (Bidgood et al (ed.), 2010) maximum daily limit was four grams while MCC was two to three gram based upon body weight for the injection formulation.

The WHO list (Bidgood et al (ed.), 2010) list did not reflect details in respect of dose, frequency or maximum daily limit.

4.2.2.2 MHRA (United Kingdom. Medicines and Healthcare Products Authority)

The MHRA approved dosages for paracetamol were the same as described under MCC approved source (chapter 4.2.1).

4.2.2.3 FDA (United States of America. Food and Drugs Administration)

The FDA (United States. Food and Drugs Administration, Organ-Specific Warnings, 2009) stipulated a maximum daily dose for over-the-counter paracetamol (acetaminophen) as not exceeding four gram daily with a single dose not to exceed one gram. The FDA (United States of America. Food and Drugs Administration) advisory panel recommended single dose range of 160-480 mg for children aged two to eleven years with no more than five doses in a 24 hour period (Brunton, 2011).

4.3. Overdose or poisoning with paracetamol

There was no difference in overdose treatment for adults or children (South Africa. Medicines Control Council, Standardised text, 2010 and Brayfield (ed.), Acetylcysteine, 2014). Acute overdose is not intentional in children (Gazarain, Drew and Bennett, 2014) but chronic use or supradoses have resulted in “unintentional overdose” (Brayfield (ed), Paracetamol, 2014)).

The recommended treatment of overdose was similar between MCC and its accepted source. When reviewed further, the differences were in the administration time of activated charcoal, the NAC intravenous diluents and NAC administration time as summarised in table 4.

Table 4: Differences of paracetamol overdose treatment

A summary of the differences of paracetamol overdose treatment recommended by MCC and Martindale (Brayfield (ed.), Acetylcysteine, 2014)

Detail	*MCC*	*Martindale*
Activated charcoal: time of administration (hours)	4	1
Intravenous diluents for NAC	Dextrose solution	5% glucose solution
Administration period (minutes)	15	60

The longer infusion time was thought to reduce the incidence and severity reactions (Acetylcycteine (acetadote) for acetaminophen, 2005).

A note was made for the adjustment of the intravenous fluid for children weighing less than 40 kg with no indication on whether the volume should be adjusted up or down (South Africa. Medicines Control Council, Standardised text, 2010). Intravenous volume adjustment for children should be halved (United Kingdom. BNFc, April 2014).

The dose for oral NAC treatment was the same, though the Martindale (Brayfield (ed.), Acetylcysteine, 2014) recommended administration as a 5% solution. Methionine is an alternate option but was not available on the South African market (MIMS, May 2012).

Overdose in pregnancy was addressed as recommended (Wilkes, Clark and Herrera , 2005) treatment but not addressed in MCC 2010 guideline (South Africa. Medicines Control Council, Standardised text, 2010). Pre-pregnancy body weight should be used to determine toxic levels with actual pregnant body weight to calculate NAC dose.

Overdose treatment is a medical emergency (Rossiter (ed.), 2012); however, the recommendations from the DoH (South Africa. Department of Health) and Goodman and Gilman (Bruton (ed.), 2011) were not included in this research project in respect of overdose treatment.

Intravenous paracetamol overdose resulted from dosage errors but rarely have resulted in substantial overdose (Brayfield (ed.), 2014).

No reported overdosage from rectal administration was found during the literature review.

The interval to initiate NAC treatment is important (Brok, Buckley and Gludd, 2006) with the rate of administration not a deciding or contributing factor in the successful overdose treatment outcome. The concentration of the solution to be used for dilution needs to be clarified in the guideline issued by MCC (South Africa. Medicines Control Council, 2010) to determine if there is any significance to using either dextrose or glucose solution as the intravenous diluent.

4.4 Medical device

The MCC had made allowance for the regulation of medical devices (South Africa, Medicines and Related Substances Act 101) but these have not yet been implemented as regulations need to be finalised.
No legislation requirements existed that liquid preparations must include a medicine measure which could deliver either a 2,5 or 5 ml dose, either in the pack of at dispensing stage.

Thus validation of volume delivery was confirmed, via experimentation on twelve devices, by the researcher and author as medical devices had to be either purchased or provided to the caregiver when the preparation was dispensed. Results are recorded under Appendix 9.

The two standard marked medicines measures, graded plastic teaspoons, provided the same volume. When the equivalent was determined when compared with syringes of 3 ml, 5 ml (two different brands) and 10 ml, the volume in the syringe was approximately 0,5 ml above the medicine measure marking.

Three droppers evaluated were unsuccessful as the rubber suction was ineffective to allow the correct volume to be drawn up in one single draw or even repeatedly.

The two household teaspoons provided differing volumes with one providing 4 ml while the other 2,5 ml. The tablespoon used provided a volume of 10 ml.

The medicine measures and syringes provided the same volume delivery and it could be assumed they were correct as the volume from one device is equivalent to the other. Droppers with rubber plastic suctions and household items did not provide the same volume of 5 ml which is the recommended dose delivery volume.

Medical devices must be provided with paracetamol liquid preparations in the UK (United Kingdom. Medicines and Healthcare Products Regulatory Authority) and USA (United States of America. Food and Drug Administration).

4.5 Products

4.5.1 Paracetamol Preparations

A total of 27 product labelling were evaluated. 88,88% were oral preparations, 45,83% of which were liquid preparations and 54,17% available as solid dosage forms. The remaining preparations were a common product labelling for the suppositories and two separate injectable strengths. Consolidated data can be found under appendices 10 & 11.

The reviewed product labelling, or package insert, is the only officially approved source of information by the MCC (South Africa. Medicines and Related Substances Act 101 and Medicines Control Council, Guideline Package insert for Human Use).

4.5.1.1 Liquids

Ten of the eleven preparations contained 120 mg per 5 ml with the eleventh strength of 0,6 g per 0,6 ml claiming to be an infant drop preparation.
However, only one product reflected a dose for children under the age of 3 months and was also indicated for use in older children.

Analysis of the various components of the dosing information revealed that all eleven product labelling had the age group of three to twelve months; seven products had indicated the age groups of one to five years and six to twelve years, two products reflected one to six years and seven to twelve years. One product had reflected the

age groups as one to two years and three to six years and then six to twelve years; the latter in common with the other products. The last product had reflected the age groups as one to four years, five to eight years and nine to twelve years. None of the products reflected 12 years and older age group.

The recommended dosage ranged from 60 to 480 mg, or 2,5 to 20 ml, per single dose across the age groups.

The starting dose was 60 mg for four products while six reflected a range of 60 to 120 mg. Two products have a single dose of 120 mg while eight products have a range of 120 to 240 mg. One product has a single dose of 240 mg; one had a range of 240 to 360 mg, while the remaining eight products have a range of 240 to 480 mg.

The frequency of administration reflected for two products were four hourly, one product had a frequency of four to six hourly while the recommended frequency for eight products was six to eight hours.

One product had not listed a maximum daily limit within 24 hours with differing maximum limits reflected across the balance of the products.

Seven of the ten products had a maximum of 480 mg while three products reflected half this value at 240 mg for the age group of three to twelve months. Where the age group was set at one to five years, six products reflected a maximum of 960 mg. In the similar age group of one to six years the one product indicated the maximum as 480 mg whilst the other was double at 960 mg.

For the age group of six to twelve years, the maximum set was 1920 mg for six products. In the similar age group of seven to twelve years, the one product had a maximum limit of 960 mg while the other was doubled.

The one product that had a narrower age group band reflected the maximum at 480 mg for one to four years, 960 mg for five to eight years and 1440 mg for nine to twelve years.

4.5.1.2 Tablets

A total of thirteen solid dosage forms were evaluated which included an effervescent formulation. Over 92% of the products had 500 mg paracetamol per tablet or capsule with 125 mg per tablet for the remainder of the product aimed specifically for children.

From eleven products, 81,81% reflected the age group of six to twelve years. Only 18,18%, or two products, reflected the wording for children 12 years and older with 90,9% indicating an adult dosage. As the labelling specially indicated a younger group it was assumed that the adult dosage would be applicable for children twelve to eighteen years of age.

The recommended dosage was half to one tablet, or 250 mg to 500 mg, for the age group of six to twelve years in 81,81% of the products whilst 54,54% indicated that the tablet was not recommended for children under six years. The recommended dose for 90,90% in the age group adults, or children over twelve years was one to two tablets. However 9,09% indicated paracetamol should not be used for children under twelve years whilst the same percentage had a dose of two tablets. The effervescent tablet had a dose of half a tablet but the tablet had no breakline which could lead to incorrect dosing (Bachynsky, Wiens and Melnychuk, 2002).

In terms of administration frequency, 9,09% had a three hour interval with a recommendation of one tablet, 9,09% had no frequency and 9,09% had a six to eight

hourly interval. A four hourly interval was recommended by 27,27% while 54,54%, or double, recommended a four to six hourly administration.

The daily maximum limit recommended for six to twelve years was 2 g as reflected by 72,72% while 9,09% had no limit indication. The maximum reflected by 81,81% was 4 g for children above twelve years while another 12,18% had no daily limit.

The capsule formulation had a restriction that it should not be used in children younger than nine years, with a narrow age group of nine to twelve years and maximum of 2 g; however, no frequency was specified. In children above twelve, the details corresponded to the tablet of one to two capsules with a daily maximum of 4 g and a four hourly administration frequency.

The dedicated children formulation had the age group of one to five years with an administration of one to two tablets administered four hourly and a maximum of 1 g for a period of five days.

4.5.1.3 Suppository

The dosing information was reflected on a common leaflet for both rectal preparations with the age group from 3 months up to 5 years only. The administration frequency was six to eight hourly and a maximum of 500 mg for the age group of three months to twelve months and 1 g for one to five year old.

4.5.1.4 Injection

The same company marketed the intravenous preparations where weight was used for dose calculation with a minimum of four hours between doses and a maximum of 60 mg/kg for children older than one year and with a body weight of 33 kg or less. For children over 33 kg, the daily maximum was not more than 4 g. The dose was the same across all ages of 15 mg/kg.

4.5.2 Comparisons

4.5.2.1 Comparison of the different ZA formulations

Based on a generalisation of the product labelling, there were some common areas within the age group, frequency of administration and the maximum allowed as summarised in Table 5.

In the age group of three to twelve months, the dosing frequency was the same for liquid and rectal administration of six to eight hours. The dosage range for the liquid was 60 to 120 mg whereas rectal dose was 125 mg. The maximum daily limit was 480 mg for liquids and 500 mg for suppositories. The maximum limit set for the intravenous preparation was 2 g with dose calculated on body weight. There were no dose recommendations discrepancies for the solid dosage form set at 4 g within 24 hours.

For one to five years, the similarity across the liquid, solid (tablet) and suppository preparations was the maximum daily dose of 960 mg for the liquid and 1 g for the solid and suppository formulation. The dosing frequency for liquids and suppositories was six to eight hourly while the tablets were more frequent at four to six hourly. The dose for tablets and liquids were similar at 125 to 250 mg and 120 to 240 mg respectively. The suppository dose recommended was 250 mg.

Table 5: Comparison of different formulations in ZA

A generalised representation from the product labelling of the various paracetamol dosage forms on the South African market.

Label information	***3-12 months***	***1-5 years***	***6-12 years***	***12-18 years***
LIQUID				
Dose (mg)	60-120	120-240	240-480	Not reflected
Administration Frequency (hourly)	6-8	6-8	6-8	
Daily Maximum Limit (g)	0,480	0,960	1,920	
SOLID				
Dose (mg)	Not recommended	125-250	250-500	500-1000
Administration Frequency (hourly)		4-6	4-6	4-6
Daily Maximum Limit (g)		1,000	2,000	4,000
RECTAL				
Dose (mg)	125	250	No recommenda-tion	No recommenda-tion
Administration Frequency (hourly)	6-8	6-8		
Daily Maximum Limit (g)	0,500	1,000		
INTRAVENOUS				
Dose (mg/kg)	At discretion of physician	15	15	15
Administration Frequency (hourly)		4	4	4
Daily Maximum Limit (mg/kg)		60	60	60 or 4 g

In the six to twelve year group, the dose was 240 to 480 mg for liquids and 250 to 500 mg for solid formulations. The maximum daily dose for the liquid was 1920 mg

while of the tablet was 2 g. Thus dose and maximum daily intake were similar for the liquid and solid formulations. The difference was the dosing frequency with the liquid administered less frequently at six to eight hourly intervals when compared to the tablet which was administered at four to six hourly intervals.

Both the intravenous and solid forms had a maximum daily limit of 4 g with a minimum dose frequency of four hourly for children twelve to eighteen years.

Individual differences were specific for the various dosage forms and were discussed under chapter 4.5.1.

4.5.2.3 Comparison to DoH (South Africa. Department of Health)

The dosage as recommended by the South African DoH in their standard treatment guidelines at primary level (South Africa. Department of Health, Standard treatment guidelines and essential list, primary care, 2008) and hospital level (paediatric level) (South Africa. Department of Health, Standard treatment guidelines and essential medicines list for South Africa, Hospital Level paediatrics, 2013) differed from the MCC approved labelling in respect of age groups.

At primary level the dose was reflected using both weight and age. There is a clear indication that paracetamol dose must be calculated based on weight for children under 6 months. The primary level reflected the dose based on an ‘infant’ formulation which was not listed on the procurement list (South Africa. Department of Health, Essential Medicines Programme, Essential Medicines catalogue, 2014).

The DoH (South Africa. Department of Health) documents did not confirm if the intravenous form could be used.

4.5.2.2.1: Oral

Upon comparison of the product labelling to the DoH (South Africa. Department of Health) recommendation, the product labelling had 4 age group bands whereas the DoH had nine age bands with the split focussed more in the younger age group. Comparison of age group, dose frequency and maximum daily dose are reflected in Table 6.

Table 6: Comparison of DOH recommendation to product labelling: Oral

The tabulation was a comparison of the DoH (South Africa. Department of Health) recommendation to the generalised product labelling (shaded in tabulation) for the oral dosage form (liquids and tablets).

DoH	DoH	Label-ling	DoH	Label-ling	Common	DoH	Label-ling	Label-ling
Age	**Dose (mg)**		**Frequency (hours)**		**Maximum (dose)**	**Maximum (mg)**		**Age**
1-3 months	48	none	4-6	none	4 doses	192	none	none
3-6 months	60	60-120	4-6	6-8		240	240-480	3-12 months
6-12 months	96		4-6			384		
1-3 years/ 18 months – 3 years	120	120-240	4-6	6-8		480	480-960	1-5 years
3-5 years	180		4-6			720		
5-11 years	240 or 250	240 or 250	4-6	6-8 or 4-6		960 or 1000	960-1000	6-12 years
11-15 years	500	Up to 1000	4-6	4-6		2000	4000	Adult
Adults	Up to 1000		4-6			4000		

The DoH had a dosage for children up to 15 years. Thereafter the adult dose was recommended.

The DOH had a dose for one to three months while this was not reflected on product labelling which resulted in the first difference. The dose was 48 mg. The second differentiation was the ages between three and twelve months. The DoH differed from product labelling to reflect three to six months old with the lower dose of 60 mg as indicated on the product labelling with the same daily maximum dose. For the six to twelve month old, the DoH reflected a changed dose of 96 mg which yielded a daily dose of 384 mg when the labelling reflected a dose of 120 mg and a maximum of 480 mg. For these two age groups the DoH had an administration frequency of four to six hours while the labelling suggested a longer period between administrations of six to eight hours.

For older age groups the DoH was consistent in the daily maximum of 4 doses with a suggested four to six hourly administration frequency. Maximum of four doses was common across both the labelling and DoH recommendations for liquid formulations.

A third segregation was the age groups of 12 months to five years. The DoH has divided this into two; namely, twelve months to three years and three to five years. The lower dose of 120 mg concurred for one to three years. The DoH suggested 180 mg whereas that on the labelling was higher at 240 mg which yielded maximum doses of 480 mg for the lower age group but 720 mg or 960 mg for the DoH and labelling respectively.

The DoH had an age group of five to eleven years whist the labelling was six to twelve years, fourth difference. The suggested dose was the same for both which produced the same maximum dose.

The fifth difference was that the DoH reflected the age group of eleven to fifteen years which was nonexistent on the product labelling. The dose recommended was 500 mg with a maximum daily dose of 2 g.

4.5.2.2.2 Rectal:

The DoH and product labelled differed in the dose, frequency and maximum limit as summarised in Table 7.

Table 7: Comparison of DOH recommendation to product labelling: Rectal

The tabulation was a comparison of the DoH (South Africa. Department of Health) recommendation to the generalised product labelling (shaded in tabulation) for the rectal dosage form.

DoH	DoH	Label-ling	DoH	Label-ling	DoH	Label-ling	Label-ling
Age	Dose (mg)		Frequency (hours)		Maximum limit (mg)		Age
3-12 months	62,5-125	125	4-6	6-8	250-500	500	**3-12 months**
1-5 years	125-250	250	4-6	6-8	500-1000	1000	**1-5 years**
6-12 years	250-500		4-6	n/a	2000	n/a	**n/a**

The age group of three to twelve months and one to five years was the same.

The dose recommended by the DoH was 62,5 mg to 125 mg, administered four to six hourly with maximum limit of 250 to 500 mg dependent on the dose administered for three to twelve months. The labelling only had one dose of 125 mg, administered every six to eight hours thus a maximum of 500 mg.

The suppositories did not have a dividing score thus a 60 or 62,5 mg dose raised the concern of the management of dosing accuracy within a hospital or home setting.

The American Academy of Pediatrics Committee had indicated that dividing suppositories to provide lower doses may not provide predictable doses (AAPC, 2001).

The DoH recommended 125 to 250 mg for one to five years every four to six hours with a maximum of 1 g based on the highest dose. The labelling dose was 250 mg administered six to eight hourly with a maximum of 1 g.

The DoH added six to twelve years old group with a recommended dose of 250 to 500 mg every four to six hours thus a maximum of 2 g concurring with solid preparation recommendation.

4.5.2.3 Comparison to MCC accepted source:

4.5.2.3.1 Oral:

When the product labelling and MCC accepted source were compared, the labelling had four age group bands whereas the source had nine bands. However unlike the DoH (South Africa. Department of Health) where the split was over younger age group, the source had a two year gap for most of the ranges as depicted in table 8.

Similar to the DoH, the frequency was four to six hourly with a maximum of four doses in a day with the exception of one to three month where the frequency was eight hourly.

The recommended single dose for this age group was 30 to 60 mg which made this the lowest administered dose. The maximum was 120 to 240 mg.

The second age range concurred with the DOH recommendations.

The third differed from the DoH in that the age group was narrowed to six to twenty four months when compared to the DoH of six to thirty six months. The dose was 120 mg with a maximum of 480 mg.

Table 8: Comparison to MCC accepted source.

The tabulation was a summary of the recommended dose strength, the frequency of administration and maximum daily limit from the MCC accepted source, the DoH (South Africa, Department of Health) recommendation and the generalised product labelling for the oral dosage forms.

Age Months or years	Dose (mg)			Frequency (hours)			Maximum (dose per day)		
	MCC	***DoH***	***Label***	***MCC***	***DoH***	***Label***	***MCC***	***DoH***	***Label***
1-3	30-60	48	None	8	4-6	none	4	4	4
3-6	60	60	60-120	4-6		6-8 (liquid) or 4-6 (solid)			
6-12	120	96							
12-24		120	120-240						
2	180								
3		180							
4	240								
5		240-250							
6	240-250		240-480						
7									
8	360-375								
9									
10	480-500								
11		500							
12	480-750		Adult/ 500-1000			4-6			
13									
14									
15									
16	500-1000	Adult							
17	Adult								
18									

The fourth band was two to four years with a dose of 180 mg and a maximum of 720 mg which coincided with the DoH recommendation for three to five years.

The fifth band was four to six years with a dose of 240 mg and a maximum of 960 mg which correlated to the labelling maximum single dose for one to five years.

The sixth band was six to eight years with the dose of 240 mg or 250 mg and a maximum of 960 mg or 1 g. This coincided to five to eleven years DoH recommendation.

The seventh band was eight to ten years with 360 to 375 mg dose and a maximum of 1440 to 1500 mg.

The eighth band was ten to twelve years with 480 to 500 mg dose and a maximum of 1,920 to 2 g.

The last band was twelve to sixteen years with a dose of 480 to 750 mg and a maximum of 1,920 to 3 g.

4.5.2.3.2 Rectal:

The age groups, the dosage, frequency of administration and maximum limit suggested by the DoH coincided with the MCC reference with the exception of two details. The first was a lower dose of 60 mg suggested for three to twelve month old in the source while the DoH recommended 62,5 mg. The second point was the last age group where the source began with five years and the DoH with six. The MCC source removed doubt on treatment for children between the ages five to six years.

4.5.3 International product review

The full prescribing information for Tylenol™ from the United States indicated-that children over 12 years of age should be given the same as the adult dose and that there was no FDA approved dose for children younger than 2 years.

Panadol™ from the UK was available in a variety of strengths as solid dosage form and was not recommended for children under 6 years, the same as South African

labelling. A narrower age band as per MHRA recommendation for liquid preparations had not been defined. This could be attributed to the difficulty of administration of ¾ tablet as the tablet scoring would then have to be cross score lines to provide 375 mg paracetamol per dose (Bachynsky, Wiens and Melnychuk, 2002).

Another product, Boots Paracetamol 3 Month Plus™ was reviewed. The recommended doses are up to six years of age which corresponded to the dose and age group as described in chapter 4.2.1.

4.5.4 N-acetylcysteine

For the intravenous treatment of overdose, the NAC specific labelling (MIMS, May 2012) corresponded to the MCC standardised texts including the vague statement that volume needs to be adjusted in children with no special dose recommendation.

The review of paracetamol labelling information in respect of overdose had reflected no distinction between the various pharmaceutical formulations as overdose is a component of distribution, metabolism and elimination of paracetamol occurring following absorption.

27 paracetamol products were evaluated. Only 25,93% (7 products) met the MCC standardised text requirements (Medicines Control Council, Standardised text, 2010) while 51,85% did not conform to the requirement. Labelling information could not be sourced for 11,11% of products whilst 11,11% were no longer listed in MIMS (MIMS, August 2013). Pharmacies did not stock all preparations at any given moment due to shelf space resources constraints.

Tylenol™ labelling detailed the full dosing requirement as per the MCC requirement. In the United Kingdom, reference was made to treatment as soon as possible and the use of charcoal and NAC but no specific details were listed on the actual product labelling.

The labelling details as prescribed by the MHRA (United Kingdom. Medicines and Healthcare Products Regulatory Authority) focussed on the ingredient, paracetamol, and not on the overdose ingredient NAC. In addition, paracetamol overdose was an emergency condition that required treatment in a clinical environment (Rossiter, 2012).

4.6 Restriction of sale

The restriction of sale (South Africa. Medicines and Related Substances Act 101, Schedules) is based on the total quantity per pack and on the dosage form. Products classified as OTC or Schedule 0 (South Africa. Medicines and Related Substances Act 101, schedules), met the conditions as specified in the Schedules (South Africa. Medicines and Related Substances Act 101,.

In the United States, over-the-counter product were only available for age 2 years and older (Tylenol™ prescribing information) and there was a restriction of pack size as in most other parts of the world (Waitemata District Health Board, 2012).

The United Kingdom had a firmer control on pack size restrictions. They had allowed 16 tablets per pack to be sold by a general dealer, a pharmacy pack size not to exceed 32 tablets and pack sizes above 100 must be prescribed (Hawkins et al, 2007). Furthermore, the MHRA (United Kingdom. Medicines and Healthcare

Products Regulatory Authority) had initiated a sale restriction of two packs per sale. No other regulator had instituted this control of restriction.

4.7 Child

The Children's Act (South Africa. Children's Act 38) concurred with the National Health Act (South Africa. National Health Act 61) to define the age of a children to be anyone eighteen years or younger.

The United Kingdom used the terminology paediatric population where the definition of age coincided to ZA (United Kingdom, Medicines and Healthcare Products Regulatory authority, Medicines for Children).

The WHO model formulary for children was intended for children up to the age of 12 years (Bidgood et al, 2010). This principle was adopted by the FDA (Tylenol™ prescribing information).

4. 8 Surveys

The surveys were conducted over a period of four weeks beginning 20th March 2014 until the 15th April 2014 by the researcher conducting face-to-face interviews with all respondents. Prior to the actual survey, various general dealers and pharmacist were approached personally or via telephone to request their assistance in the research. The respondents were given the survey forms to complete and clarification provided by the researcher where necessary. When requested, the research completed the form but read the form together with the respondent before addressing each point. The time varied for each survey as a result of other general discussions with the period for the survey varying from 10 minutes to 30 minutes per survey.

Common questions asked of caregivers and pharmacists were on dose recommended, the frequency of administration, the review of product labelling and whether a medicine measure was considered. Please refer appendices 2 – 5 for a template of the survey documentation. Appendices 13 and 14 provide a consolidation of the responses received from all the respondents.

The dose recommended by 80% of pharmacists was in millilitres where the dose was per product labelling. 20% of pharmacists recommended using a teaspoon while 20% recommended the solid form for children older than six years.

80% of caregivers indicated that they reviewed the product labelling while 20% used paracetamol as recommended by their pharmacist. 40% of caregivers used a teaspoon to administer liquid paracetamol while 60% indicated that they administered the product in millilitres. The doses administered met the product labelling but was on the lower end for all age groups.

Neither pharmacist nor caregiver exceeded 10 ml per dose while labelling indicated a dose of up to 20 ml for the age group of six to twelve years.

The labelling frequency of administration was six to eight hourly with a six hourly recommendation by 80% of pharmacists while 20% relayed the doctor's instructions to the caregiver.

Doses administered by caregivers ranged from four to eight hourly. The distribution was 30% each at four and eight hours, while 40% administered paracetamol at six hourly intervals.

70% of caregivers and 40% of pharmacists had reviewed the labelling in the last month. All pharmacists had reviewed the labelling within the last twelve months while

the figure for caregivers was 80%. 20% of caregivers previously reviewed the labelling more than twelve months ago.

Household items were the preferred device for administration of paracetamol liquid preparations. 60% preferred a teaspoon while 30% used a tablespoon. Only 10% used a syringe. None of the respondents used a dedicated medicine measure. 100% of pharmacists which served the low income groups handed out medicines measures to caregivers whereas pharmacists in the middle suburb sold medical devices as separate items.

Caregivers did not inform any healthcare profession when they thought paracetamol was ineffective in 60% of the cases which implied that there was a lack of pharmacovigilance reporting.

4.9 Hypothesis testing

The dependent variable of MCC information was based on MCC's accepted source and the independent variable assessed were the product labelling, use in practice by caregivers and the pharmacist recommendations within the private sector and the DoH (South Africa. Department of Health) treatment guidelines for public sector recommendations.

Parameters assessed were age, dose, frequency and maximum daily limit across the different dosage forms based on the findings reported under chapter 4. The results were coded 0 or 1 as described under chapter 3.2. The comparisons are described in tables 9 and 10 below.

Table 9: Product labelling evaluation

The score rating for the determination of conformance of product labelling to MCC accepted recommended, frequency of administration and daily maximum limit for children.

Dosage form	*Age*	*Dose*	*Frequency*	*Maximum*
Liquid	0	0	0	1
Tablet	0	0	0	1
Rectal	0	0	0	1
Intravenous	1	1	1	1

Therefore the only dosage form that met the regulator standard was the intravenous preparation accessible in a clinical setting.

The rectal form was available from pharmacy only and met the maximum daily dose. Age and dose did not conform to the standard.

The liquid and solid dosage forms were easily accessible to caregivers and met the maximum dose only. Age and dose did not meet the standard.
Medical device use was not assessed as a parameter due to lack of legislation enforcement.

As more than 50% of pharmacists and caregivers referred to the product labelling, it confirmed the importance of product labelling.

Therefore, for the private sector, 7,41% of the labelling met regulator standards.

Table 10: DoH recommendation evaluation

The score rating for the determination of conformance of DOH (South Africa, Department of Health) recommendations to MCC accepted recommended, frequency of administration and daily maximum limit for children.

Dosage form	*Age*	*Dose*	*Frequency*	*Maximum*
Liquid	0	0	1	1
Tablet	0	0	1	1
Rectal	1	1	1	1
Intravenous	n/a	n/a	n/a	n/a

The rectal form met all the regulator conformance parameters. The differences of dose (under 4%) and age (five years and six years had to same dose) were acceptable.

All dosage forms met the frequency and maximum requirement. However liquid and tablet preparations did not meet the dose or age parameter.

Medical devices were procured by the department (South Africa. Department of Health, Medical and Pharmaceutical contracts, 2014) but the practice setting was not established in this research project.

Therefore in the public sector, the only dosage form to meet the regulator standard was the rectal preparation. All other dosage forms did not meet the requirements although the DoH had eight age group bands.

In terms of consideration of children, neither the private nor the public sector met the definition of the eighteen years of age requirement.

It is concluded that the null hypothesis is met.

5. Conclusions and/or Recommendations

Paracetamol is the most used drug (South Africa. Department of Health, Tenders liquids and solid dosage forms, 2012 and IMS, 2014) available both over-the-counter and in pharmacy used by both children and adults (Brayfield (ed.), 2014). This research focussed on the use of paracetamol in children on the basis of their vulnerability when administered medicines by caregivers.

An extensive review of the South African legislation with specific reference to paracetamol yielded information on the strength per unit dose, pack size restriction, point of sale, labelling requirements and overdose treatment. There was no specific suggestion to dosing or labelling requirements in children apart from alcohol content for oral medicines (Medicines Control Council, Alcohol Content, 2003).

The paracetamol recommendations from the national Department of Health of South was reviewed as the department of health are responsible for legislating the control of medicines in addition to principles governing professional practice of all healthcare providers within South Africa.

Specific product labelling was reviewed as MCC scrutinized all labelling at the time of assessment prior to granting a marketing authorisation (South Africa. Medicines and Related Substances Act 101, Section 15). Subsequent labelling changes are initiated by the marketing authorisation holder or in very rare instances as a result of a MCC directive (Medicines Control Council, Medicines Safety Alert, Cough and Cold preparations, 2011). MCC (Medicines Control Council, Package inserts for Human use, 2014) had initiated that product labelling should reflect registration and amendment dates on the package insert. However; would the community pharmacist

or even a caregiver realize the value of this information to them warrants further investigation as it indicates when last the package insert was updated by the pharmaceutical company.

Paracetamol is well-known and well-established molecule should be referenced to *The Complete Drug Reference*, or simply *Martindale* as per MCC (Medicines Control Council, Package inserts for Human use, 2010) accepted reference. Therefore changes made in Martindale must be filtered down to product specific labelling. The ultimate aim is to provide users including caregivers and healthcare professionals with updated safety information (Gray, May 2014).

Paracetamol in liquid preparations are available only in two strengths in South Africa. This correlated to the 2009 FDA (United States of America, Food and Drugs Administration) ruling that paracetamol liquid preparations be available in limited strengths to minimise dosage errors (Food and Drugs Administration, 2009).

In 2011, the MHRA (United Kingdom. Medicines and Healthcare Products Regulatory authority, 2011) made a ruling to narrow the age band for liquid preparations to ensure that younger children were not overdosed and that older children were not under dosed. The MHRA recommended doses, can be administered and used in children based on the 120 mg/5 ml strength formulation available in ZA, as preparations reflected doses up to the age of twelve and can be extended to include dosing instructions for children older than twelve years.

As a consequence of the MHRA decision, the United Kingdom recommended dose was revised in the British National Formulary. The dose was reflected in milligram and not limited to a particular dosage form. The MHRA dose revision affects the

tablet formulation but has not yet been incorporated onto the product labelling (Panadol^{TM} SmPC) which could be due to a lack of the MHRA directive on addressing the tablet formulations. There were only two marketed strengths for solid preparations in ZA. For the common 500 mg strength, there was conflicting recommendations in administration to children six to twelve years, generally the same dose was recommended for six to twelve year olds with fewer than twenty percent of the labelling specifically addressing a dose for children over the age of twelve.

Paracetamol strengths for rectal or intravenous preparations were similar to that available internationally in terms of dose and frequency of administration.

There was commonality for the maximum daily doses across all dosage forms. Children doses ranged from 60 mg to 4 g from birth until eighteen years of age. Adult doses were recommended for children over fifteen by the DoH at primary and hospital level (South Africa. Department of Health, 2008 and 2013) and over sixteen in Martindale (Brayfield (ed.), Paracetamol 2014). It was identified that product labelling does not adequately address the children age group of twelve to eighteen years in South Africa.

Finding of the research revealed that administration frequency differed across dosage forms and even across the same dosage form notably for liquids in South Africa. Martindale (Brayfield (ed.), Paracetamol, 2014) and the DoH (South Africa. Department of Health) had a rectal dose for children up to the age of twelve whilst the product labelling in ZA terminated at five years.

There were differences in the age group bands and therefore there were dose differences across the different preparations marketed in ZA (MIMS, May 2012). This was applicable when comparing the MCC approved product labelling to the DOH recommendations. The DoH recommendations were similar to that ascribed in Martindale (Brayfield (ed.), Paracetamol, 2014) but differed to the approved labelling.

There are eleven official languages in South Africa; however, labelling must be captured in “English and one other official language” (Medicines and Related Substances Act 101, Regulations 8, 9 and 10) with Afrikaans being the other language based on previous legislation. Apart from being instructed by healthcare professionals at the time of dispensing, there is no further progress to inform illiterate care-givers on the safe administration of medicines to children.

Paracetamol’s narrow therapeutic index makes it necessary to inform caregivers and healthcare professionals of the signs, symptoms and treatment regimen as a result of a paracetamol overdose. Due to the seriousness of hepatic failure associated with paracetamol overdose (Brayfield (ed.), Paracetamol, 2014), treatment had been classified as a medical emergency worldwide. However internationally there was no consensus on the type of treatment, intravenous or oral, or the rate of administration when using acetylcysteine. However, consensus exists that treatment of paracetamol overdose should begin as soon as possible.

The United Kingdom was the only country that had a limitation on the quantity that could be sold in a single purchase and limited pack for pharmacist initiated therapy (PAGB, 2013). However given that paracetamol are freely available at general store outlets in South Africa, the practicality of a similar recommendation for South Africa might not be feasible. The Advertising Standards Authority code in South Africa(ASA

2014) did not curb the sale of medicines either in terms of age or pack size to children in South Africa. However, there is a limitation on the sale of medicines to children over the age of fourteen in pharmacy (South Africa, Medicines and Related Substances Act 101, Section 22A).

From the surveys conducted during the research, it was established that product labelling does play an important role when pharmacists or caregivers prescribe or administer medicines to children as the dose is confirmed from the package insert. In addition, the survey revealed that caregivers were not aware that a household teaspoon and a medicines measure teaspoon did not provide the same volume. The medicine measure or the recommended product labelling unit dose is provided in volume units of 5 ml. The finding confirmed that a household teaspoon provides a volume less than 5 ml; and therefore, it is concluded that children under dosed when given liquid paracetamol preparations. Of the caregivers surveyed, none administered the tablet to children and was a shortcoming that was not anticipated and thus not addressed in the survey questionnaire. The survey revealed that the children population in South Africa are being under dosed with paracetamol liquid, similar to the finding by Kazouini(Kazouini A et al, 2011).

All surveys were conducted within pharmacies, with no pharmacist indicating that they initiated therapy with a suppository and none of the caregivers mentioned the rectal form during the face-to-face discussions. There were no modified release paracetamol preparations on the market (MIMS, August 2013)

Upon concluding this research, it is noted that product labelling needs to take into consideration the recommended target population for the particular drug; and in

addition, to address formulations limitations should more than one dosage form exist as is the case with paracetamol.

A recommendation is that the “main panel” wording as stipulated by MCC (Medicines and Related Substances Act 101, Schedules) be revisited as caregivers did not recognise a drug by its international non-proprietary name, or generic name, but were conscious of brand names as observed when the survey interviews were conducted by the researcher. Therefore, it was concluded that the boxed warning required on the front panel, does not provide any heightened awareness of the dangers of overdosing with paracetamol. Furthermore, the definition of a main panel in labelling needs to be clarified at this was the only molecule (Medicines and Related Substances Act 101, schedules) that had this limitation in South Africa.

A consolidated review of the multiple pharmaceutical forms was enlightening.
For liquid preparations, the dose was reflected in millilitres while this is not a household item. The research conducted has shown that caregivers equated a teaspoon to provide a 5 ml dose.
Fortunately the opportunity has just presented itself to comment on the proposed medical devices regulations in ZA. The recommendation will be for the inclusion of a medicine measure or equivalent device to be provided with all medical liquid preparations sold.

Paracetamol is presented in the same strength in tablet or capsule form to be swallowed, as an effervescent tablet to be dissolved just before administration or a meltab that could dissolved on the tongue. Yet there is no guidance at which age group the solid form may be given to children. As an illustration, one product

indicated that it was not recommended for children under the age of twelve but yet other preparations reflected a tablet dose for children from six to twelve years.

There was a recommendation that half a tablet be administered on a product package insert; but this product did not have a score line to allow for the tablet to be broken and to deliver this half a tablet dose. Similarly, it could be concluded that a child would find it easier to be given a meltab, which is a thin film, that disintegrates in the mouth rather than a tablet to swallow yet the meltab is not recommend for children under the age of twelve. This re-emphasizes that the target population should be considered during the product design phase and dosage form limitations captured on product labelling.

This research project has uncovered the importance of updating product labelling especially when the benefit risk ratio is modified or could impact the safe use of a product (Medicines Control Council, Safety-related Package insert notifications, 2014) particularly when a preparation is made available directly to the consumer with no healthcare provider intervention. Therefore it is imperative that MCC issue consumer directives as practised by other established regulators such as the MHRA and the FDA. These consumer directives will provide a clear and unambiguous leadership from the regulator in managing the safe and effect use of medicines used by the public which it, the MCC, serves to protect.

A limitation was that the research project did not provide any answers of research conducted previously to indicate at what age a child might be independent enough to use medication without caregiver supervision. The Medicines and Related Substances Act 101 (South Africa. Medicines and Related Substances Act 101) provided some guidance as it indicated that medication can only be sold to children

older than fourteen years but did not address to whom medicines can be sold at general dealer outlets.

Another restriction is that no single clause or rule can be assessed on its own and that many aspects or clauses need to be taken into consideration when medicines are administered to children. It was not possible to address all within this research project.

Further investigations should include the review of labelling for products that are supplied to the DoH (South Africa. Department of Health) including determining if a medicine measure in included in the pack, public sector practice recommendation for paracetamol preparations, evaluation of prescribing habits by authorised prescribers, re-imbursement trends, and an analysis into the paracetamol overdose treatment in South Africa.

It is essential that MCC and the pharmaceutical industry be cognisant of dosage recommended for children, their age group breakdown, the differing international definition of a child and other international trends especially those that relate to effective administration of medicines to children.

The observations noted from the recommended dosage review of the product labelling and that used in practice from the results of the survey, is that children are not being given the recommended dose as per product labelling. However, product labelling does not correlate to MCC’s accepted source. Therefore, children are not receiving the correct therapeutic dose of paracetamol.

The null hypothesis has been proven and therefore it is concluded that paracetamol is not being used or prescribed at the correct therapeutic dose in the children population within South Africa.

References:

1. Acetylcysteine (Acetadote) for acetaminophen overdosage (2005). *Med Lett Drugs Ther* 2005; 47: 70–1.
2. Advertising Standards Authority of South Africa (ASA), Code of Marketing Practice. Available at: http://www.asasa.org.za/ (Accessed 23 February 2014
3. American Academy of Pediatrics Committee on Drugs (AAPC) (2001), Acetaminophen toxicity in children. Pediatrics. 2001; 108:1020-4. [PubMed] [IDIS 470914]
4. Ashcroft, R., Dawson A., Draper H. and McMillan J.R. (ed) (2007), Principles of health care ethics, second edition. Ebrary [Online] Available at: www.mphar.hiberniacollege.net/ebrary. (Accessed: 01 July 2012)
5. Bachynsky J., Wiens C. and Melnychuk K. (2002), The practice of splitting tablets: Cost and therapeutic aspects, Pharmacoeconomics 20 (5): 339-346
6. Bertolini A. et al (2006), Paracetamol: new vistas of an old drug. CNS Drug Reviews, 12(3-4):250-75
7. Bidgood M, Donohoo E, Gunewardhane N, Harvey A, Hoa V, Hunter S, Keen S and Wroth O (ed)(2010), WHO Model Formulary for Children 2010. [Online] Available at: www.who.int/en/ (Accessed 21 March 2014)
8. BMJ Group (2014), British National Formulary April 2014, Acetylcysteine, [online] London: Pharmaceutical Press [Online] Available at: http://www.medicinescomplete.com. (Accessed: 20 April 2014)
9. Brayfield A (Ed), Martindale: The Complete Drug Reference, Acetylcysteine, [online] London: Pharmaceutical Press [Online]. Available at: http://www.medicinescomplete.com. (Accessed: 16 November 2013)
10. Brayfield A (Ed), Martindale: The Complete Drug Reference, Paracetamol, [online] London: Pharmaceutical Press [Online] Available at: http://www.medicinescomplete.com. (Accessed: 16 November 2013)
11. Brok J., Buckley N,Gludd C. (2006)*. Interventions for paracetamol (acetaminophen) overdose,* Apr 19;(2):CD003328. Cochrane Database of Systematic Reviews [Online]. Available at http://www.ncbi.nlm.nih.gov/pubmed/; Issue 2. Chichester: John Wiley; 2006; (Accessed: 13 October 2006).
12. Brunton L.L (Ed) (2011), Goodman and Gilman's The Pharmacological Basis of Therapeutics, Chapter 34, Anti-inflammatory, antipyretic and analgesic agents: pharmacotherapy of gout, 12th Edition, pages 982 – 984.
13. Cranswick N and Coglan D (2000), Paracetamol efficacy and safety in children: the first 40 years. American Journal of Therapeutics Mar; Vol. 7 (2), pp. 135 – 41, ESBSCO [Online]. Available at: http://resources.hiberniacollege.net:2162/ehost/delivery.(Accessed: 14 April 2014)
14. Gazarain M, Drew A. And Bennett A (2014), Medical mishaps, Intravenous paracetamol in paediatrics: cause for caution, Australian Prescriber, Volume 37, Number 1, February 2014, 24-25 [Online], Available at: http://www.australianprescriber.com/magazine (Accessed: 25 April 2014)
15. Generic Dictionary (2014). Available at: www.generic.co.za (Accessed: 31 January 2014

16. Gray A. (2014), Picking the right lever – expanding the cube to prepare for NHI, Pharmaceutical Society of South Africa, Conference May 2014, 9-11 May 2014
17. Hawkins L.C. Edwards J.N., Dargan P.I. (2007), Impact of Restricting Paracetamol Pack Sizes on Paracetamol Poisoning in the United Kingdom: a literature review, Drug Safety 2007; 30 (6): 465-479
18. Heard K. J. (2008), Acetylcysteine for acetaminophen poisoning, New England Journal of Medicine, 2008, 359:285-292
19. Intekom (2014), South African Electronic Package Inserts (SAEPI). Available at: www.intekom.com (Accessed: 28 April 2014)
20. Intercontinental Marketing Service (IMS) Health South Africa (2014), International Marketing Surveys South Africa, Data on Panado ATC, 19 April 2014
21. International Conference on Harmonisation (ICH) (1996), International conference on harmonisation Tripartite guideline, Guidelines for Good Clinical Practice E6(R1), 10 June 1996 [Online] Available at: http://www.ich.org/products/guidelines/efficacy. (Accessed: 24 July 2012).
22. Kazouini A, Mohammed B. S., Simpson C.R., Helms P. J. And McLay J.S. (2011), Paracetamol prescribing in primary care: too little and too much, British Journal Clinical Pharmacology, 72: 3, pp 500 – 504.
23. McEvoy (ed), American Hospital Formulary System (AHFS) Drug Information, Acetaminophen, [online] London: Pharmaceutical Press. Available at: http://www.medicinescomplete.com.(Accessed: 16 November 2013)
24. MIMS South Africa (2012), Monthly Index of Medical Specialities May 2012 pages 65 -68.
25. MIMS South Africa (2013), Monthly Index of Medical Specialities August 2013 pages 70 -73.
26. Patel (2013), Research Proposal, Is paracetamol being prescribed and used at the correct therapeutic dose in the children population in South Africa?, Nov 2013
27. Patel A et al (2012), Quality of generic medicines in South Africa: perceptions versus reality – a qualitative study, BMC Health Services Research 2012, 12:297
28. Proprietary Association of Great Britain (PAGB) (2013), Paracetamol [Online] Available at: www.pagb.co.uk (Accessed: 21 April 2014)
29. Rossiter D (ed) (2012), South African Medicines Formulary, 12th Edition.
30. Sobhani et al (2008), Accuracy or oral liquid measuring devices: Comparison of dosing cup and oral dosing syringe, The Annals of Pharmacotherapy, Ann Pharmacotherapy January 2008 vol. 42 no. 1 46-52
31. South Africa, *Medicines and Related Substances Act 101 (1965),* Schedule 1, Control of Medicines and scheduled substances, LexisNexis [Online]. Available at: http://www.mylexisnexis.co.za. (Accessed: 18 April 2014)
32. South Africa. Department of Health (2008), Standard treatment guidelines and essential medicines list, Primary Healthcare. Available at: www.health.gov.za. (Accessed: 20/04/2014)
33. South Africa. Department of Health (2013), Standard treatment Guidelines and essential medicines List for South Africa, Hospital level Paediatrics, 2013 edition. Available at: www.doh.gov.za (Accessed: 28 February 2014)

34. South Africa. Department of Health (2014), Essential Medicines Programme (EMP), Medicines List February 2014. Available at: www.health.gov.za/docs. (Accessed: 20/04/2014)
35. South Africa. Department of Health (2014), Essential Medicines Programme (EMP), Essential Medicines Catalogue February 2014. Available at: www.health.gov.za/docs. (Accessed: 20/04/2014)
36. South Africa. Department of Health (2014), Tenders, Medical and Pharmaceutical Contracts, HP092012 Solid dosage forms, HP09-2012SD. Available at: www.health.gov.za.(Accessed: 28 February 2014)
37. South Africa. Department of Health (2014), Tenders, Medical and Pharmaceutical Contracts, HP122012, Liquids,HP12-2012LQ. Available at: www.health.gov.za. (Accessed: 28 February 2014)
38. South Africa. Department of Health (2014), Tenders, Medical and Pharmaceutical Contracts, HP082012, Semi-solids, HP08-2012SSD. Available at: www.health.gov.za. (Accessed: 2 May 2014)
39. South Africa. Department of Health (2014), Tenders, Medical and Pharmaceutical Contracts, HM04-2013SG, Surgical sundries. Available at: www.health.gov.za. (Accessed: 2 May 2014
40. South Africa. Department of Health, Medicines and Related substances control Act, Act 101 of 1965. Available at:www.mccza.com.
41. South Africa. Department of Social Development (2014), Children's Act 2005; Act 38 of 2005. Available at: http://www.ci.org.za/depts/ci/pubs/pdf/lawreform/billsacts/consolidated_childrens_act_1april2010. (Accessed: 23/02/2014)
42. South Africa. Marketing code authority (MCA) 2013, Final SA Code of Marketing Practice, September 2013. Available at: http://www.marketingcode.co.za. (Accessed: 23 February 2014)
43. South Africa. Medicines and Related Substances Act, Act 101 of 1965, Schedules, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za (Accessed: 5 April 2014)
44. South Africa. Medicines and Related Substances Act, Act 101 of 1965, Section 22A, Control of Medicines and scheduled substances, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za (Accessed: 05 April 2014)
45. South Africa. Medicines and Related Substances Act, Act 101 of 1965,, Definitions, Medicine, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 05 April 2014)
46. South Africa. Medicines and Related Substances Act, Act 101 of 1965,, Regulation 8 Labelling of Medicines, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 5 April 2014)
47. South Africa. Medicines and Related Substances Act, Act 101 of 1965, Regulation 9 Package inserts for medicines for human use, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 20 February 2014)
48. South Africa. Medicines and Related Substances Act, Act 101 of 1965, Regulation 10 Patient Information Leaflet, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 20 February 2014)

49. South Africa. Medicines and Related Substances Act, Act 101 of 1965, Section 15, Registration of medicines, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 7 May 2014)
50. South Africa. Medicines and Related Substances Act, Act 101 of 1965, Regulation 45, Advertising of medicines, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 21 April 2014)
51. South Africa. Medicines and Related Substances Act, Act 101 of 1965, Regulation 25, Categories and classification of medicines, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 21 April 2014)
52. South Africa. Medicines and Related Substances Act, Act 101 of 1965, My LexisNexis (2014), South African Pharmacy Council (2014), Dispensary, References Sources; electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za (Accessed: 23 February 2014.
53. South Africa. Medicines Control Council (2010), Guidelines and Forms, 2.20 Package inserts for Human Medicines Standardised texts, February 2010, v1. Available at: www.mccza.com (Accessed: 15 February 2014)
54. South Africa. Medicines Control Council (2014), Guidelines and Forms, 2.14 Patient information leaflets (PIL). Available at: www.mccza.com (Accessed: 15 February 2014)
55. South Africa. Medicines Control Council (2014), Guidelines and Forms, 2.16 Package Inserts for human use. Available at: www.mccza.com (Accessed: 15 February 2014)
56. South Africa. Medicines Control Council (2014), Guidelines Human Medicines, 2.17 Safety Related Package Insert notifications (SR-PINs), Available at: www.mccza.com (Accessed: 13 March 2014)
57. South Africa. Medicines Control Council (December 2003), Alcohol content of medicines, 2.03 Alcohol content Dec03 v1, December 2003. Available at: www.mccza.com (Accessed: 10 April 2014)
58. South Africa. Medicines Control Council (November 2011), Medicines safety Alert, Cough and Cold medicines no longer to be used in children under the age of two years, 21.6_MSA_Cough_and_Cold_Medicines_Nov11_v1, June 2012 Available at: www.mccza.com (Accessed: 03 March 2014)
59. South Africa. National Health Act, Act 61 of 2003, Definitions; child, electronic Publishing Legislation; My LexisNexis (2014) [Online] Available at: www.mylexisnexis.co.za. (Accessed: 02 January 2014)
60. Tylenol full prescribing information (2010) Available at: http://www.tylenolprofessional.com (Accessed: 28 April 2014)
61. United Kingdom. Electronic Medicines Compendium (eMC) (2014), Summary of product Characteristics, Panadol Advanced 500 g T. Available at: http://www.medicines.org.uk/emc. (Accessed: 2 January 2014)
62. United Kingdom. Electronic Medicines Compendium (eMC) (2014), Summary of product Characteristics, Boots Paracetamol 3 Month. Available at: http://www.medicines.org.uk/emc/. (Accessed: 2 January 2014)
63. United Kingdom. Medicines and Healthcare Products Regulatory Authority (MHRA) (2011), MHRA UK Public Assessment Report, Liquid paracetamol for children: revised UK dosing instructions have been introduced, November 2011. Available at: www.mhra.gov.uk (Accessed 01 February 2014)

64. United Kingdom. Medicines and Healthcare Products Regulatory Authority (MHRA), Medicines for Children. [Online]. Available at: www.mhra.gov.uk (Accessed 27 January 2014)
65. United States of America. Food and Drugs Administration (FDA) (2009), Federal Register, Organ-Specific Warnings; Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over- the-Counter Human Use; Final Monograph, Rules and regulations, Vol 74, no. 81, 29 April 2009
66. Vale JA, *et al.* Treatment of acetaminophen poisoning: the use of oral methionine.*Arch Intern Med* 1981; 141: 394–6.
67. Veale, D.J.H., Wium, C.A and Müller, G.J.(2013), Toxicovigilance I: A survey of acute poisonings in South Africa based on Tygerberg Poison Information Centre data, South African Medical Journal, 2013;103(5):293-297. DOI:10.7196/SAMJ.6647 [Online]. Available at: www.ajol.info/index.php/samj/article/download/88038/77680 (Accessed: 30 January 2015)
68. Waitemata District Health Board (2012), Safer: Safer use of high risk medicines: Paracetamol – safe prescribing – mind that child, No:0182-01-026, Issued Dec 12,
69. Wilkes JM, Clark L.E, Herrera J.L. (2005). Acetaminophen overdose in pregnancy. *South Med J* 2005; 98:1118–22.
70. World Health Organisation (WHO) (2013), WHO Model List of Essential Medicines for Children, 4th List final amendment October 2013 [Online] Available at: www.who.int/medicines/.../essentialmedicines (Accessed: 15 January 2014)

Bibliography:

1. (September 2012), Safety warnings and messages for medicines, Paracetamol overdose: simplification of the use of intravenous acetylcysteine, 9 September 2012, http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON178225; accessed 22/03/2012
2. , http://www.fda.gov/Drugs/DrugSafety/ucm284741.htm; accessed 22/03/2014
3. Advertising Standards Authority of South Africa, http://www.asasa.org.za/, accessed 23/02/2014
4. Buzzle (2014), Average weight for children by age, http://www.buzzle.com/articles/average-weight-for-children-by-age.html; accessed 26 February 2014
5. Chetley A, et al (2007), How to improve the use of medicines by consumers, WHO PUBLICATION, http://www.who.int/medicines/areas/rational_use/Manual2_HowtoImprove.pdf; accessed 21/03/2014
6. Children's Act 2005; Act 38 of 2005, http://www.ci.org.za/depts/ci/pubs/pdf/lawreform/billsacts/consolidated_childrens_act_1april2010accessed 23/02/2014,
7. Dal Pan G.J. (2009), Acetaminophen: Background and Overview, 29 June 2009, Office of Surveillance and Epidemiology, Centre for drug Evaluation and Research
8. Department of Health, South African medicines procurement registry, Published documents, Database of Medicine process 30 Jan 2014, http://www.mpr.gov.za/, accessed 31/01/2014
9. Electronic medicines compendium (2014), eMC, www.medicines.org.uk, accessed 23/03/2014
10. EMA (2001), Directive 2001/83/EC as amended, Title V, Labelling and package leaflets, http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004481.pdf; accessed 22/03/2014
11. EMA (2010), Report on the survey of all paediatric uses of medicinal products in Europe, EMA/794083/2009, Human Medicines Development and Evaluation, http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500101006.pdf, accessed 22/03/2014
12. EMA (2014), European Medicines Agency, www.ema.europa.eu; accessed 22/03/2014
13. EMA (July 2011), Drug Safety update, Paracetamol: updated dosing for children to be introduced, http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON123113; accessed 22/03/2014
14. FDA (2009), Federal Register, Organ-Specific Warnings; Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over- the-Counter Human Use; Final Monograph , [Docket No. FDA–1977–N–0013] (formerly Docket No. 1977N–0094L), Federal Register/ Vol. 74, No. 81 / Wednesday, April 29, 2009 / Rules and Regulations

15. FDA (2011), FDA Drug Safety Communication: Addition of another concentration of liquid acetaminophen marketed for infants
16. FDA (2013), Don't Double Up on Acetaminophen
17. FDA (2013), Drug Safety and availability, NCPDP Recommendations for Improved Prescription Container Labels for Medicines Containing Acetaminophen, version 1.1, 2013, http://www.fda.gov/downloads/Drugs/DrugSafety/UCM266631.pdf; accessed 22/03/2014
18. FDA (2013), Guidance for Industry and Review Staff Pediatric Information Incorporated into Human Prescription Drug and Biological Products Labelling Good Review Practice, DRAFT GUIDANCE, Feb 2013, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM341394.pdf, accessed 22/03/2014
19. FDA (2014), Acetaminophen information, http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm, accessed 22/03/2014
20. FDA (June 2013), Drug Safety and Availability, Acetaminophen toxicity, http://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/ucm230396.htm, accessed 22/03/2014
21. Ford D et al (not known), Introduction to the CE mark (presentation), http://www.medmarc.com/Life-Sciences-News-and-Resources/Webinars/Webinar%20Files/CE%20Mark/TheCEMark.pdf; accessed on the 27 February 2014
22. Forty-third report of the WHO Expert Committee on specifications for pharmaceutical preparations. (2009) (WHO technical report series; no. 953), 1. Pharmaceutical preparations - standards. 2. Technology, Pharmaceuticals - standards. ,3. Drug industry - legislation. 4. Quality control. I. World Health Organization. II. Series., http://www.who.int/medicines/publications/pharmprep/pdf_trs953.pdf?ua=1, accessed 21/03/2014
23. Generic Dictionary, www.generic.co.za; accessed 31/01/2014
24. Health Canada (2009), Guidance Document; Acetaminophen Labelling standard (Oct 2009), http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/prodpharma/applic-demande/guide-ld/label_stand_guide_ld-eng.pdf, accessed 21/03/2014
25. Hibernia College (2012), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Ethics
26. Hibernia College (2012), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Writing and evaluating a CTD
27. Hibernia College (2012), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Pharmacovigilance
28. Hibernia College (2012), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Regulatory Affairs
29. Hibernia College (2013), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Research Methods
30. Hibernia College (2013), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Generics and Biosimilars
31. Hibernia College (2013), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Medical devices

32. Hibernia College (2013), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Leadership and Negotiation
33. Hibernia College (2013), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, Module Research Methods
34. Hibernia College (2014), M.Sc. Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences, eLibray
35. http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm336581.htm, accessed 22/03/2014
36. Medicaid (2014), United Stated Public Health, www.medicaid.gov.; accessed 23/03/2014
37. Medicines Control Council (MCC website); accessed 17/01/2014
38. MHRA (2011), Safety warnings and messages for medicines, Liquid paracetamol for children, 14/11/2011, http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON134919, accessed 22/03/2014
39. MHRA (2012), STATUTORY WARNINGS FOR ALL MEDICINES CONTAINING PARACETAMOL, http://www.mhra.gov.uk/home/groups/pl-a/documents/websiteresources/con207166.pdf; accessed 22/03/2014
40. MHRA (2012), The Blue Guide, Advertising and promotion of medicines in the UK, Medicines and Healthcare Products Regulatory Agency, 3rd Edition, August 2012, http://www.mhra.gov.uk/home/groups/pl-a/documents/publication/con2022589.pdf, accessed 22/03/2014
41. MHRA/PEAG (2009), Prescription trends in analgesics 2003-2008 - before, during and after the withdrawal of co-proxamol, http://www.mhra.gov.uk/home/groups/es-foi/documents/foidisclosure/con100023.pdf, and accessed 22/03/2014
42. Mims Desk Reference (MDR) 2009, Volume 44
43. MIMS, Monthly Index of Medical Specialities, Volume 52, Number 5, May 2012
44. MIMS, Monthly Index of Medical Specialities, Volume 71, August 2013
45. My LexisNexis (2014) [online], National Health Act, Act 61 of 2003
46. National Department of Health (2014), Database of Medicine Prices 27Feb2014; http://www.health.gov.za/edp.php; accessed 28 February 2014
47. National Department of Health (2014), Tenders, Medical and Pharmaceutical Contracts, Supply and delivery of pharmaceutical liquids, alcohol, ether, glycerine and methylated spirits to the Department of Health, HP12-2012LQ, http://www.health.gov.za/docs/contructs/HP122012LQContract, accessed 28 February 2014.
48. National Department of Health (2014), Tenders, Medical and Pharmaceutical Contracts, Supply and delivery of solid dosage forms and transdermal patches to the Department of Health, HP09-20125D, http://www.health.gov.za/docs/contructs/HP09122012SDContractCir; accessed 28 February 2014.
49. NHS (2014), NHS Choices, Medicine Guides, Paracetamol 500 mg tablets, http://www.nhs.uk/medicine-guides/pages/MedicineOverview.aspx?condition=Pain&medicine=paracetamol; accessed 23/03/2014

50. Physician Desk Reference (2014), Tylenol (acetaminophen) Full prescribing information McNeil Consumer Healthcare, http://www.pdr.net/full-prescribing-information/tylenol?druglabelid=317#topPage, accessed 23/03/2014
51. Rossiter D (Ed) (2012), South African Medicines Formulary (SAMF), Faculty of Health Sciences University of the Western Cape, 10th Edition, Paediatric Prescribing, pages 5 – 6
52. Rossiter D (Ed) (2012), South African Medicines Formulary (SAMF), Faculty of Health Sciences University of the Western Cape, 10th Edition, Anilides, Paracetamol, pages 437 – 438
53. Snyman J. (Ed) (2009), MIMS Desk Reference (2009), Volume 44, Drug Therapy in children, pages 62a – 63a.
54. South African Electronic Package Inserts (SAEPI), Collection of marketed product package inserts, www.home.interkom.com, accessed 31/01/2014
55. Standard Treatment Guidelines and Essential Medicines List for South Africa, Paediatric Level Hospital, 2013 edition
56. Standard Treatment Guidelines and Essential Medicines List for South Africa, Primary Health Care Level, 2008, 4th edition
57. The South African Medical Devices Industry Association (SAMED) (2014), SAMED members, http://www.samed.org.za/Members-View, accessed 26 February 2014
58. TITLE 21--FOOD AND DRUGS, CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES, SUBCHAPTER C--DRUGS: GENERAL, PART 201. LABELING, 201.326 - Over-the-counter drug products containing internal analgesic/antipyretic active ingredients; required warnings and other labelling, http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=201, accessed 22/03/2014
59. Turner L. (2010), Daily drug Use, A guide for the Health Care Professional, 9th Edition, Drug use in different age groups - use in children, page 8
60. Turner L. (2010), Daily drug Use, A guide for the Health Care Professional, 9th Edition, Anilides, Paracetamol, page 410
61. Wellkang Tech Consulting, http://www.ce-marking.org/, accessed 27 February 2014
62. WHO (???), National Medicines Price sources, http://www.who.int/medicines/areas/access/sources_prices/national_medicine_price_sources.pdf, accessed 23/03/2014
63. WHO (2003), Bulletin of the World Health Organisation, evidence on the use of paracetamol in febrile children, Volume 81, No. 5, Jan 2003; http://www.scielosp.org/scielo.php?pid=S0042-96862003000500011&script=sci_arttext&tlng=pt; accessed 23/03/2014
64. WHO (2003), WHO Pharmaceuticals Newsletter No. 2, 2003, http://www.who.int/medicines/publications/newsletter/en/news2003_2.pdf?ua=1; accessed 21/03/2014
65. WHO (2007), PROMOTING SAFETY OF MEDICINES FOR CHILDREN, http://www.who.int/medicines/publications/essentialmedicines/Promotion_safe_med_childrens.pdf?ua=1, accessed 21/03/2014
66. WHO (2010), 45th Expert Committee on Specification for pharmaceutical products, regulatory guidance, development of paediatric medicines, Point to consider,

http://www.who.int/medicines/services/expertcommittees/pharmprep/Rev2-PaediatricMedicinesDevelopment, accessed 16/03/2014

67. WHO (2010), 45th Expert Committee on Specification for pharmaceutical products, Draft Paracetamol solution for the International Pharmacopoeia, ParacetamolSolution-QAS10-385_29092010.doc; accessed 16/03/2014
68. WHO (2010), 45th Expert Committee on Specification for pharmaceutical products, Draft Paracetamol solution for the International Pharmacopoeia, ParacetamolSuspension-QAS10-386_29092010.doc; accessed 16/03/2014
69. WHO (2011), Guidance for availability and accessibility of controlled medicines, http://www.who.int/medicines/areas/quality_safety/, accessed 16/03/2014
70. WHO (2013) Model List of Essential Medicines for Children, 4th list (April 2013), (Final Amendments – October 2013), http://apps.who.int/iris/bitstream/10665/93143/1/EMLc_4_eng.pdf?ua=1, accessed 21/03/2014
71. WHO (2013) Pocket book of Hospital care for children, 2nd edition, 2013 edition, http://apps.who.int/iris/bitstream/10665/81170/1/9789241548373_eng.pdf?ua=1, accessed 21/03/2014
72. WHO (2013), Health topics, Behind the essential medicines list, March 2013, http://www.who-cc.dk/features/2013/essential_medicines_list/en/; accessed 23/03/2014
73. WHO model formulary for children 2010 based on the Second Model List of Essential Medicines for Children 2009, http://apps.who.int/medicinedocs/documents/s17151e/s17151e.pdf, accessed 21/03/2014
74. WHO Technical Report Series (2006), THE SELECTION AND USE OF ESSENTIAL MEDICINES including the 14th Model list of essential medicines, (933) http://www.who.int/medicines/services/expertcommittees/essentialmedicines/TRS933SelectionUseEM.pdf?ua=1; accessed 21/03/2014
75. WHO (2013), Model List of Essential Medicines, 18th list, finalised Oct 2013, http://apps.who.int/iris/bitstream/10665/93142/1/EML_18_eng.pdf?ua=1, accessed 21/03/2014

Appendices:

No.	*Detail*	
1.	Research proposal_Aadila Patel Modified Jan 2014	Research Proposal
2.	Survey for professional	Professional survey
3.	Survey for caregiver	Caregiver survey
4.	Consent form for participation in survey	Participant consent form
5.	Participant Information Leaflet	Participant Information leaflet
6.	Medical device: Experiment method	Device experiment method
7.	MIMS May 2012 Paracetamol products	MIMS 2012 paracetamol products
8.	MIMS May 2012: NAC products	MIMS 2012 NAC products
9.	Medical device: Results of experiment	Devices experiment results
10.	Product Labelling: Source of data	Product Labelling source

No.	*Detail*	
11.	Summary of Paracetamol product labelling	Product labelling summary
12.	Summary of paracetamol overdose	Summary of overdose review
13.	Survey results: Professional	Professional surevy results
14.	Survey results: Caregivers	Caregiver survey results

University of the Western Cape
in partnership with
Hibernia College, Ireland

MASTER OF SCIENCE IN PHARMACY ADMINISTRATION AND PHARMACY POLICY SPECIALISING IN REGULATORY SCIENCES

COVER PAGE

Name:	Aadila Patel
Student Number:	MRESC001
Student Cohort:	APRIL 2012
Assessment Title:	RESEARCH PROPOSAL
Word Limit as per CA details:	500 - 1 000
Word Count (excl. title pages, references & attachments):	734
Submission Date:	18 NOVEMBER 2013

I agree that I have researched and written the work submitted in this assessment, and that the work submitted is my own. Any information and opinions drawn from other sources are attributed by means of a reference to that source.

✓

Title: Is paracetamol being prescribed and used at the correct therapeutic dose in the children population in South Africa?

Writer: Aadila Patel

Student at the University of Western Cape and Hibernia College; research proposal is toward the partial fulfilment of the award of M.Sc. in Pharmacy Administration and Pharmacy Policy specialising in regulatory sciences.

Current qualification: BPharm

South African, +27 (0)836407565, aadilapqp@hotmail.com,

Date of submission: 18 November 2013

Date of completion: 12 May 2014

Institution: Western Cape University, South African and Hibernia College, Ireland

Supervisors: Miriam O'Donoghue Research Project Supervisor
modonoghue@hiberniacollege.net

Peter Eagles Research Project Co-Supervisor
peagles@uwc,ac.za

Title:

Is paracetamol being prescribed and used at the correct therapeutic dose in the children population in South Africa?

Introduction

Paracetamol is first line treatment as an analgesic (treatment of pain) and antipyretic (treatment of fever) especially in children (Brayfield). It is one of two[1] orally administered analgesic and antipyretic available without prescription[2] at pharmacies or can be purchased from a general dealer store (LexisNexis). Paracetamol was first commercialised in 1953 in the United States and subsequently introduced to other parts of the world (Sneader).

Although highly effective, paracetamol has a narrow therapeutic index (FDA) and therefore needs to be administered to children correctly. Paracetamol is less irritant on the stomach lining when compared to non-steroidal anti-inflammatory agents and is therefore the treatment of choice in children (Brayfield).

There are options of different pharmaceutical dosage forms for paracetamol. Paracetamol is available as a syrup having the strength of 120 mg per 5 ml, as a tablet or capsule containing 500 mg, as suppositories containing either 125 mg or 250 mg per suppository, as melt tabs (or effervescent tablets) containing either 125 mg or 500 mg per tablet or as a solution for infusion containing 1 g per 100 ml (MIMS).

With the different dosage forms containing variable quantities of paracetamol, the research will review the current legislation on paracetamol, the therapeutic dose of paracetamol and the manner of administration (medical device) to ensure correct use of paracetamol preparations in children.

[1] The other preparation contains aspirin

[2] Prescription is the term used in South Africa and is the same as a script for medicines

The focus of the research in children is as a result of the conflicting classification of children internationally versus that of South Africa. The reason for this research is to increase awareness for the correct and effective use of paracetamol preparations in children population.

Hypothesis:

Paracetamol is effective within a defined therapeutic range however are prescribers and caregivers using paracetamol as authorized by regulators.

Methodology

The methodology for this research will be a mixed methods approach using both quantitative and qualitative study. A closed structured survey has been developed (attachments 6 and 7) whereby data will be collected. This will ensure data reliability. If the participants (respondents) do have additional time, this may present the opportunity for continuation into open-ended discussions. It is anticipated that data collection will be via completion of the survey form and an audio recording.

The data from the survey will be captured during the interviews. Should open-ended discussions take place, these will be captured electronically and summarised in hard copy. Aadila Patel will be solely be responsible for collecting the data and will use face validity.

The data collection will focus on the dose and medical devices that are used to administer the paracetamol preparation to the child.

Data collection sites will be from private pharmacies at different practice settings, different social economics groups at pharmacy level and at different retail outlets. Data collection will not be conducted in the public sector at this stage due to the time limitation to complete the research and the slow progress of authorisation that needs to be obtained from the Department of Health. However, any relevant research that is available in the public domain will be included in the study.

In terms of legislation, data collection will consist of the review of current legislation in South Africa and internationally. In addition, there will be a review of the various scientific package inserts on the South African market. A comparison will be performed against one product from the United States and another from the United Kingdom.

Ethical considerations

Children have been classified as a vulnerable group (ICH). It is important that as adults we continually review the safety of medicines, be this from the perspective of a caregiver or as healthcare professional. The latter could constitute the delivery of effective healthcare or as a component of continuing professional development.

Data collection for this research project will be confidential, although the survey does not require any personal information to be shared in respect of any child.

The principle investigator of this research will be Aadila Patel. The focus of the research will be practice ethics in terms of responsibility of updating information, if required. Clinical ethics (treatment delivery and care) will be considered. The role of the regulator will be reviewed to determine if they are responsible for public ethics (Ashcroft) and informing the public of new safety information in the effective use of paracetamol.

The sponsor[3] responsibility in this research project is Pharmaceutical Quality Partner.

[3] Limited to funding only

References:

1) Ashcroft at el (2007), Principles of health care ethics, second edition, accessed via Hibernia ebrary

2) Brayfield A (ed), Martindale: The Complete Drug Reference, Paracetamol, [online] London: Pharmaceutical Press <http://www.medicinescomplete.com>, accessed on 16 November 2013,

3) FDA, Foodstuff and Drug Administration, Cosmetic

4) Hibernia (2013), UWC Research Project Student Handbook_Apr 12 Cohort

5) ICH (1996), International conference on harmonisation Tripartite guideline, Guidelines for Good Clinical Practice E6(R1), 10 June 1996.

6) MIMS (2012), Monthly Index of Medical Specialities May 2012 pages 65 -68.

7) MyLexisNexis (2013) [online], Medicines and Related Substances Control Act, Act 101 of 1965, Electronic Publishing Legislation, accessed 16 November 2013

8) Sneader W (2005) Drug Discovery: A History. Hoboken, N.J.: Wiley. p. 439.

9) Study Guides and strategies, http://www.studygs.net/proposal.htm; accessed 16 November 2013

10) WHO (2013), WHO Model List of Essential Medicines for Children, 4th List final amendment October 2013.

Attachments

Attachment 1:	Cover letter to the ethics research committee
Attachment 2:	Hibernia College Research Ethics Committee Application Form v1_Aadila Patel
Attachment 3:	Hibernia College Research Ethics Committee Consent Form v1_Aadila Patel
Attachment 4:	Hibernia College Research Ethics Committee Information leaflet v1_Aadila Patel
Attachment 5:	Introduction to research document, check for principal investigator
Attachment 6:	Survey for healthcare professional
Attachment 7:	Survey for caregiver
Attachment 8:	Curriculum vita principle investigator: Aadila Patel

PARACETAMOL SURVEY: CHILDREN 12 YEARS AND UNDER

Pharmacy ☐ Independent ☐ Corporate

Profession: ☐ Pharmacist ☐ Pharmacy Assistant
☐ Nurse ☐ Other: _____

1. Do you use paracetamol as first line treatment:

   Yes No

2. What is the dose that you recommend:

   _____

3. What is the frequency of the dose:

   4 hours 6 hours 8 hours

4. Do you look at the package insert of the product that is being dispensed:

   Yes No

5. When last have you looked at the package insert:

Last month last 3 months last 12 months over 12 months ago

6. Do you hand out a medicine measure:

   No Yes

7. Do you ask if the caregiver has an adequate dispensing device (medicine measure) to dose the child

   No Yes

PARACETAMOL SURVEY: CHILDREN 12 YEARS AND UNDER[1]

Caregiver ☐ Parent ☐ Grandparent
☐ Guardian ☐ Day caregiver

Purchase: ☐ Independent Pharmacy ☐ General dealer
☐ Corporate pharmacy ☐ Other: ----------

1. Why do you give your child (or child under your care) paracetamol?

☐ Pain ☐ Fever ☐ Other: ----------

2. Do you use paracetamol as first line of treatment:

Yes No

3. What is the dose that you give to the child:

---

4. How often do you give the child paracetamol:

4 hours 6 hours 8 hours

5. Do you look at the package insert of the product before giving the paracetamol syrup:

Yes No

6. When last have you looked at the package insert:

Last month last 3 months last 12 months over 12 months ago

7. How do you give the child paracetamol:

☐ Teaspoon ☐ Tablespoon ☐ Medicine measure
☐ Syringe ☐ Other: ----------

8. Do you tell the pharmacist or doctor if you think that the product is not working

No Yes

9. For how long do you use paracetamol before you go to seek the advice of your pharmacist or doctor

☐ 3 - 5 days ☐ 10 days ☐ Other: ----------

[1] Age group in line with paracetamol dosage in preparations for children in South Africa

CONSENT FORM[1]

Protocol Title:

Is paracetamol being prescribed and used at the correct therapeutic dose in the children population in South Africa?

Please tick the appropriate answer.

I confirm that I have read and understood the Information Leaflet dated **Nov 2013 v1** attached, and that I have had ample opportunity to ask questions all of which have been satisfactorily answered. ☐**Yes** ☐**No**

I understand that my participation in this study is entirely **voluntary** and that I may withdraw at any time, without giving reason, and without this decision affecting my future participation in further research. ☐**Yes** ☐**No**

I understand that my identity (or that of my child/ren) will remain confidential at all times. ☐**Yes** ☐**No**

I have been given a copy of the Information Leaflet and a copy of a Consent form for my records. ☐**Yes** ☐**No**

FUTURE USE OF ANONYMOUS DATA:

I agree that I will not restrict the use to which the results of this study may be applied. I give my approval that unidentifiable data concerning my person (or of my child/ren) may be stored or electronically processed for the purpose of scientific research and may be used in related or other studies in the future. (This would be subject to approval by an independent body, which safeguards the welfare and rights of people in biomedical research studies) ☐**Yes** ☐**No**

Participant :_____ _____

Signature Name in block capitals

[1] To be completed by all participants; healthcare professional and parent/caregiver

Date _____

To be completed by the Investigator (in the presence of the participant).

I the undersigned, have taken the time to fully explain to the above participant the nature and purpose of this study in a manner that he/she could understand. I have explained the risks involved, the reason for research, as well as the possible benefits and have invited him/here to ask questions on any aspect of the survey that concerns them.

_____	_Aadila Patel_____	_BPharm____	_____
Signature:	**Name in Block Capitals:**	**Qualification:**	**Date:**

_____

Site name

2 copies to be completed: 1 for patient and 1 for Principal investigator.

Participant Information Leaflet

Protocol Title:

Is paracetamol being prescribed and used at the correct therapeutic dose in the children population in South Africa?

Principal Investigator's Name: **__Aadila Patel_____**

Principal Investigator's Title: **__Pharmacist_____**

Telephone No. of Principal Investigator: **_0217013594_____**

You are being invited to take part in a clinical research study carried out at [*to be completed at site*].

Before you decide whether or not you wish to take part, you should read the information provided below carefully and if you wish to discuss it with your family, friends or pharmacist.
Take time to ask questions – do not feel rushed or under any obligation to make a hasty judgement.
You should clearly understand the risks and benefits of participating in this study so that you can make a decision that is right for you and your child/ren – this process is known as **Informed Consent** as per international research requirements.

You are not obliged to take part in this study and failure to participate will have no effect on your future care.

You may change your mind at any time (before the start of the study or even after you have commenced the study) for whatever reason without having to justify your decision and without any negative impact on the care you will continue to receive from your pharmacist or the pharmacy staff.

WHY IS THIS STUDY BEING DONE?
This study is being done because I am conducting research to determine if paracetamol preparations are used correctly in children as reflected on the scientific package insert.

WHO IS ORGANISING AND FUNDING THIS STUDY?
Aadila Patel is the name of the person that is conducting this study in the form of a survey.
Aadila is doing her research for the purposes of attaining a masters degree through the University of Western Cape.

This research is not being funded and is being conducted solely for attaining a master qualification.

There will be no remuneration to you for participating in this study.

HOW WILL IT BE CARRIED OUT?

The survey commences in December 2013 and will be completed by the end of February 2014.

The survey will be done by collecting responses from 5 pharmacists and 10 caregivers. The survey will be conducted at various sites in Cape Town.

The selection of participants will be dependent on their willingness to assist in the survey in response to specific set of questions and informed consent.

WHAT WILL HAPPEN TO ME IF I AGREE TO TAKE PART?
There is no financial compensation to you for taking part in the survey.
Your input is required to clarify how and when you give your child/ren a paracetamol preparation.
In the case of a pharmacist, the input will be to determine how and when they prescribe paracetamol preparations for a child/ren.

It is anticipated that your participation in the research will be 10 minutes. You will be required to read this information leaflet, complete the informed consent form and completing the survey.

BENEFITS:
There will be no personal benefit to you in participating in this research. The benefit is determining if South Africa is in line with international requirements and practices for the use of paracetamol preparations in children.

RISKS:
There is no risk to you or your child/ren as this survey is being done to gather information on the use of the paracetamol product that has been purchased/dispensed.

WHAT IF SOMETHING GOES WRONG AS A RESULT OF MY PARTICIPATION IN THIS STUDY?
There is no chance that anything will go wrong with your participation in this study as the data will be analysed to determine how paracetamol preparations is being used.

YOUR RESPONSIBILITIES AS A PARTICIPANT
Your participation requires that you be honest and do not provide answers that you think are correct or answers that you think I should be told.
Provide your consent in the use of the data that is gathered from the survey.

MY RESPONSIBILITIES TO YOU AS AN INVESTIGATOR
I will treat you with respect and dignity. To treat all your response in confidence.

CONFIDENTIALITY ISSUES

I will be keeping the data for a period 5 years. 5 years has been chosen to be in line with the time that the South African receiver of revenue requires for the retention of papers or documentation.

At the end of the 5-year period, the paper copies will be destroyed by means of shredding and the electronic copies will be deleted from the hard drives and other backups copies that are made.

Please be aware that the data may be used in future research.
Do you consent to this? Yes/No

IF YOU REQUIRE FURTHER INFORMATION

If you have any further questions about the study, or if you wish to withdraw from the study you may do so without justifying your decision and your future treatment will not be effected.

For additional information now or any future time, please contact:
Name: Aadila Patel Phone No: 0217013594

PROCESS TO DETERMINE VOLUME: MEDICAL DEVICE

1. Images were captured of the various devices in their initial wrapping as purchased from the
2. Images were then captured with the medical device being visible next to its packaging, where relevant
3. Decision made to use Medi-Rite medicine measure as base measuring device
4. Images of product in each device has been captured

Actual process

5 ml

1. Emptied product into the Medi-Rite unit up to the 5 ml/1 tsp mark
2. Transferred contents into medicine measure
3. When dropper and syringe used, the contents were emptied into the Medi-Rite medicine measure
4. Unless you are trained to use a syringe, there is no instruction to the positioning of the black plunger. For this exercise plunger at bottom tip was used

10 ml

1. Same as 5 ml
2. Investigated devices that could deliver 10 ml in single administration

2,5 ml

1. Same as per 5 ml
2. Investigated devices that could measure 2,5 ml

7,5 ml

1. Same process as 5 ml
2. Investigated devices that could deliver 7,5 ml in a single administration

Tablespoon

1. Contents of 10 ml where emptied from Medi-rite spoon into tablespoon
2. Content remaining was determined.
3. If necessary add product in 5 ml increments until table spoon is full.

Dosage: Init. 1 tab 6 hrly. Inadeq.relief./sev. intractible pain incr.subseq.by ½ tab increm. Max. 3 tabs.
Contra-indications: *Resp.depress., asthma, head inj., rais. IC-press., MAOI's, ulc.colit., sev.hepat./ ren. impairm., labour, lactat., bil./ren.spasm.*
Side-effects: *Resp.depress., poss.addict., sedat., GI / CNS effs.*
Special precautions: *Hypotens., resp.insuff., hypothyroid., prostat.hypertrophy, phaeochromocyt.*

3.2. Analgesics and antipyretics

(See also 4.1)

ADCO-MEFENAMIC ACID, (Adco Generics) Al Pharm Ltd [P/S]
Mefenamic acid.
Indications:
(S3) *Mild to mod.pain in ac.& chron.condits. includ. traumat/arthrit.or musc.origin. pain, dysmenorrh., headache , dent.pain, menorrh. & pyrex.*
(S2) *Post-traum.condits.e.g.pain, swell., inflamm. for max. per.of 5 days.*
(S3) & (S2) SUSP, [P/S] 28/2.7/0220. 50 mg/5 ml.
875643-019: 100 ml, R9,37
875643-027: 200 ml, R18,73
Dosage: Admin.with meals. for max.7 days. Childr. 6 mnths-1 yr: 5 ml. 3xdly. 2-4 yrs: 10 ml 3xdly. 5-8 yrs: 10 ml. 4xdly. 9-12 yrs: 15 ml 4xdly.
(S3) & (S2) CAPS, [P/S] 28/2.7/0019
883102-004: 250 mg, 18, R10,19
883102-012: 250 mg, 250, R141,47
Dosage: Admin.3xdly.with food for max.7days. Adults: 1-2 caps.
Contra-indications: *NSAID cross-sens., pept. ulc., GI bleed.hist., inflammat.bowel dis., safety in pregn.& lactat. not est., epilept., imp. hepat.funct.*
Side-effects: *GI disturbs.incl.bleed., drowsin., dizz., nervousn., vis.disturbs., bld.dyscras., allerg. glomerulonephrit., ac.allerg.reacts., abnorm.ren./ liv.funct., bronchoconstrict.in asthmat.pts.with aspir.sens., platel.funct.aff.*
Special precautions: *Poss.enhanc.eff.of anticoags., discont.if diarrh./skin rash occurs, monit.ren./liv.funct.dur. prolong.ther., asthma, excl.uterine & other pathology bef. prescrib.for menorrh.*

ADCO-PARACETAMOL, Al Pharm Ltd [P/S]
Paracet.
Indications: *Mild to mod.pain & fev.*
(S0) SYRUP. U/2.7/118. 120 mg/5 ml.
894281-003: 100 ml, R6,73
Dosage: Admin.3-4xdly.as reqd. Max. 4 dos.dly. Infts.3-12 mnths: 2,5-5 ml. Childr. 1-5 yrs: 5–10 ml. 6-12 yrs: 10-20 ml.
Contra-indications: *Sev.liv.funct.impairm.*
Side-effects: *Pancreatit., skin/allerg.reacts., bld.disords.*
Special precautions: *Liv./kidn.dis.*

ADVIL, (Wyeth) Pfizer Consum. [P/S]
Ibuprofen.
Indications: *Mild to mod.pain, e.g. min.musc. aches & strains, headache., menstr./dent.pain, pain assoc.wth migraine.*
(S2) LIQUI-GELS CAPS, 34/2.7/0193
892302-005: 200 mg, 20, R31,81.
Dosage: Admin.with food.
Adults & childr.over 12 yrs: 1-2 caps.4-6 hrly. Max.6 caps/24 hrs.
Contra-indications: *Pept.ulcerat./hist., bld. disords., CV dis., aspir.& NSAID sens., pregn., childr.und.12 yrs.*
Side-effects: *GI disturbs.incl.bleed., CNS effs., hypersens.reacts.incl.Steven.-Johnson/ tox. epiderm. necrolys./ hepatotoxic.& asept.meningit., vis.disturbs., bronchosp.in asthmat., cystit., haematur., ac.ren.fail., interstit.nephrit., nephrot. syndr., fluid retent., bld.dyscras., revers.inhibit.of platelet aggregat., photosens., alveolit., pulmon. eosinophil., pancreatit., colit.induct./exacerbat., abnorm.liv.funct.test.*
Special precautions: *Asthma/bronchosp./bleed. disords./ CV dis./pept.ulcerat.hist., anticoag. ther., discont.if vis. disturbs.exper., collag.dis., HF poss. precipitat.in comprom. pts., may mask sympts.of infect., imp.ren./hepat./CV funct., elderly, concom. prot.bound meds., hypertens..*
Drug interactions: *Effs.of oral anticoags. enhanc., Li/ methotrex./& card.glycoside plasma conc.incr., incr. nephrotox.risk with ACE-inhibit./ cyclospor/tacrolim.& diuret., hyperkalaem.risk incr. with ACE-inhib.& K+-spar. diuret, anti-hypertens. effs.of some anti-hypertens. agents poss.reduc., poss. convuls. with quinolones, effs.of phenytoin & sulphonylurea anti-diabet.enhanc., NSAID assoc. GI bleed.risk incr.with corticoster./alcoh/ bisphosphonate/oxpentifylline, SSRI's, antiplatelet. clopidogrel & ticlopidine incr. haemotox. with zidovudine.*

ANTALGIC, CAPS [P/S]
Paracet.
Indications: *Fever, mild to mod.pain.*
SF SYRUP, [P/S] X/2.8/64. 120 mg/5 ml.
798983-019: 100 ml, R3,86
Dosage: Dos.may be repeat. 4 hrly.up to 4x/day. Infts. 3-12 mnths: 2,5 ml. Childr. 1-6 yrs: 5 ml. 7-12 yrs: 5-10 ml.
500 T TABS, [P/S] 27/2.8/0022.
805467-009: 500 mg, 1 000, R65,19
805467-017: 500 mg, 5 000, R325,31
Dosage: Adults: 1-2 tabs 4-6 hrly. Max. 8 tabs/ 24 hrs. Childr.6-12 yrs: ½-1 tab 4-6 hrly. Max 4 tabs/24 hrs. Childr.und.6 yrs: Not recomm.
Side-effects: *Revers.skin rash, bld.disords.*
Special precautions: *Liver/kidn.dis.*

AUSTELL-PARACETAMOL, Austell [P/S]
Paracet.
Indications: *Mild to mod.pain & fever.*
(S0) TABS. 28/2.8/0406
713153-001: 500 mg, 10, R4,29.
713153-002: 500 mg, 20, R8,57
Dosage: Do not exceed recomm.dos. Adults: 1-2 tabs 4-6 hrly. Max.8 tabs./24 hrs. Childr 6-12 yrs: ½-1 tab 4-6 hrly. Max.4 dos./24 hrs.
Contra-indications: *Sev.liv.impairm., safety in pregn. & lactat.not est.*
Side-effects: *Bld dyscras., ren.colic./-fail., hepatit., hypersens.reacts.incl.revers.skin rash.*
Special precautions: *Imp.kidn./liv.funct., exceed. recomm.dos.may cause sev.liv.damage, contact near.med. facility immed.in event of suspect. overdos., alcoh.incr.liv. toxic.risk esp.in alcohol.with high dos.& prolong.use.*
Drug interactions: *Concom.potent.hepatotox. drugs/ drugs induc.liv.microsom.enzyme poss.incr. toxic.risk, metoclopramide accelert.absorpt., cholestyramine reduc. absorpt.if given within 1 hr., probenecid may affect.excret.*

BE-TABS ASPIRIN, Be-Tabs [P/S]
Aspirin
Indications: *Mild to mod.pain, febr.condits.*
(S0) TABS. E/2.7/104
798533-005: 300 mg, 100, R21,83
798533-013: 300 mg, 1000, R74,95
798533-021: 300 mg, 5 000, R358,88
Dosage: Adults: 1-2 tabs 4 hrly. max.10 days. Childr.3-4 yrs: ¼-½ tab.4 hrly. 5-7 yrs: ½-¾ tab.4 hrly. 7-12 yrs: ¾-1 tab.4 hrly.
Contra-indications: *Pregn., pept.ulc., haemophil., sev. ren.impairm., oral anticoag.ther.*
Side-effects: *Dizz., gastr.mucosa irrit.& bleed. incl. malaena, bld.dyscras., pept.ulc.& ren.papill. necros.with prolong./high dos.use.*
Special precautions: *Reye's syndr., asthmat. notable sensit., imp.ren.funct., dyspeps., anaem., dehydrat.*
Drug interactions: *Enhanc.eff.of coumarin anti-coag., oral antidiabet.& sulphonam., diminish.eff. of antigout preps., barbit.& other sedat.may enhanc.toxic.& mask resp.sympt.of aspir.OD.*

BEDORAL, Be-Tabs [P/S]
Ketorolac tromethamine.
Indications: *Short-term mod.post-op pain relief*
(S4) INJ, A40/2.7/0147
709803-001: 30 mg/ml, 10x1 ml amps., R147,59
Dosage: IV/IM use. Admin.should not exceed. 2 days with max.IV infus.durat.not exceed. 24 hrs. Admin.low.eff. dos. Concom.opiate analges.for furth. pain relief if requir. Ensure adeq.fluid & electrol. bal.bef.IV infus. Admin.bolus dos.over min. 15 secs.
Sngl.dos.treatm: IM admin: Admin.slow./deep IM. Pts.<65 yrs: One dos.of 10-60 mg.accord.to sev.of pain. Pts.≥65 yrs/mild ren. impairm: One dos. of 10-30 mg. IV admin: Pts.<65 yrs: One dos. of 10-30 mg. Pts.≥65 yrs/ mild ren. impairm: One dos.of 10-15 mg.
Multiple-dos.treatm: (IV or IM). Dos.adjustm. accord.to sever.of pain & pt.respons. Max. combin. durat.of multip. bolus IM/IV dos.not to exceed 2 days.
Pts.<65 yrs: Max.dly.dos.not.exceed.90 mg. IM dos: Init.10-30 mg follow.by 10-30 mg 4-6 hrly.as reqd.upto max.dly.dos. IV dos: IV bolus: Init.10-30 mg follow.by 10-30 mg 6 hrly.as reqd.up to max. dly.dos.
Contin.IV infus: Init: 30 mg follow.by contin. infus. at rate of up to 5 mg/hr for up to 24 hrs.up to max. dly.dos.
Pts.≥65 yrs/ren. impairm: Max.dly.dos.not to exceed 60 mg. IM dos: 10-15 mg 4-6 hrly.as reqd. up to max.dly dos. IV dos: IV bolus: 10-15 mg 6 hrly.as reqd.up to max. dly. dos. Contin.IV infus.not recomm.in this age group.
Contra-indications: *NSAID cross sens., hist./ act. pept.ulc./GI bleed., haemorrhag.diathes.incl. coagulat. disords,, full anticoag.ther.incl. prophylact. low dos. heparin, susp./confirm. cerebrovasc. bleed., ops.with high risk of haemorrh./ incompl.haemostas., mod.to sev.ren. impairm., pts.at risk of ren.fail.due to vol.deplet. /dehydrat., pregn.& lactat., safety & effic.in childr. und.16 yrs.not est., prophylact.analges. bef.surg., intra-op.use, neuraxial admin., concom. oxpentifylline/other NSAIDs. chron.painf.condits.*
Side-effects: *Hypersens.reacts.incl.anaphylax., GI/ CNS/ CV effs., dos.depend.GI bleed./perforat. esp.in elderly & debilit., pancreatit., sweat., convuls., thirst, hyperkines., asept.meningit., psychot.reacts., paraesthes., vertigo, myalg., incr. urin.freq., oligur., ac.ren.fail., haemolyt. uraem. syndr., flank pain, interstit.nephrit., hyponatraem., hyperkalaem., urin.retent., nephrot. syndr., hyper-/ hypotens., hepatit., cholestat. jaund., liv.fail., dyspn., asthma, pulm. oed., skin reacts.incl.Lyell's & Stevens-Johnson syndr., purpura, thrombocytopen., post-op wound haemorrh., epistax., haematoma, incr.bleed.time, abnorm. vis., hear.loss, tinnit., oed., weight gain, inj.site reacts., fev., asthen., inhib.platel. aggregat., fluid retent.*
Special precautions: *Angioed.hist., asthma, compl./ part.syndr.of nasal polyps, bronchosp., concom. methotrexate., imp.ren.funct., HF, liv. dysfunct., concom. diuret., kidn.dis.hist., poss. incr.uter.haemorrh.risk dur. labour/deliv., hypovolaem. correct.bef.admin., precipit.will occur if mix. in small vol.with morphine sulph./ pethidine/ promethazine/hydroxyzine HCl, elderly, coagulat.disords., ops.where strict haemostas.is critic.eg.cosmet./day case surg., card. decompensat., hypertens.*
Drug interactions: *Addit.S/E with other NSAIDs, oxpentifylline incr.bleed.tendenc, poss. reduc.methotrex. clear., incr.Li plasma conc., plasma conc.incr.with salicylate, poss.incr. ren.impairm.with ACE-inhibit.partic. vol.deplet. pts., reduc.diuret.respons. to furosemide.*

BETAGESIC, Al Pharm Ltd [P/S]
Ibuprofen.
Indications: *Pain, musc.-skelet.pain, fever.*
(S2) TABS. U/2.7/20.
708186-009: 200 mg, 20, R18,58
Dosage: Adults & childr.over 12 yrs: Init.2 tabs then 1-2 tabs 4 hrly if necess. Max 6 tabs/24 hrs.
Contra-indications: *Pregn., bleed.disords., CV dis., pept. ulcerat./hist.thereof, aspir.sens., childr. und.12 yrs.*
Side-effects: *Dyspeps., GI intol.& bleed., nervousn., skin rash, prurit., tinnit., oed., depress., drowsin., insomn., vis. disturbs., hypersens. reacts., bld.dyscras, ren.fail.*
Special precautions: *Coumarin anticoag., revers. ren. funct.impairm.*

CALPOL, GSK [P/S]
Paracet.
Indications: *Mild to mod.pain & fev., headache, sore throat, toothache, teeth.pains, fev.assoc.with colds & flu.*
PAED.SYRUP. B/2.7/767. 120 mg/5 ml.
711993-009: 100 ml, R27,68
Dosage: Admin. 3-4xdly.at 4 hrly.interv. 3 mnths-1 yr: 2,5 ml. 1-2 yrs: 5 ml. 3-6 yrs: 10 ml. Infts. und.3 mnths: Not recomm.
Side-effects: *Revers.skin rash/bld.dyscras., papill.necros.*
Special precautions: *Hepat./ren.dysfunct.*

Drug interferences with laboratory tests and physical incompatibilities common with parenteral solutions have not been included.

DISPRIN, Reckitt Benckiser [P/S]
Aspirin.
Indications: *Mild to mod.pain, fever.*
(S0) REGULAR STRENGTH TABS, [P/S] B/2.7/570.
720577-004: 300 mg, 12, R10,99
720577-012: 300 mg, 24, R19,99
720577-020: 300 mg, 48, R33,99
720577-039: 300 mg, 96, R59,99
Dosage: **Adults:** 1-3 tabs 4 hrly if necess. Max. 12 tabs/24 hrs. **Childr:** 2-4 yrs: ½ tab.max 4xdly. 4-6 yrs: ½-1 tab.max 4xdly. Over 12 yrs 1-2 tabs. Max. 4xdly. Max 10 tabs/24 hrs.
(S0) EXTRA STRENGTH TABS, [P/S] M/2.7/292.
847283-004: 500 mg, 16, R19,99
720585-015: 500 mg, 24, R29,99
720585-023: 500 mg, 48, R49,99
Dosage: Adults: 1-2 tabs 4 hrly.if necess. Max. 8 tabs/24 hrs. Childr.over 12 yrs: 1 tab 4 hrly if necess.
(S0) MELTS, [P/S], R/2.8/99
807206-008: 300 mg, 32, R38,99
Dosage: Adults: 1-3 tabs 4 hrly if necess. Max. 12 tabs./24 hrs. **Childr over 12 yrs:** 1-2 tabs max.4xdly. Max 10 tabs./24 hrs.
Contra-indications: *Pept.ulc., haemophil., sev. ren. impairm., oral anticoag., 1st & 3rd trimest. pregn. & lactat.*
Side-effects: *Dizz., GI-irrit., result.dyspeps., erosion, ulcerat., haematemes., melaena, skin erupt., urticar., angioed., paroxysm.bronchosp.& dyspn., bld.dyscras.with prolong.high dos.*
Special precautions: *Incr.risk of gastr.irrit.with other gastr.irritants eg NSAID's, withdr.1 wk.bef. surg.because of poss.incr.bleed.time, asthma, imp. ren.funct., dyspeps., anaem., dehydrat.*
Drug interactions: *Enhanc.act.of coumarin anticoag. / methotrex./oral antidiabet.& sulphonam., dimin.eff.of anti-gout preps., barbit.& other sedat.enhanc.aspir.toxicity & poss mask resp. sympt.*
Warnings: *Reye's syndr.*

ECOTRIN, Pharmafrica [P/S]
Aspirin.
Indications: *Pain & fev.*
(S0) EC TABS, 29/2.7/0767
823481-018: 81 mg, 50, R32,46
823481-026: 81 mg, 100, R60,04
Dosage: 4-8 tabs.every 4 hrs.if need.not exceed. 48 tabs./24hrs.
Contra-indications: *Haemorrhag.disords., gout, aspirin sens.asthmat., sev.ren.impairm., oral anticoag., 1st & 3rd trimest.pregn., lactat.*
Side-effects: *Dizz., GI-irrit./disturbs., skin erupt., angio-oed., rhinit., paroxysm.bronchosp.& dyspn., incr.bleed.time.*
Special precautions: *Imp.hepat./ren.funct., withdr. 1 wk.bef.surg., asthma, dyspeps., anaem., dehydrat.*
Drug interactions: *Enhanc.act.of coumarin anticoag., sulphonylurea, hypoglycaem.agents, methotrex., phenytoin, valproic acid, dimin.eff.of anti-gout preps.*
Warnings: *Reye's syndr.*

EMPAPED, Nycomed [P/S]
Paracet.
Indications: *Mild to mod.pain & fever when oral therapy not feasible.*
(S2) SUPPS. X/2.7/193, 194.
819697-001: 125 mg 10, R38,26
819700-002: 250 mg, 10, R48,45
Dosage: Admin.up to 4xdly.
Infts. 3-12 mnths: 125 mg. **Childr: 1-5 yrs:** 250 mg.
Contra-indications: *Imp.kidn./liv.funct.*
Side-effects: *Skin rash, other allerg.reacts., bld dyscras.*
Special precautions: *Liv./kidn.dis.*

FENAMIN, (Aspen Pharmacare: Pharma) Pharmacare [P/S]
Mefenamic acid.
Indications (S3): *Mild to mod.pain from rheumat., soft tiss.injur., painf.musc-.skelet. condits., dysmenorrh.*
Indications (S2): *Post-traumat.condits.(eg.pain, swell.& inflamm.) x max 5 days.*
(S2) (S3) SUSP, [P/S] 27/2.7/0283. 50 mg/5 ml.
797014-004: 100 ml, R11,27
(S2) & (S3) CAPS, [P/S] 27/2.7/0281.
797707-026: 250 mg, 250, R144,78
(S2) & (S3) TABS, [P/S] 27/2.7/0282.
797715-010: 500 mg, 100, R153,48
Dosage: Admin.for max. 7 days.
Mild to mod.pain: 500 mg 3xdly.
Ac.pain: **Adults :** Init. 500 mg thereaft. 250 mg 6 hrly. **Childr.** Rep.up to 3xdly. **6 mnths-1 yr:** 5 ml. **2-4 yrs:** 10 ml. **5-8 yrs:** 15 ml. **9-12 yrs:** 20 ml.
Contra-indications: *NSAID cross-sens., GIT ulcerat./ inflamm., epilept., imp.hepat.funct.*
Side-effects: *GI disturbs.incl.haemorrh., CNS eff., vis. disturbs., ac.hypersens.reacts., skin rash, bld.dyscras.*
Special precautions: *Imp.ren./liv.funct., elderly with dehydrat./ pre-exist.ren.dis.*
Drug interactions: *Eff.of coumar.anticoags. enhanc.*

GO-PAIN P, (Glenmark) MDI [P/S]
Paracet.
Indications: *Mild to mod.pain & fev.*
SYRUP, X/2.7/242
895199-009: 120 mg/5 ml, 100 ml, R9,17
Dosage: Admin.6-8 hrly. Max: 4 dos.dly.
Infts.3-12 mnths: 2,5 ml. **Childr: 1-6 yrs:** 5 –10 ml. **7-12 yrs:** 10-20 ml.
Side-effects: *Skin rash, allerg.reacts., bld. dyscras.*
Special precautions: *Liv./kidn.dis.*

IBUCINE, (Goldex) Pharm.Contractors [P/S]
Ibuprofen.
Indications: (S2) When recomm.paed.dos.does not exceed 20 mg/kg
(S3) Inflamm.joint dis.treatm.
Mild to mod.pain & inflammat., fev., musculosket. & joint disord.& soft tiss.disords.
(S2) & (S3) PAED.SUSP, 36/3.1/0436
700315-001: 100 mg/5 ml, 100 ml, R15,71
Dosage: Do not admin.to childr.<7 kg/und.1 yr.
Juvenile rheumat.arthrit: 20 mg/kg dly.in div. dos upto 40 mg/kg/day.
Pain: 5 mg/kg bm.with a second dos.aft.2 hrs.if necess. thereaft.4-6 hrly.
Fev: 5 mg/kg bm.6 hrly.
Childr.1-2 yrs (7-12 kg): 2,5 ml 3-4xdly. **3-7 yrs (14-23 kg):** 2,5-5 ml 3-4xdly. **8-12 yrs (25-40 kg):** 10 ml 3-4xdly.
Contra-indications: *Pept.ulc., pregn.in 3rd trimest., NSAID cross-sens.*
Side-effects: *GI disturbs.incl.bleed./pept.ulc., CNS effs., hypersens.reacts.incl.hepatotox.& asept.meningit., vis. disturbs.incl.tox.amblyop., bld.dyscras., interstit.nephrit., nephrot.syndr., ren.fail., bronchosp. in asthmat.pts., cystit., haematur.*
Special precautions: *Pept.ulcerat.hist., bleed. disords., asthma, aspir./NSAID's sens., hyppertens., imp.ren./ card./hepat.funct., bld./ kidn./liv.or eye disord.developm., elderly, concom. oral anticoags./Li/methotrex.& card. glycosides, incr.risk of asept.meningit.in pts.with collagen dis., discont.in case of blurr./dimin./changes in colour vis.*

MYOPRIN, Desatnik [P/S]
Aspirin.
Indications: *Mild to mod.pain & fev.*
EFFERVESC.TABS. B/2.8/1117.
845590-001: 100 mg, 30. R14,31
Dosage: Adults: 3-6 tabs 4 hrly.as reqd. Max. 40 tabs/24 hrs.
Contra-indications: *Haemorrhag.disords., gout, aspirin sens.asthmat., 1st & 3rd trimest.of pregn., lactat.*
Side-effects: *Dizz., GI disturbs., eros., ulcerat., haematemes., melaena, hypersens.reacts.notably asthmat., hypoprothrombinaem., hepatotox. partic. in juven.arthrit.& other connect.tiss.disords.*
Special precautions: *Imp.ren./hepat.funct., discont.1 wk.bef. sched.surg., Reyes syndr., dyspeps., anaem., dehydrat.*
Drug interactions: *Enhanc.eff.of coumarin anti-coag., dimin.eff.of probenecid.& sulphinpyrazone.*

NAPAMOL, Al Pharm Ltd [P/S]
Paracet.
Indications: *Mild to mod.pain, fev.*
(S0) TABS, [P/S] B/2.7/1404.
745723-136: 500 mg, 5 000, R274,71
(S0) ELIX, [P/S] B/2.7/1409. 120 mg/5 ml.
745715-028: 100 ml, R10,47
Dosage: Adults: 1 -2 tabs 4-6 hrly. Max.8 tabs. dly. Childr: Admin. elixir 3-4xdly.as reqd. Max. 4 dos. dly. **3-12 mnths:** 2,5-5 ml **1-5 yrs:** 5-10 ml **6-12 yrs:** ½-1 tab./10 -20 ml
Contra-indications: *Sev.liv.funct.impairm.*
Side-effects: *Allerg.reacts.incl.skin rash.& pancreatit., bld.dyscras.*
Special precautions: *Liv./kidn.dis.*

NUROFEN, Reckitt Benckiser [P/S]
Ibuprofen.
Indications: *Headache & back pain of musculo-skelet. origin, fever, musc.aches & pain, menstrual & dent.pain, migraine.*
(S1) TABS, [P/S] S/2.7/123.
748560-009: 200 mg, 12, R15,19
748560-017: 200 mg, 24, R30,34
748560-025: 200 mg, 48, R60,63
748560-033: 200 mg, 96, R121,24
Dosage: Childr.und.12 yrs: Not to be given.
Adults & childr.over 12 yrs: Init. 2 tabs, then 1-2 tabs.if necess. 4 hrly. Max. 6 tabs./24 hrs.
Migraine: 2 tabs. 3xdly.
(S1) PERIOD PAIN TABS, [P/S] W/2.7/142
897984-005: 400 mg, 12, R22,09
Dosage: 1 200 mg dly in div.dos. Max: 3 tabs/ 24 hrs. Not for childr.und.12 yrs.
(S2) CHILDR.SUGAR-FREE SUSP, [P/S] 31/2.7/0466
700695-001: 100 mg/5 ml, 100 ml, R28,77
Dosage: Do not admin.to childr.und.3 mnths. Childr: 20 mg/kg bm dly in div.dos. **Childr.und. 5,6 kg/und.3 mnths:** consult physic. Not to exceed 20 mg/kg bm/day. **3-6 mnths. (5,6 -7 kg):** 2,5 ml up to 3xdly. **6-12 mnths (7-10 kg):** 2,5 ml up to 3xdly. **1-2 yrs (7-12 kg):** 2,5 ml up to 3-4xdly. **3-7 yrs (14-23 kg):** 2,5-5 ml up to 3-4xdly. **8-12 yrs (25-40 kg):** 10 ml up to 3-4xdly. For pain a second dos.may be giv.aft.2 hrs.if necess.thereaft.6 hrly.
(S2) CHILD.STRAWBERRY SUSP, A40/2.7/0092
Indications: *Fev./pain & inflammat.assoc.with cold & flu, sore throat, earache, headache, dent. pain, min.aches & sprains.*
712683-001: 100 mg/5 ml, 100 ml, R28,77
Dosage: Do not admin.to childr.<5,6 kg/und.3 mnths.
Pain: Init.dos.5 mg/kg bm.a second dos.may be giv. aft.2 hrs.if necess.thereaft.6 hrly.
Fev: Init.dos.5 mg/kg bm.6 hrly.
Childr: 20 mg/kg bm dly in div.dos. **Childr.und. 5,6 kg/ und.3 mnths:** consult physic. Not to exceed 20 mg/kg bm/ day. **3-6 mnths. (5,6 -7 kg):** 2,5 ml up to 3xdly. **6-12 mnths (7-10 kg):** 2,5 ml up to 3xdly. **1-2 yrs (7-12 kg):** 2,5 ml up to 3-4xdly. **3-7 yrs (14-23 kg):** 2,5-5 ml up to 3-4xdly. **8-12 yrs (25-40 kg):** 10 ml up to 3-4xdly.
Contra-indications: *Pept.ulc./hist., bleed. disords., CV dis., aspir.sens., NSAID cross-sens., GI bleed.of perforat. relat.to NSAID's, act.hist.of recurr. ulc./haemorrh./ perforat., HF, childr.und.3 mnths.(susp), sev.liv.& ren funct. impairm., pregn. in 3rd trimest., uncontr.asthma*
Side-effects: *GI disturbs.incl.bleed./pept.ulc. activat., CNS effs., hypersens.reacts.incl. hepatotox. & asept. meningit., bronchosp.in asthma pts., cystit., haematur., ac. revers.ren.fail., interstit. nephrit., nephrot.syndr., bld. dyscras., vis.disturbs. incl.tox.amblyop., photosens., skin peel., revers. platelet aggregat., fluid retent., alveolit., pulm. eosinophil., pancreatit., ser.skin reacts.incl.Stev. John.syndr.& tox.epiderm.necrolys.*
Special precautions: *Asthma, bronchosp., elderly, bleed. disords., CV dis., CHF, hypertens. hist., pept.ulcerat.hist., GI bleed.risk incr.with incr.NSAID dos.with ulc.hist./elderly, GI dis.hist., liv./ ren.impairm., cirrhos., diuret.-induc.vol. deplet., discont.in case of vis.chang., incr.asept. meningit. risk with collagen dis., poss.masks sympts. of infect., anaem., stomatit.*
Drug interactions: *Concom.coumar.anticoags./ antihypertens./diurets./Li/methotrexate/aspir.& other NSAIDs, incr GI bleed.& ulcerat.risk with concom.alcoh./ corticoster./clopidrogel/ticlopidine/biphosphonates/ pentoxyfylline & SSRI's, hypoglycaem. effs. of antidiabet. meds.& anticoags. effs.poss.incr., incr.ser.digox.conc with digox., incr.nephrotoxic.risk with nephrotox.meds., antihypertens.eff.of antihypertens./diuret.poss. reduc./ revers., effs.of bone marr.depress.incr.*
See Also MDR Page 1563

PAINAMOL, Be-Tabs [P/S]
Paracet.
Indications: *Mild to mod.pain & fev.*
(S0) For packs less than 100 ml of syrup
(S1) For packs over 100 ml of syrup.
SYRUP, [P/S] E/2.7/106. 120 mg/5 ml
752118-021: 50 ml, R4,05
752118-005: 100 ml, R5,36
752118-013: 2,5 L, R75,52
Dosage: Admin. 3-4xdly. Max.4 dos.dly.
Infnts 3 mths.to 1 yr: 2,5 -5 ml. 1-5 yrs: 5-10 ml. 6-12 yrs: 10-20 ml.
TABS, [P/S] E/2.7/105.
(S0) For packs less than 25 tablets
(S1) For packs over 25 tablets.
752142-143: 500 mg 10, R6,27
752142-003: 500 mg, 20, R11,40
752142-011: 500 mg, 100, R9,96
799629-014: 500 mg, 1 000, R99,88
799629-006: 500 mg, 5 000, R499,34
Dosage: Adults: 1-2 tabs 4-6 hrly. Max. 8 tabs/ 24 hrs. Childr. 6-12 yrs: ½-1 tab 6 hrly. Over 12 yrs: 1 tab 4-6 hrly.
Contra-indication: Childr.und.6 yrs.
Side-effects: *Revers.skin rash/bld.disords.*
Special precautions: *Liv./ kidn.dis.*

PANADO, Al Pharm Ltd [P/S]
Paracet.
Indications: *Mild to mod.pain & fever.*
(S0) TABS, [P/S] B/2.8/858.
752274-015: 500 mg, 50, R23,17
752274-066: 500 mg, 12, R7,27
752274-058: 500 mg, 24, R10,85
752274-023: 500 mg, 100, R46,36
Dosage: Admin.3-4 hrly. Not for childr.und.6 yrs.
Adults: 1-2 tabs. Max. 8 tabs/24 hrs. Childr. 6-12 yrs: ½-1 tab. Max. 4 doses/24 hrs.
(S0) MELTABS SUGAR FREE, A39/2.7/0059
708438-001: 500 mg, 12, R14,31
Dosage: Dissolv.in mouth/dispers.in small amnt.water. Do not chew.
Adults: 1-2 tabs.4-6 hrly while sympts persist. Max.8 tabs/24 hrs.
(S0) CAPS, [P/S] S/2.8/57.
752355-007: 500 mg, 20, R13,15
Dosage: Admin. 3-4 hrly.
Adults: 1-2 caps.if reqd. Max.8 caps/24 hrs. Childr. 9-12 yrs: 1 cap.if reqd. Max.4 dos./24 hrs.
(S0) INFT.DROPS, [P/S] V/2.7/209.
788945-009: 60 mg/0,6 ml, 20 ml, R18,35
Dosage: Infts. 3 mnths-1 yr: 0,6-1,2 ml 4 hrly if necess. Max. 4 dos./24 hrs.
(S0) CHILDR.MELTABS, A39/2.7/0060
708432-001: 125 mg, 12, R12,88
Dosage: Dissolv.in mouth/dispers.in small amnt. water. Do not chew.
Childr. 1-5 yrs: 1-2 tabs.4 hrly.while sympts. persist. Max.4 dos./24 hrs.for max.5 days
(S0) PAED.SYRUP SUGAR & ALCOHOL FREE, [P/S] V/2.8/208. 120 mg/5 ml
788953-001: 100 ml, R19,81
(S0) SYRUP, [P/S] B/2.7/1143. 120 mg/5 ml
752282-026: 50 ml, R10,88
752282-018: 100 ml, R19,81
Dosage: Admin. 6-8 hrly with max. 4 dos/24 hrs.
Infts. 3 mnth-1 yr: 2,5-5 ml. Childr. 1-5 yrs: 5-10 ml. 6-12 yrs: 10-20 ml.
(S0) PAED.SYRUP STRAWBERRY, 35/2.7/0112. 120 mg/5 ml.
703118-001: 50 ml, R10,88
703118-002: 100 ml, R19,81
Dosage: Childr.6-12 yrs: 10-20 ml. 1-5 yrs: 5-10 ml. Infts.3 mnths-1 yr: 2,5-5 ml. Repeat dos.4-6 hrly if necess. Max.4 dos./24hrs.
Contra-indications: *Sev.liv.funct.impairm., safety in pregn.& lactat.not est.*
Side-effects: *Bld.dyscras., ren.colic, ren.fail., sterile pyuria, hepatit., pancreatit., dermatit., skin rash, allerg. reacts.*
Special precautions: *Do not exceed recomm. dos., liv.& kidn.dis., alcoh., depend., Meltabs & Childr.Meltabs: Phenylketonurics as contains phenylalanine*
Drug interactions: *Hepatotox.meds.& enzyme induc.meds.incr.hepatotox.risk, therapeut. eff.poss. decr. by enzyme induc.meds., absorpt. accelerat.by metoclopramide, cholestyramine reduc.absorpt.if given within 1 hr., incr.risk of advers.ren.effs.with longterm salicylates.*

PARACET, Be-Tabs [P/S]
Paracet.
Indications: *Mild to mod.pain & fev.assoc.with colds & flu.*
(S1) TABS. 33/2.7/0203
704719-001: 500 mg, 1000, R71,50
Dosage: Not for childr.und.6 yrs.
Childr. 6-12 yrs.: ½ to 1 tab.6 hrly. Childr.over 12 yrs: 1 tab 4-6 hrly. Adults: 1-2 tabs 4-6 hrly.
Contra-indications: *Sev.liv.funct.impairm.*
Side-effects: *Sev.liv.funct.impairm.with excess dos., pancreatit., skin rash, other allerg.reacts., bld.disords.*
Special precautions: *Liv./kidn.dis., not for use long. than 10 days.*

PERFALGAN, BM Squibb [P/S]
Paracetamol
Indication: *Short term treatm.(not exceed.24 hrs.) of mild to mod.pain, & fev.when oral route unsuit.*
(S3) SOL.FOR INFUS, A38/3.2/0561. 1 g/100 ml.
705103-001: 12x100 ml vials, R516,25
Dosage: Admin.as 15 min.infus., Use oral analges. ther. as soon as poss.
Adults & adolesc.weigh.>50 kg: 1 g/admin upto 4x/day. Min.interv.betw.each admin.4 hrs. Max. dly. dos: 4 g. Childr.weigh.>33 kg (approx. 11 yrs) /adults & adolesc.weigh. <50 kg: 15 mg/kg (i.e. 1,5 ml sol./kg) per admin. Admin. interv.betw.each admin.4 hrs. Max.dly. dos: 60 mg/kg without exceed.4 g.
Contra-indications: *Sev.hepatocellul.insuffic., safety & effic.not est.in childr.weigh.less than 33 kg.*
Side-effects: *Malaise, hypersens.incl. anaphylax., hypotens., thrombocytopen., bld. dyscras., ren.colic/fail., hepatit., pancreatit., dermatit.*
Special precautions: *Ensure no concom.meds. contain paracet.to minim.OD risk., exceed. recomm. dos.may cause sev.liv.damage, hepatocellul. insuffic., chron.alcohol./ malnutrit., recov. from liv.dis., ren.dis., concom.enzyme-induc. subst., assess.risk vs.benef.in pregn.as exper.of IV admin.limit., dehydrat.*
Drug interactions: *Probenec.reduc.clear., salicylam. prolong eliminat.half-life.*
See Also MDR Page 592

PERFALGAN PAEDIATRIC, BM Squibb [P/S]
Paracetamol
Indications: *Short term treatm.(not exceed.24 hrs.) of mild to mod.pain & fev.when IV route justif.& when other admin.routes not poss.in childr. 1 yr & old.*
(S3) SOL.FOR INFUS, A40/3.2/0053. 10 mg/ml.
709807-001: 500 mg, 12x50 ml vials, R359,10
Dosage: Use oral analges.ther.as soon as poss. Do not exceed recomm.dos. Admin.as 15 min. infus. Sngl.use only. Do not mix.with other meds.
Childr.1 yr & old.up to 33 kg (approx.11 yrs): 15 mg/kg/admin (ie.1,5 ml sol./kg) upto 4x/day. Min.interv.betw.each admin.4 hrs. Max.dly.dos: 60 mg/kg.
Contra-indications: *Sev.hepatocellul.insuffic., childr. und.1 yr., safety in pregn.& lactat.not demonstrat.*
Side-effects: *Malaise, hypersens.incl. anaphylax., hypotens., thrombocytopen., bld. dyscras.*
Special precautions: *Ensure no concom.meds. contain paracet.to minim.OD risk., exceed. recomm. dos.may cause sev.liv.damage, hepatocellul. insuffic., chron.alcohol./ malnutrit., recov. from liv.dis., sev.ren.insuffic., ren.dis., concom.enzyme-induc.subst., dehydrat.*
Drug interactions: *Probenec.reduc.clear., salicylam. prolong eliminat.half-life.*
See Also MDR Page 596

PONAC, (Aspen Pharmacare: Consum) Pharmacare [P/S]
Mefenamic acid.
Indications (S3): *Mild to mod.pain from rheumat.condits., soft tiss.injur., dysmenorrh.& other painf.musculoskelet.condits.*
Indications (S2): *Post traumat.condits.such as pain, swell., & inflammat.for max.5 days.*
(S2) & (S3) SUSP, [P/S] Y/2.7/192. 50 mg/5 ml.
793264-006: 100 ml, R10,55
793264-014: 200 ml, R21,10
(S2) & (S3) FORTE TABS, [P/S] Y/2.7/158.
794201-008: 500 mg, 50, R80,94
(S2) & (S3) CAPS, [P/S] Y/2.7/157.
796433-003: 250 mg, 100, R59,82
Dosage: Admin.with meals for max.x7 days.
Adults **Mild to mod.pain**: 500 mg 3xdly.
Ac.pain: Init. 500 mg, thereaft. 250 mg 6 hrly. Childr: 25 mg/kg/bm.dly.in div.dos. May be rep. 3xdly. 6 mnths.-1 yr. 5 ml. 2-4 yrs: 10 ml. 5-8 yrs: 15 ml. 9-12 yrs: 20 ml.
Contra-indications: *Sens.to other NSAID's with prostaglandin synthetase inhibit.activ., GI ulcerat. / inflamm., epilep., imp.hepat.funct., safety in pregn.& lactat.not est.*
Side-effects: *GI disturb.& bleed., pept.ulcerat., headache, drowsin., dizz., nervousn., vis.disturb., hypersens./ haematol.reacts., asthma, skin rash.*
Special precautions: *Imp.hepat./ren.funct., poss.NSAID cross-sens., avoid in elderly with dehydrat., pre-exist.ren.dis.*
Drug interactions: *May enhanc.coumarin anti-coag.eff.*

PONSTAN, (Pharmacia) Pfizer [P/S]
Mefenamic acid.
Indications (S3): *Mild to mod.pain in ac.& chron. condits., incl.pain of traumat./arthrit.or musc. origin, prim. dysmenorrh., headache, dent.pain, menorrhag.when due to ovulat.dysfunct.bleed., anti-pyret.in febrile condits.*
Indications (S2): *Post-traumat.condits.for a max. 5 days., prim.dysmenorrh.x max.3 days.*
(S2) & (S3) CAPS, [P/S] B/2.7/560.
756148-112: 250 mg, 20, R18,30
Dosage: GI irrit.reduc.if admin.with meals. Max. durat: 7 days.
Adults: 500 mg 3x/day.
Menorrhag: 500 mg 3x/day with onset of menstr. flow x5 days or until cessat.of flow whichever is less.
Prim.dysmenorrh: 500 mg 3x/day commenc.at onset contin.for max. 3 days while sympts.persist
(S2) & (S3) FORTE TABS, [P/S] H/2.7/13.
756164-001: 500 mg, 50, R86,91
Dosage: Adults: 500 mg 3xdly.
(S2) & (S3) SUSP, [P/S] B/2.7/561. 50 mg/5 ml.
756156-009: 100 ml, R12,31
756156-017: 200 ml, R24,64
Dosage: Admin.as necess.upto 3xdly.
6 mnths-1 yr: 5 ml. 2-4 yrs: 10 ml. 5-8 yrs: 15 ml. 9-12 yrs: 20 ml
(S3) PAED.SUPPS, [P/S] 27/2.7/0561.
Indications: *Pain & fev.in childr.6 mnths-2 yrs. when oral ther.not poss.*
807435-007: 125 mg, 5, R42,17
Dosage: Use for long.than 24 hrs not recomm.
Childr.6 mnths-2 yrs.weigh.not less than 10 kg: 1 supp. rect. 3x/day at 6-8 hr.interv.
Contra-indications: *Pept.ulc./intest.ulcerat., imp. ren./hepat.funct., other NSAIDs sensitiv., drug induc. bronchosp./allerg.rhinit./urticar., chron.GIT inflammat., epilep., concom.anticoag.ther.unless contin.prothrombin.& fact.VII/IX & X monit.avail., safety in pregn.& lactat. not est.*
Side-effects: *GI disturbs., hepatit., pancreatit., pept. ulcerat.with/without GI haemorrh., haemolyt. anaem., bld. dyscras., anaphylax., gluc.intol.in diab., hyponatrem., CNS effs., vis.disturbs., convuls., ear pain, palpitat., hypotens., asthma, bronchosp., dyspn., fac.oed., angioed., laryng. oed., skin & subcutan.tiss.disords.incl Stev.-Johns.syndr. / Lyell's syndr./erythema multiforme., ren.& urin. disords., nephrot.syndr.*
Special precautions: *Poss.NSAID cross-sens., discont.if diarrh/skin rash exper., monit.bld.counts. & liv.funct. with prolong.ther., GI bleed.poss. without warn.signs, dehydrat., ren.dis., elderly, asthma, pre-ren.condits.lead.to reduct.in ren.bld. flow/vol., excl.uter./other pathology bef.prescrib. for menorrh., ther.not to exceed 7 days*
Drug interactions: *Anticoags effs.enhanc., poss. Li toxic.*

PONSTEL, Al Pharm Ltd [P/S]
Mefenamic acid.
Indications (S3): *Mild to mod.pain in ac.& chron. condits. include.traumat., arthrit.or muscul. origin. pain, dysmenorrh., menorrh.& pyrex.*

Indications (S2): *Post traumat.condits.for max.of 5 days.*
(S2) & (S3) SUSP, [P/S] 28/2.7/0704. 50 mg/5 ml.
810398-001: 100 ml, R12,22
810398-028: 200 ml, R24,44
Dosage: Admin.3xdly.with meals. Not to be cont.for long. than 7 days.
Childr.6 mnths & old: 25 mg/kg bm dly in div.dos or **6 mnths-1 yr:** 5 ml. **2-4 yrs:** 10 ml. **5-8 yrs:** 15 ml. **9-12 yrs:** 20 ml. May be repeat.as necess. up to 3xdly.
(S2) & (S3) CAPS, [P/S] 28/2.7/0703.
812250-001: 250 mg, 20, R18,16
812250-036: 250 mg, 250, R227,01
(S2) & (S3) FORTE TABS, [P/S] 28/2.7/0548.
810371-006: 500 mg, 50, R86,20
Dosage: Adults: 500 mg 3xdly.with meals.
Menorrh: 500 mg 3x/day with onset of menstr. flow x 5 days or unt.flow cessat.whichev.is less.
Prim.dysmenorrh: 500 mg 3x/day commenc.at pain onset contin.for max.3 days while sympt. persist.
Contra-indications: *NSAID cross-sens., inflammat. bowel dis., pept.ulc./ intest.ulcerat. hist., imp.ren./hepat. funct., epilept., safety in pregn.& lactat.not est.*
Side-effects: *GI disturbs.incl. bleed./ulcerat./ cholestat. jaund./ hepatit., CNS effs., convuls., vis. disturbs., ear pain, hypotens., asthma, palpits., dyspn., haemolyt. anaem., bld.dyscras. incl. bone marr.aplas., ac.hypersens. reacts., oed. esp.laryng., Stevens-Johnson syndr., Lyell's syndr., perspirat., exfoll.dermatit., ren.fail., allerg. glomerulonephrit., papill.haematur., dysur., hyponatraem., ac.interstit.nephrit., nephrot.syndr.*
Special precautions: *Excl.uter./other pathology bef. prescrib.for menorrh., discont.in case of diarrh./ skin rash, regul.bld.counts /LFT advis.dur. longt. ther., elderly & debilit., gluc.intol.in diab., dehydrat., ren.dis., asthmat.pts. with aspir.sens., HF, liv.dysfunct., concom.diurets/Li.*
Drug interactions: *Anticoag.prolong.prothromb. time, poss.toxic.with Li.*

PROLIEF, AI Pharm Ltd [P/S]
Paracet.
Indications: *Mild to mod.pain, fev.*
(S0) TABS. B/2.7/1259.
757403-107: 500 mg, 5 000, R288,61
757403-113: 500 mg, 20 000, R1 154,44
Dosage: Admin 4 hrly when necess.
Adults: 1-2 tabs. Max. 8 tabs/24 hrs. **Childr. 6-12 yrs:** ½-1 tab. Max. 4 tabs/24 hrs.
Contra-indications: *Sev.liv.funct.impairm., childr. und.6 yrs.not recomm.*
Side-effects: *Revers.skin rash/bld.disords.*
Special precautions: *Liv./kidn.dis.*

RAYZON, Pfizer
See Section 4.1.3.

TORA-DOL, (Akacia) Roche [P/S]
Ketorolac tromethamine.
Indications: *Short-term mod.post-op pain relief*
(S4) INJ, [P/S] 28/2.7/0570, 0571
819344-028: 10 mg/ml, 5x1 ml amps., R85,77
819352-012: 30 mg/ml, 5x1 ml amps, R145,97
Dosage: IV/IM use. Admin.should not exceed. 2 days with max.IV infus.durat.not exceed. 24 hrs. Admin.low. eff. dos. Concom.opiate analges.for furth. pain relief if requir. Dly.morphine dos. equir. is less than norm.requir.follow. major surg if used in assoc.with Tora-Dol. Ensure adeq. fluid & electrol. bal.bef.IV infus. Admin.bolus dos.over min. 15 secs.
Sngl.dos.treatm: IM admin: Admin.slow./deep IM. Pts.<65 yrs: One dos.of 10-60 mg.accord.to sev.of pain. **Pts.≥65 yrs/mild ren.impairm:** One dos. of 10-30 mg. IV admin: **Pts.<65 yrs:** One dos. of 10-30 mg. **Pts.≥65 yrs/ mild ren. impairm:** One dos.of 10-15 mg.
Multiple-dos.treatm: (IV or IM). Dos.adjustm. accord.to sever.of pain & pt.respons. Max. combin. durat.of multip. bolus IM/IV dos.not to exceed 2 days. **Pts.<65 yrs:** Max. dly.dos.not. exceed.90 mg. IM dos: Init.10-30 mg follow. by 10-30 mg 4-6 hrly.as reqd.upto max.dly.dos. IV dos: IV bolus: Init.10-30 mg follow.by 10-30 mg 6 hrly.as reqd. up to max.dly.dos. Contin.IV infus: Init: 30 mg follow.by contin.infus.at rate of up to 5 mg/hr for up to 24 hrs.up to max.dly.dos. **Pts.≥65 yrs/ren.impairm:** Max.dly.dos.not to exceed 60 mg. IM dos: 10-15 mg 4-6 hrly.as reqd. up to max.dly dos. **IV dos:** IV bolus: 10-15 mg 6 hrly. as reqd. up to max. dly.dos. Contin.IV infus. not recomm.in this age group as limit.exper.
(S4) TABS, [P/S] 28/2.7/0572
819336-017: 10 mg, 100, R646,97
Dosage: Short term use only for up to 5 days. When transf.from inj., tot.combin.dly.dos.of all forms of ketorolac on day of transit.should not exceed 90 mg for pts.≤65 yrs.& 60 mg for pts.>65 yrs., ren.impair pts.& pts.weigh.less than 50 kg. Tot.oral dos.should not exceed 40 mg on the day change is made.
Sngl.dos: One dos.of 10 mg.
Multip.dos: Recomm.1 tab.4-6 hrly as requir. with max.40 mg/day.
Contra-indications: *Hist./ act. pept.ulc./GI bleed./ perforat., full anticoag.ther.incl. prophylact. low dos.heparin, haemorrhag. diathes.incl. coagulat.disords., NSAID cross sens., susp./confirm.cerebrovasc.bleed., ops.with high risk of haemorrh./incompl.haemostas., mod. to sev.ren.impairm., pts.at risk of ren.fail.due to vol. deplet./dehydrat., dur.pregn./ labour/deliv. /lactat., safety & effic.in childr.und.16 yrs.not est., prophylact.analges.bef.surg., intra-op.use, neuraxial admin., concom.oxpentifylline/other NSAIDs/ chron.painf. condits., high haemorrh. risk surg./incompl.haemostas.*
Side-effects: *Hypersens.reacts.incl.anaphylax., GI disturbs. incl.fulln./rect.bleed./stomatit./ pancreatit., dos.depend. GI bleed./perforat.esp.in elderly & debilit., sweat., excess. thirst, CNS eff., dizzin., headache, pareasthes., convuls., vertigo, myalg., hyperkines., asept.meningit., psychot. reacts., incr.urin.freq., oligur., ac.ren.fail., hyponatraem., hyperkalaem., haemolyt.uraem. syndr., flank pain, interstit. nephrit., urin.retent., nephrot. syndr., flush., bradycard., pallor, hyper-/hypotens., palpitat., chest pain, hepatit., cholestat. jaund., liv.fail., dyspn., asthma, pulm. oed., skin reacts.incl.Lyell's & Stevens-Johnson syndr./exfolliative dermatit., purpura, thrombocytopen., post-op wound haemorrh., epistax., haematoma, incr.bleed.time, abnorm. taste/vis., hear.loss, tinnit., asthen., oed., weight gain, inj. site reacts., fev., inhib.platel. aggregat., prolongs bleed.time, fluid retent., poss.laryng./ angio-oed.with/without aspir. hypersens., ser.GI toxic.with/without prev.sympt.*
Special precautions: *Poss. incr.uter.haemorrh. risk dur. labour/deliv., precipit.will occur if mix. in small vol.with morphine sulph./ pethidine/ promethazine /hydroxyzine HCl, hypovolaem. correct.bef.admin., elderly, imp.ren. funct., kidn. dis.hist., ops.where strict haemostas.is critic. eg. cosmet./day case surg., card.decompensat., hypertens., concom.methotrexate, discont.ther.if S&S of liv.dis.devel., angioed.hist., asthma, compl./ part.syndr.of nasal polyps, bronchosp., consid.opioid S/E when used concom.esp.dur. day surg., HF, liv. dysfunct., concom.diuret., bleed. risk.*
Drug interactions: *Addit.S/E with other NSAIDs, oxpentifylline incr.bleed.tendenc, alterat. in pharmacokinet.with probenicid, poss. reduc.methotrex. clear., incr.Li plasma conc., reduc. diuret.respons. to furosemide, poss.incr. ren. impairm.with ACE-inhibit.partic. vol. deplet. pts.*

VARIPAN, (Specpharm) LeBasi [P/S]
Paracet.
Indications: *Mild to mod.pain, fev.*
(S0) TABS, 33/2.7/0435
701140-003: 500 mg, 20, R8,39
Dosage: Adults: 1-2 tabs.4-6 hrly. Max.8 tabs/24 hrs. Childr.6-12 yrs: ½ -1 tab. 6-8 hrly. Max.4 dos. / 24 hrs.
Contra-indications: *Sev.liv.funct.impairm., childr.und.6 yrs.not recomm.*
Side-effects: *Pancreatit., skin rash, allerg.reacts., bld. dyscras.*
Special precautions: *Imp.kidn./liv.funct.*
Drug interactions: *Absorpt.accelerat.by metoclopramide, probenecid alters plasma conc.*

VIBURCOL, Heel [P/S]
Chamomilla D1 1,1 mg, belladonna D2 1,1 mg, dulcamara D4 1,1 mg, plantago major D3 1,1 mg, pulsatilla D2 2,2 mg, calcium carbonicum hahnemanni D8 4,4 mg.
Indications: *Restless.with/without fever in infts.& childr.*
SUPPS. U5677.
812943-007: 12, R92,15
Dosage: Ac.condit: 1 suppos.to be rep.on sev. occasions. Aft.alleviat.insert 1 suppos. 2-3xdly. **Infts.up to 6 mnths:** Max.1 suppos.2xdly.

WOODWARD'S PARACETAMOL, (Aspen Pharmacare: Consum.) Pharmacare [P/S]
Paracet.
Indications: *Mild to mod.pain & fev.*
(S0) ALCOHOL & SUGAR FREE SYRUP, X/2.7/207.
726176-001: 120 mg/5 ml, 100 ml, R19,15
Dosage: Rep. 4-6 hrly.if necess. Max. 4 dos./day. Infts. 3-12 mnths: 2,5 ml. **1-4 yrs:** 2,5-5 ml. **5-8 yrs:** 5-10 ml. **9-12 yrs:** 10-15 ml.
Contra-indications: *Sev.liv.funct.impairm.*
Side-effects: *Skin rash, bld.disords.*
Special precautions: *Imp.ren./liv.funct.*

XEFO, Nycomed [P/S]
Lornoxicam
Indications: *Short term treatm.of mild to mod. pain when oral admin.inappropr*
(S3) INJ, 33/3.1/0249.
860670-007: 8 mg/vial, 5 vials, R125,53
Dosage: Admin.IV/IM
Admin.in 8 mg dos. Dly.dos.not exceed.16 mg. A further 8 mg within 1st 24 hrs.could be need.
(S3) TABS, 33/3.1/0247, 0248.
Indications *Short term.treatm.of mild to mod. pain assoc. with extra artic.inflamm, symptomat. treatm.of pain & inflammat.in osteoarthrit.& rheumat.arthrit.*
860654-001: 4 mg, 20, R67,35
860662-004: 8 mg, 20, R96,06
860662-012: 8 mg, 100, R480,28
Dosage: Admin.bef.meals. Individualise.
Pain: 8-16 mg/day in 2-3 div.dos. Max.tot.dly. dos.16 mg.
Contra-indications: *Prev.hypersens.reacts.to other NSAID meds.incl.acetyl.salicyl.acid., GI/ cerebrovasc. bleed., bleed. & coagulat.disords., act. pept.ulcerat./ hist.of recurr. pept. ulcerat., sev.liv./ren.impairm., thrombocytopen., sev./ uncontrol.card.fail., elderly (>65 yrs), pregn.& lactat., childr.und.18 yrs.,* **Tabs also:** *elderly (>65 yrs) & weigh.< 50 kg & for ac. surg.,* **Inj also:** *hypovolaem./dehydrat.*
Side-effects: *Loc.reacts., CNS effs., sweat., oed., allerg. reacts., vis.disords., GI disturbs.incl. pept. ulcerat.with / without bleed., haemorrhoid./ rect. bleed., bld.dyscras., musculo-skelet.disords., migraine, paraesthes., taste pervers., tinnit.& trem., resp.& skin disords., micturit. disords. palpitat., tachycard., chngs.in BP.*
Special precautions: *Discont.therapy with appropr. therapeut.act.if GI ulcerat./bleed. develops, prev. cerebrovasc.haemorrh., SLE, ulc. colit., Crohn's dis., porphyr., haematopoiet. disords., reduc.card.funct., hepat. dis., coagulat. disords., treatm.long.than 3 mnths., elderly (>65yrs.), imp.ren.funct., monit.ren.funct.in pts.for maj.surg./ comprom.ren.funct./CF/concom. diuret./ nephrotox. meds.*
Drug interactions: *Poss.prolong.bleed.time with concom. anticoagul./platel.aggregat.inhib., poss. incr. hypoglcaem. eff.with sulphonylureas., incr. risk of S/E with other NSAID & aspr., decr.effic.of loop diuret.drugs., decr.eff.of ACE inhib.& risk of ac. ren. insuff., incr.Li peak conc., high dos. methotrexate, high.plasma conc.with cimetidine, decr. ren.clearance of digoxin, incr.ren.toxic.with cyclosporin, CYP2C9 induc.& inhibit.*
See Also MDR Page 1388

3.3. Combinations

ABFLEX-4, (Cipla Medpro) First Pharm [P/S]
Paracet.450 mg, doxylamine succin.5 mg, caff. 30 mg, cod. phosph.10 mg.
Indications: *Mild to mod.pain assoc.with tens.*
(S2) TABS, 28/2.8/0383
826766-022: 20, R8,49
826766-013: 100, R42,45
826766-023: 1 000, R424,51
Dosage: Adults & childr.12 yrs.& old: 2 tabs 4 hrly as necess. Max.8 tabs./day.
Contra-indications: *Resp.depress.esp.in pres.of cyanosis & excess.bronch.secret., aft.bil.tract. ops., ac.alcohol., head injur.& condit.in which IC-press.rais., bronch.asthma attack, HF second.to chron.lung dis., MAOI, safety in pregn.& lactat.not est.*
Side-effects: *Skin rash incl.prurit./urticar., allerg. reacts., bld.disords., resp.depress., bradycard., circulat.fail.,*

...caus.by *Salmonella typhi* &
...nfer.against paratyphoid fev./ill by non-
...ae, emphas. imp.of person.& food hygiene
... thrombocytopen/bleed.disords.
...ractions: *Adeq.respons.may not be achiev. with ...ess.treatm./ immunodefic. pts.*

... Sanofi Aventis [P/S]
...polysacchar.of *Salmonella typhi* (Ty 2 strain) ...dos.
...ns: *Act.immunisat.against typhoid fev. caus. by ...phi.intend.for inhabit.of/ travell. to endem. ...nts, health care work., catering & food indust. ...person.*
...FOR INJ. 29/30.1/0091.
... 1x sngl.dos.pre-fill.syringe, R176,61
...in.of childr.und.2 yrs.depends on dis. expos.risk.
...ildr: Sngl.dos.of 0,5 ml by deep SC/IM inj.at ... prior to potent.expos. Revaccin. every 3 yrs.

...dications: *Life-threaten.react.aft.prev. admin. ...acc.contain.same subst., safety in pregn. not ...wn if excret.in breast milk, intravasc.admin.*
...cts: *Loc.reacts., fev., headache, asthma, ..., arthralg., myalg., GI disturbs., allerg. ...ser.sickn/anaphylax.*
...recautions: *Postpone vaccin.in case of ... fev., protect.not conferr.against paratyphoid ...s.by non-invas. Salmonellae., formaldehyde ... traces thereof pres., immunosuppress. ...munodefic. reduc.immune response theref. ...ccinat.to end of treatm., vaccinat.pts. with ...nodefic.even if antibody response limit., may ...me time as other vacc. using diff.sites, childr. ...r show sub-optim. respons.but as typhoid rare ...roup base vaccinat.decis.on expos.risk, poss. ...f admin.at same time as other meds. contain. ...sap adrenaline avail.in case of anaphylact. ...mbocytopen., bleed. disords.*
...MDR Page 1869

... GSK [P/S]
...at.varicella-zoster virus vaccine.
...ns: *Act.immunisat.of healthy infts.from 9 ...& adolesc./suscept high-risk pts.& suscept. ...s.*
... 30.1/0468. 2 000 pfu/0,5 ml
... 1x 3 ml vial, R258,11
...min.SC only. Admin.entire contents immed.aft. ... sngl.dos. Allow swab area to dry bef.admin. ...ths.-12 yrs: 1 dos. 13 yrs.& old: 2 dos.with ...os.of a minim.of 6 wks. Add.dos.may be ... risk pts.
...dications: *Total lymphocyte count of <1 200/ ...evid.of cellul.immune compet., neomycin ...pregn., no avail.evid.in lactat., ac.sev.febrile ...ncom.live attenuat.vacc.admin.in high risk ...m./ IV admin., mix.with other vacc.in same*

...cts: *Loc.reacts., papulo-vesicul.erupts., fev.*
...recautions: *Avoid pregn.for 3 mnths. post ... disinfect.agents on skin poss. inactiv.virus ...at.bef.admin., monit.x 30 mins.for poss. ...delay immunisat. x3mnths.in pts.who have ...e globul./ bld.transfus., other vaccinat.poss. ...at the same time, observ.1 mnth.interv.aft. ...nat.*

VAXIGRIP, Sanofi Aventis [P/S]
Flu vaccine. Formula varies each year accord.to WHO recommendat. for adults & childr.
Indications: *Flu prophylax.*
(S2) INJ. T/30.1/674.
836597-003: 1x paed.prefill.syr.0,25 ml, R36,89
825670-004: 10 sngl.dos.prefill.syr.0,5 ml, R546,96
Dosage: IM/deep SC admin.
Adults & childr.over 36 mnths: 0,5 ml. Childr.6-35 mnths: 0,25 ml. Childr.und.8 yrs. not prev. vaccinat. should receive 2nd dos.aft.an interv.of at least 4 wks.
...-indications: *Ac.fev., egg/chicken prot./neomycin ... IV admin., childr.und.6 mnths.*
...cts: *Loc./syst./allerg.reacts., gen.skin reacts., ..., neuralg., parasthes., vasculit., convuls., trans. ...topen., neurit., encephalomyelit., Guillain Barre syndr.*
Special precautions: *Immunosuppress., pts. show. allerg./abnorm.reacts.to prev.vaccin., febr. react.poss. precipit.an attack in sickle cell dis., pregn.*
Drug interactions: *Dimish.immunolog.respon.in pts.on immunosuppress.treatm.*
See Also MDR Page 1872

VAZIGAM IM, NBI [P/S]
Human varicella-zoster immunoglobulin deriv.from pooled human plasma with high titre of antibodies to varicella-zoster virus, test.& found non-react.to HBsAg & antibodies to HCV, HIV-1 & HIV-2 viruses.
Indications: *Post.expos.prophylax.of varicella in high risk pts.who have had expos.*
(S4) IM INJ. T/30.2/749. 100 IU/ml.
793078-008: 1x2 ml amp, R457,80
Dosage: IM admin Warm to body temp.bef.use
Up to 5 yrs: 2 ml. 6-10 yrs: 4 ml. 11-14 yrs: 5 ml. 15 yrs.& older: 6 ml.
Contra-indications: *Immune adults/childr., clinic. varicella/ shingles treatm., disseminat.zoster prophylax., weigh risk-benefit ratio pts.with IgA defic. hist./sev. anaphylact.reacts.to plasma prod., IV admin., bleed. disords., safety in pregn.not est.*
Side-effects: *Loc./ anaphylact./skin reacts., headache, fev., chills, flush., lightheadedn., backache, naus., IgA sensitisat., imp.effic.of live attenuat.vit. vaccines.*
Special precautions: *Do not admin.more than 96 hrs. aft.expos., as infect.dis.transmiss cannot be tot. exclud. consid.vaccinat.where appropr.*

VERORAB, Sanofi Aventis [P/S]
Rabies vir.using Wistar rabies PM/WI 38 1503-3M strain obt.from cult.on Vero cell lines, inactiv.with beta-propiolactone.
Indications: *Rabies pre-expos.prophylax.in indiv. at incr. expos., rabies prev.aft.confirm/suspect. expos.*
(S4) INJ. V/30.1/220.
1 immunis.dos.equal to or great.than 2,5 IU/0,5 ml reconstit.dos.
814970-001: 1 vial+syringe with dil., R300,42
Dosage: Strict IM! admin.direct.into deltoid musc. Adapt accord.to circumst.& pts.rabies immune status.
Pre-expos.prophylax: Prim.vaccinat: 3 inj.of 0,5 ml on days D0, D7 & D28 follow.by a booster 1 yr.aft.1st inj. D28 inj.may be admin.on D21. **Boosters:** thereaft.one inj.every 5 yrs.aft.the last inj.
Post-expos.prophylax: Flush wound with soap/ detergent immed.follow.bite, then admin.curat. vaccinat. und.med.supervis. Non-immunis.subj: Adults & childr: 5x0,5 ml inj.on days 0, 3, 7, 14, 28. Complement.passive immunisat.on day 0 with human rabies immunoglobulin at 20 IU/kg bm. infiltrat.as much as poss.around wound with remainder.inj.IM into glut.reg. In cases of sev.les./ proximity to CNS/late consultat/pt.immunodefic.2 x0,5 ml dos.on Day 0 poss.justif. In cases of sev. bites admin 20 iu/ kg bm of specif.human rabies immune globul.in conjunct. with 1st dos.to provide immed.protect.antibod. Vaccinat. of pre-immunis. indiv: If less than 5 yrs.aft.last.vaccinat. dos: 2 booster inj.of 0,5 ml on days D0 & D3. Pts vaccinat. more than 5 yrs.prev./vaccinat.incomplete to be treat.as unvaccinat.subj.
Contra-indications: Pre-expos: *Postpone in event of fev./ac.illn./chron.evolut.dis., assess benef. vs.risk bef. admin.dur.pregn.* Post expos: *No contra-indicat.as rabies ... human rabies immunoglobul.& vacc.in same syringe/inj. at same site.*
Side-effects: *Loc.reacts; ... System. reacts ... malaise, asthen., headaches, dizzin., arthralg., myalg., GI disturbs., allerg.skin reacts., anaphylact.react.*
Special precautions: *... every 2-3 yrs.aft.booster at 1 yr.& 5 yrs where expos.risk freq., in immunodefic. indiv.serolog... last 2-4 wks.aft. vaccinat.admin.boost./addit.inj.if antibody titre <0,5 IU/ml, neomycin hypersens., adhere strict.to method of admin.as fatal at.report.when not follow.*
Drug interactions: *Corticoster.& immunosuppress. ther. may lead to vaccinat.fail.*
See Also MDR Page 1874
See Also MDR Page 1874

27. ENZYMES

(See also 8.3, 12.1, 26)

ACTILYSE, Ing. Pharma
See Section 8.3.

CREON, Abbott
See Section 12.1.

HYALASE, (Mylan) Xixia [P/S]
Hyaluronidase.
Indications: *Hypodermoclysis, prevent.post-partum haemorrh., radiography, obstet.anaesth., aid to loc. anaesth.in ophthalmol.& fract.reduct.*
(S4) INJ, H2874. 1500 iu/amp
731560-035: 10 amps, R2 834,04
For further details refer to manuf.product lit.

METALYSE, Ing. Pharma
See Section 8.3.

28. POISON ANTIDOTES

PARVOLEX, Aspen Pharmacare: Pharma) Pharmacare [P/S]
N-acetylcysteine.
Indications: *Paracet.overdos.*
(S2) INJ. NX/34/156. 200 mg/ml.
788740-008: 10x10 ml, R2 621,55
Dosage: Adults: Init. 150 mg/kg bm.IV infus.in 200 ml dextr. 5% over 15 min., then 50 mg/kg bm in 500 ml over next 4 hrs., then 100 mg/kg bm in 1 L over next 16 hrs. Modify quantit.IV fluid used for childr.accord.to age & bm.
Contra-indications: *Ineffect.15 hrs.aft.overdos.*
Side-effects: *Rash, anaphylax., hypokalaem., ECG chang.*
Special precautions: *Asthma/hist.thereof, monit. plasma K+ conc.*

PREMIER DICOBALT EDETATE, (Restan) AI Pharm Ltd [P/S]
Dicobalt edetate
Indications: *Cyanide poison.antidote (in addit.to standard treatm.).*
(S1) IV INJ. H2798. 300 mg/20 ml.
735108-005: 6x20 ml, R1 180,07
Dosage: 20 ml stat.IV over 1 min.foll.by 50 ml IV dextr. May be rep. 2x.
Side-effects: *Vomit., fall in BP, tachycard.*
Warnings: *Premier dicobalt edetate itself is toxic., avoid use as precaut.meas., use only when pt.is tend.to lose/has lost consciousn.*

TOXOGONIN, (Merck Serono) Merck [P/S]
Obidoxime chloride.
Indications: *Organophosph.poison.*
(S4) INJ. E/5.3/79.
771376-006: 250 mg/ml, 5x1 ml, R363,35
Dosage: Pretreat pt.with atropine sulph., then admin.IV. Adults: 3-5 mg/kg stat. Rep.aft. 2 hrs.if satisfact. respon. IV/IM. Childr: 4-8 mg/kg stat.

...nteral solutions

...es: MIMS reflects the single exit price inclusive of VAT in line with pricing legislation (Government Notice, Gazette ...4 of 30 April 2004). Prescribers are reminded that this price excludes any professional fees that may be applicable and will not necessarily be what their patients will pay.

...ept.ulcerat., observe for dis.contr.decline, ...es on-demand treatm., insuffic.contr. diabet. ...gle glauc., halogen.anaesthet.
...ractions: *Poss.addit.CV effs.with concom. ...et., incr.risk arrythm.with card. glycosid., ...'s.*
...DR Page 1004

... Aspen Pharmacare) GSK, [PWR]
... µg, fluticasone propionate 100 µg, (250 µg ... ster
...ns: *Reg.prophylact.treatm.of atop. asthma ...s.on identic.dos.of compon., chron. COPD incl. ...mphysema, sev. COPD & hist of rep.exacerbat. ...sympts. despite reg.bronchodilat.ther.*
...HALER, 42/21.5.4/0581, 0582, 0583
...0/100 µg, 60 blisters, R180,19
...0/250 µg, 60 blisters, R249,80
...0/500 µg, 60 blisters, R332,46
... low.dos.effect.contr.sympt. **Adolesc. 12** ... inhalat.of reqd. strength 2xdly. **Childr.4 yrs &** ... 50/100 ug strength 2xdly.
...ct.pulm.dis: **Adults:** 1 inhalat. 50/250 ug ... strength 2xdly.
...ER, 42/21.5.4/0244, 0245, 0246
... µg, fluticasone propionate 50 µg, (125 µg & ...
...ns: *Reg.prophylact.treatm.of atop. asthma when ...entic.dos.of compon.*
...5/50 µg, 120 actuat., R142,50
...5/125 µg, 120 actuat., R191,52
...5/250 µg, 120 actuat., R257,64
...st be used regular.even when asymptomat. ...s.effect.contr.sympt.
...ildr.12 yrs.& old: 2 inhalat.of requir. strength

...ndications: *Safety in pregn.& lactat.not est., no ... childr.und.4 yrs.for accuhal.*
...ects: *Rash, trem., headache, palpitat., ... hypersens.reacts.incl.oed.& angioed., ... card.arrhythm., oropharyng. irrit., arthralg., ...at candidias., hoarsen., adren.suppress., ...at. in childr.& adolesc., decr.bone min. ...ract, glauc., paradoxic.bronchosp.*
...recautions: *Not for relief of ac. sympts., ...d.deteriorat.of asthma control, corticoster. ... animals, treat. concurr.infects., no abrupt withdr., ...se of paradoxic.bronchosp., transf.from other ...teroids, medic.or surg.emerg./elect.proced. / ...poss.unmask.of underly.eosinophil. condits., ...eight.if treatm.prolong., act. /quiesc.pulmon. TB, ...poss. adrenocortic. suppress.with corticoster.ther.*
...eractions: *Poss.interact.with substrates /inhibit. ... avoid both non-select.& select. ß-block.unless ...mpell.reasons.*
...MDR Page 803

... Cipla Medpro, [PWR]
...5 µg, fluticasone propionate 50 µg, (125 µg & ...at.
...ns: *Reg.prophylact.treatm.of atop. asthma when ...entic.dos.of compon.*
...NHALER, A42/21.5.4/0218, 0219, 0220
... 25/50 µg, 120 dos., R142,50
... 25/125 µg, 120 dos., R191,52
... 25/250 µg, 120 dos., R257,64
... to low.dos.effect.contr.sympt.
...dolesc.12 yrs.& old: 2 inhalat.of reqd. ...y.
...ndications: *Safety in pregn.& lactat.not est.*
...ects: *Hypokalaem., headache, trem., palpitat., ...m., hypersens.reacts. incl. angioed., musc. ... arthralg., oropharyng. candidias., vag. ... Cushing syndr./ features., adren.suppress., decr.bone min.density, psych. disords., CNS effs., cataract, glauc., incr. IOP, conjunctivit., eye irrit., bronchit., nas. congest. /-discharge, rhinit., sinusit., nasopharyngit., paradox. bronchosp., otit.media., dysphon., epistax., sneez., GI disturbs., hoarsen., throat irrit., skin rash, ecchymos., contus., prurit., PID, dysmenorrh., malaise, fatig., weight gain, vir.GI/ resp.infect., eosinophil., neuropathy, keratit., chest pain, cough, rhinorrh., poss.syst. cortico-ster.effs.& adrenocortic.suppress.*
Special precautions: *Childr.may be more suscept. to infects.eg chickenpox/measles, avoid both non-select.& select. ß-block.unless there are compell.reasons, corticoster.teratogen.in animals, not for ac.sympt.relief, progress./sudd.deteriorat.of asthma control, no abrupt withdr., discont.in case of paradoxic.bronchosp., transf. from other oral/ inhal. steroids, pts.wean.of oral steroids whose adrenocortic. funct.is imp., rarely poss.unmask. underly.eosinophil.condits., monit.childr.height.if treatm. prolong., medic./surg.emerg./elect.proced. /stress, treat. concur.infects., act./quiesc.pulmon. TB, thyrotoxicos.*
Drug interactions: *Potent.incr.system.expos.to fluticasone with strong CYP 3A4 inhibit.*

SERETIDE, GSK, [PWR]
Salmeterol 50 µg, fluticasone propionate 100 µg, (250 µg & 500 µg)/blister
Indications: *Reg.prophylact.treatm.of atop. asthma when stabilis.on identic.dos.of compon., sev.COPD & hist of rep. exacerbat.with signific. sympts.despite reg.bronchodilat. ther.*
(S4) ACCUHALER, 33/21.5.4/0413, 0414, 0415
874493-005: 50/100 µg, 60 blisters, R240,26
874507-006: 50/250 µg, 60 blisters, R333,06
874515-009: 50/500 µg, 60 blisters, R443,29
Dosage: Titr.to low.dos.effect.contr.sympt. **Adults & childr.12 yrs.&old:** 1 inhalat.of reqd. strength 2xdly. **Childr.4 yrs & old:** 1 inhalat. 50/100 ug strength 2xdly. **Chron.obstruct.pulm.dis: Adults:** 1 inhalat. 50/250 ug OR 50/500 ug strength 2xdly.
(S4) CFC FREE INHALER, 35/21.5.4/0411,0412,0413
Salmeterol 25 µg, fluticasone propionate 50 µg, (125 µg & 250 µg)/actuat.
Indications: *Reg.prophylact.treatm.of atop. asthma when stabilis.on identic.dos.of compon*
894989-006: 25/50 µg, 120 actuat., R240,26
894990-004: 25/125 µg, 120 actuat., R333,06
895006-007: 25/250 µg, 120 actuat., R443,29
Dosage: Must be used regular.even when asymptomat. Titr.to low.dos.effect.contr.sympt.
Adults & childr.12 yrs.&old: 2 inhalat.of requir. strength 2xdly.
Contra-indications: *Safety in pregn.& lactat.not est.*
Side-effects: *Trem., headache, palpitat., musc. cramps, card.arrhythm., arthralg., hypersens. reacts., hypokalaem., hoarsen., candidias., poss. syst.cortico-ster.effs.& adrenocortic.suppress.*
Special precautions: *Not for relief of ac. sympts., no abrupt withdr., discont.in case of paradoxic.bronchosp., transf.from other oral/ inhal. steroids, progress./sudd. deteriorat.of asthma control, pts.wean.of oral steroids whose adrenocortic. funct.is imp., rarely poss.unmask.of underly.eosinophil.condits., monit.childr.height.if treatm. prolong., medic./surg.emerg./elect.proced. /stress, treat. concur.infects., act./quiesc.pulmon. TB, thyrotoxicos., avoid both non-select.& select. ß-block.unless there are compell. reasons, corticoster. teratogen. in animals.*
Drug interactions: *Poss.interact.with substrates /inhibit. of CYP 3A4*

SYMBICORD, AstraZeneca
Budesonide 80(160) µg, formoterol fumarate dihydrate 4,5 µg/dose.
Indications: *Asthma in adolesc.& adults where combinat. inhal. corticoster.& long act.ß-agon. ther. appropriate.*
(S4) TURBUHAL. 35/21.5.1/0404, 0405.
705986-001: 80/4,5 µg/inhal., 120 dos., R365,05
700172-001: 160/4,5 µg/inhal., 60 dos., R204,35
700173-001: 160/4,5 µg/inhal., 120 dos., R408,70
Dosage: Indiv.accord.to sev. When contr.achiev. titrat. to low.dos.at which sympt.contr.is maint. 2 treatm. approach:
Maint.ther: Adults 18 yrs.& old: 1-2 inhalat.of either strength 2xdly. Max: 4 inhalat.2xdly.as maint. /tempor.dur. worsen. **Adolesc.12-17 yrs:** 1-2 inhalat.of either strength 2xdly. Temp.incr.to max. 4 inhalat.2xdly.dur. worsen.
Maint.& reliev.ther: Adults 18 yrs.& old: Maint (80:4,5): 2 inhalat./day given as 1 inhalat.in morn. & even. OR 2 inhalat.in either morn./even. **Maint** (160:4,5): 2 inhalat./day given as 1 inhalat.in morn. & even. OR 2 inhalat.in either morn./even. Some pts. may req.2 inhalat.2xdly. Take 1 addit.inhalat. as need.in respons.to sympts. If sympts.persist.an addit.dos.may be taken.aft.a few mins. Max.6 inhalat. on any sngl.occas. Tot.dly.dos.of more than 8 inhalat.not norm.reqd.however tot.dly dos. of upto 12 inhalat.maybe used tempor.
Adolesc.12-17 yrs: Maint (80:4,5): 2 inhalat./day given as 1 inhalat.in morn.& even. OR 2 inhalat.in either morn./ even. **Maint (160:4,5):** 2 inhalat./day given as 1 inhalat. in morn.& even.OR 2 inhalat.in either morn./even. Some pts.may req.2 inhalat. 2xdly. Take 1 addit.inhalat.as need. in respons.to sympts. If sympts.persist.an addit.dos.may be taken aft.a few mins. Max.6 inhalat.on any sngl. occas. Tot. dly.dos.of more than 8 inhalat.not norm. reqd. however tot.dly dos.of upto 12 inhalat. maybe used tempor.
(S4) TURBUHAL. 320/9 µg/inhal. 38/21.5.1/0187
Budesonide 320 µg, formoterol fumarate dihydrate 9 µg/dose.
Indications: *Adult asthma where combinat.high dos. inhal.corticoster.& long act.ß-agon.ther. appropriate.*
705984-001: 320/9 µg/inhal.,60 dos., R417,91
Dosage: Indiv.accord.to sev.titrat.to low.effect. dos.for sympt.contr. Not for ac.asthma attack.
Adults & adolesc.12 –17 yrs: 1 inhalat. 2xdly.
Contra-indications: *Safety & effic.in.childr.und. 12 yrs. not est., init.ther.dur sev.exacerbat., safety in pregn.& lactat.not est., no data avail.in hepat./ ren.impairm.*
Side-effects: *Trem., palpitat., headache, candida infects. of oropharynx., throat irritat., cough., hoarsen., tachycard., naus., musc.cramps, CNS effs., card.arrhythm.assoc. with $ß_2$-agon., hypersens. reacts.incl.exanthema/urticar./ prurit.& angioed., bronchosp., skin bruis., ang.pect., S&S of system.glucocortic.effs.incl.adren.hypofunct., hyperglycaem., psych.sympts., low.ser.K^+ with high dos.*
Special precautions: *Corticoster.teratogen.in anim., sev.CV disords., diab.mellit., untreat hypokalaem., thyrotoxicos., longt.ketoconazole treatm., have separat. rapid act.bronchodil.for rescue treatm., re-assess ther.if incr. inhalat.reqd. for sympt.contr.without improv.asthma contr. within 3 days, sev.liv.cirrhos., continuat.of ther. even if asymptomat., re-assess ther.if condit. worsen., monit.childr./ adolesc.growth, transf.from oral to inhal. glucocorticoster., pts.requir.prolong. treatm.at high dos., surg./infect./condits. assoc. with sev.electrol.loss/sev.stress,consid.addit. system. corticoster.dur.stress/elect.surg.*
Drug interactions: *CYP3A4 inhibit.eg ketoconazole/ macrolides/ HIV protease inhibits. may incr.syst.expos.to budesonide, concom.ß-adrenerg.block.incl.eyedrops may inhibit./weak. eff.of formoterol, quinidine/disopyramide/ procainamide/phenothiazin./ antihistamin.eg. terfenadine, MAOI's & TCA's can prolong QTc interv. & incr.risk of ventr.arrhythm.*
See Also MDR Page 397

10.3. Mucolytics

ACC200, (Sandoz) Hexal [P/S]
N-acetylcysteine.
Indications: *Mucolyt.of non-infect.secret.in cyst.fibros.& resp.condits, paracet.overdos.*

DUOVENT HFA
Metered Dose Inhaler

S2 Duovent® HFA Metered Dose Inhaler. Each metered dose contains ipratropium bromide monohydrate corresponding to ipratropium bromide anhydrous 20 µg, and fenoterol hydrobromide 50 µg. Reg. No.: 35/10.2.1/0302. Ingelheim Pharmaceuticals (Pty) Ltd. Cpy.Reg.No.: 1966/008618/07. BI Ref. No.52/2012 (Mar 12)

Combination Therapy in a single inhaler

Boehringer Ingelheim

(S2) EFFERVESC.TABS. 29/10.2.2/0753.
824291-018: 200 mg, 25, R54,47
Dosage: Dissol.tabs.bef.admin.
Mucolyt: Childr.und. 2 yrs: 200 mg dly. 2-6 yrs: 200 mg 2xdly. Adults: 200 mg 3xdly.
Paracet.overdosage: commenc.as soon as poss. Init. 140 mg/kg then 70 mg/kg 4 hrly x17 dos.
Side-effects: *Bronchosp., GI disturbs., rhinorrh., headache, tinnit., urticar., chills, fever, anaphylax.*

AMUCO 200, (Austell) Camox [P/S]
N-acetylcysteine.
Indications: *Mucolyt.of non-infect.secret.in cyst. fibros.& resp.condits.*
(S2) EFFERVESC.TABS. 43/10.2.2/0510.
716267-001: 200 mg, 2x10, R41,38
Dosage: Dissolve tabs.bef.admin.
Childr.und. 2 yrs: 200 mg 1xdly. 2-6 yrs: 200 mg 2xdly. Adults: 200 mg 3xdly.
Contra-indications: *Safety in pregn.& lactat.not est.*
Side-effects: *Headache, drowsin., N&V, stomatit., bronchosp., rhinorrh., tinnit., allerg. dermatit., urticar., anaphylax., chills, fev., poss. disrupt. gastr.mucos.barrier.*
Special precautions: *Asthma, pept.ulc.hist.*

BETAPHLEM, Be-Tabs [P/S]
Carbocisteine.
Indications: *Adjunct.therapy in resp.tract. disords. charact.by excess muc.in absen.of infect.*
(S2) SYRUP. S/10.2.2/146.
708151-019: 250 mg/5 ml, 200 ml, R17,93
708151-027: 250 mg/5 ml, 2,5 L, R224,20
Dosage: Adults: 10-15 ml. 3x dly. Childr: 2-5 yrs: 1,25-2,5 ml. 4x dly. 6-12 yrs: 5 ml 3x dly.
Contra-indications: *Act.pept.ulc., childr.und.2 yrs. not recomm.*
Side-effects: *Naus., diarrh., headache.*
Special precautions: *Gastr./duod.ulc.hist.*

BISOLVON, Ing.Pharm [P/S]
Bromhexine HCl.
Indications: *Cough assoc.with non-purul.excess. sputum product.*
(S2) SOL, [P/S] G642. 10 mg/5 ml.
710040-006:, 50 ml, R66,12
Dosage: Oral: Adults & childr.over 10 yrs: 5-10 ml 3xdly. Childr.und.10 yrs: 2,5-5 ml 3xdly.
Inhal.from respirator: May be dil.1:1 with physiolog. NaCl. Admin.2xdly.
Adults: 4 ml. Childr.over 12 yrs: 2 ml. 6-12 yrs: 1 ml. 2-6 yrs: 10 drps. Und. 2 yrs: 5 drps.
Contra-indications: *Safety in pregn.& lactat.not est.*
Side-effects: *GI disturbs., CNS effs., sweat., cough & bronchosp.with inhalat., allerg.reacts., incr.secret.flow.*
Special precautions: *Gastr.ulc., asthmat.pt., sev.hepat./ren.impairm.*
Warnings: *1st give bronchodil.in bronchosp.*

BRONCHETTE, (Aspen Pharmacare) Pharmacare [P/S]
Carbocysteine.
Indications: *Adjunct.in respir.tract disords. charact. excess.visc.mucus in absen.of infect.*
(S2) SYRUP, [P/S] L/10.1/320.
710520-018: 250 mg/5 ml, 200 ml, R15,23
Dosage: Adults: 10-15 ml 3xdly. Childr. 5-12 yrs: 5 ml 3xdly. 2-5 yrs: 2,5 ml 2-4xdly.
Contra-indications: *Act.pept.ulc., safety in pregn.not est.*
Side-effects: *Naus., diarrh., headache, GI bleed., skin rash.*
Special precautions: *Gastr./duod.ulc.hist*

FLEMEX, J&J [P/S]
Carbocisteine.
Indications: *Resp.tract.disord.charact.by excess or visc. mucus in the absence of infect.*

(S2) SYRUP, [P/S] M/10.1/248. 250 mg/5 ml
726451-010: 200 ml, R64,60
Dosage: Admin.3xdly. Adults: 10-15 ml. Childr: 5-12 yrs: 5 ml. 2-5 yrs: 2,5 ml 2-4xdly. acc.to age.
Contra-indications: *Act.pept.ulc.*
Side-effects: *Naus., diarrh., headache.*
Special precautions: *Gastr./duod.ulc.*

FLEMLITE, (Aspen Pharmacare: Consum) Pharmacare [P/S]
Carbocysteine.
Indications: *Adjunct.therapy in resp.tract disords. charact.by excess.visc.muc.in the absence of infect.*
(S2) SYRUP, X/10.2.2/184. 250 mg/5 ml.
785164-006: 200 ml, R21,98
Dosage: Adults: 10-15 ml 3xdly. Childr: 6-12 yrs: 5 ml 3xdly. 2-5 yrs: 2,5 ml 2-4xdly.
Contra-indications: *Act.pept.ulc., childr.und.2 yrs., safety in pregn.& lactat.not est.*
Side-effects: *GI disturbs.incl.haemorrh., headache, skin rash, palpitat., dizz.*
Special precautions: *Gast./duod.ulc.hist.*

LESSMUSEC, Brunel [P/S]
Carbocisteine
Indications: *Adjunct.in resp.tract disords.charact. by excess.visc.muc.in absenc.of infect.*
(S2) CAPS, T/10.2.2/227. 375 mg.
783633-130, 30, R24,07
783633-122, 1 000, R826,42
Dosage: 2 caps 3xdly. Once satisfact. respons.reduc.to 1 cap 4xdly.
Contra-indications: *Act.pept.ulc.*
Side-effects: *Naus., diarrh., headache, skin rash, palpits.*
Special precautions: *Gastr./duod.ulc.*

MUCOSPECT, (Aspen Pharmacare: Consum) Pharmacare [P/S]
Carbocysteine.
Indications: *Resp.tract disord.charact.by excess. mucus in absence of infect.*
(S2) SYRUP, [P/S] L/10.1/318. 250 mg/5 ml
744816-009: 200 ml, R24,02
Dosage: Admin. 3xdly.
Adults: 10-15 ml. 5-12 yrs: 5 ml.
(S2) PAED.SYRUP, [P/S] W/10.1/216.
781169-003: 125 mg/5 ml, 100 ml, R24,40
Dosage: Admin. 3xdly.
Childr. 2-5 yrs: 2,5-5 ml. 5-12 yrs: 10 ml.
(S2) CAPS, [P/S] P/10.1/186.
744824-001: 375 mg, 30, R48,38
Dosage: 2 caps 3xdly red.to 1 cap 4xdly.aft. satis. respon.
Contra-indications: *Pept.ulc., safety in pregn.not est.*
Side-effects: *Naus., diarrh., headache, dizz., palpits., heartburn, skin rash, GI bleed.*
Special precautions: *Gastr./duod.ulc.*
Drug interactions: *Incompat.with pholcod.linct.*

SOLMUCOL, (Aspen Pharmacare: Consum) Pharmacare [P/S]
N-acetylcysteine.
Indications: *Adjunct.therapy in resp.condits., reduc. viscos.of non-infect.secret.in cyst.fibros., paracet.overdos.*
(S2) GRANS, [P/S] 28/10.2.2/0128, 0129.
809284-006: 200 mg, 20 sachets, R93,39
809292-009: 400 mg, 30 sachets, R161,24
(S2) LOZ, [P/S] 28/10.2.2/0451.
809306-018: 100 mg, 24, R86,54
Dosage: Dissol.gran.bef.admin.
Resp.disords: Childr.up to 2 yrs: 200 mg dly. 2-6 yrs: 200 mg 2xdly. Adults: 200 mg 3xdly.
Cyst.fibros: Childr.2-6 yrs: 200 mg 3xdly. Adults: 200-400 mg 3xdly.

Paracet.overdos: Commenc.as soon as poss. L
140 mg/kg then 70 mg/kg 4 hrly x17 dos.
Side-effects: *GI disturbs., rhinorrh., bronchosp. fev., headache, tinnit., urticar., haemoptys., anap reacts.*
Special precautions: *Elderly with resp.insuffic pts., recent gastro-duod.ulcerat.*

10.4. Anti-asthmatics

10.4.1. Glucocorticoids

ALVESCO, Nycomed [PWR]
Ciclesonide.
Indications: *Asthma sympt.prophylax.*
(S3) MET.DOSE INHALER. 37/21.5.1/0530, 05
705265-001: 80 µg, 60 met.dos, R248,79
705267-002: 160 µg, 60 met.dos, R248,79
705269-003: 160 µg, 120 met.dos, R497,59
Dosage: Inhalat.use only. Indiv.& titrat.to low. e Tot.dly.dos.range: 80-320 µg admin.as sngl.morn dos OR in 2 div.dos.
Contra-indications: *Safety & effic.in childr. no safety in pregn.& lactat.not est., status asthmat ac.asthma episod.requir. intens. ther.*
Side-effects: *Paradox.bronchosp., hoarsen., lo bad taste, oropharyng.Candidiasis, rash, eczema corticoster.eff.with high dos. over prolong.perio*
Special precautions: *Poss.incr.in ser.lev.with inhibit.of cytochrome P450 3A4 syst., no info on .with spacer, transf. of oral steroid pts., pulm.TB relief of ac.asthma sympts., pts.to keep inhal.sh bronchodilat.avail., if treatm.less effect./ requir treatm.to be re-assess, stress from emerg./elec do not stop inhal. steroids abrupt., assess risk v contin. use if paradoxic.bronchosp.occurs*

BECLATE, Cipla Medpro [PWR]
Beclomethasone dipropionate.
Indications: *Asthma.*
(S3) INHALER. 30/21.5.1/0080, 0081, 0147.
819611-018: 50 µg/actuat., 200 met.dos., R58,5
819638-005: 100 µg/actuat., 200 met.dos., R111
820083-003: 200 µg/actuat., 200 met.dos., R177
Dosage: Adults: Usual dos: 200 µg 2xdly.
Sev.cases: 600-800 µg/day reduc.when stabilis as 2-3-4 div.dos. Sev.cases/part.respons: up to 1 in div. dos.
Childr: 50-100 µg 2-3-4xdly accord.to age & resp
Contra-indications: *Ac.stat.asthmatic., safety not est.*
Side-effects: *Hoarsen., candidias.of mouth & t paradox.bronchosp.(discont.), adren. suppress.*
Special precautions: *Act./quisc.pulmon.TB, re of syst.ster.dur.stress, airway obstruct./ reduc.a transf.from syst.ster.*

BUDEFLAM, Cipla Medpro [PWR]
Budesonide.
Indications: *Asthma sympt.prophylax.*
(S3) MET.DOSE INHALER WITH GENTLE-HALI
30/21.5.1/0255, 32/21.5.1/0115
897462-004: 100 µg/dos, 300 dos, R175,71
897469-003: 200 µg/dos, 300 dos, R250,78
(S3) DP-CAPS, [PWR] 36/21.5.1/0258
704176-001: 200 µg, 60, R49,78
577802-004: DP haler device, 1, R14,58
708079-001: Revolizer device, 1, R52,17
Dosage: Admin.bronchodilat.sev.mins. bef.to m loc.S/E. Spacer use recomm.in dly.adult dos. ab µg.& in all childr.dos.for improv. lung deposit. Fo

MEDICAL DEVICE DELIVERY VOLUME *

Product used: Adco Napamol elixir

No	Medical Device	Order of product	Contents (all?)	Contents remaining	Observations	Cleaning of device
1	Medi-Rite Medicine spoon	1	n/a	n/a	1) Pouring the product into the medicine spoon can only be done in one way because of the scoop shape 2) During pouring, the grading marks are not visible to the individual therefore making it difficulty to ensure that the correct volume id being poured. 3) Pouring from device into a mouth (at lips) is impracticable as there is much spillage due to the device design having an upward shape. 4) However if the device is placed halfway into the mouth there is no spillage. This latter was performed by the researcher and not on a child younger than 18 years	1) As per house hold item 2) No special requirements
2	Medicine measure 5 ml	2	All emptied with no wastage	none	1) It is easy to empty the product from the Medi-rite spoon	
	Medicine measure 2,5 ml	14	All contents were emptied	none	As per 5 ml	
3	Dis-chem Super Dropper	5	From dropper to Medi-Rite (4,5 ml to 3/4 tsp [3,75 ml])	under by 1/4 tsp	1) Instruction to rinse device after each use noted on the actual device. 2) In drawing up the product, the vacuum suction provided by the flexible rubber gave a maximum of 4,5 ml reading after several attempts. 3) Volume obtained varied from 3/4 tsp (3,75 ml) to 4,5 ml. It was not possible to get to 5 ml in one draw. 4) Repeat with water only draw between 4,5 ml and 5 ml	1) Rubber stopper can be removed 2) However practicality after use has not been evaluated; that is will the rubber continue to provide adequate suction to deliver dose

No	Medical Device	Order of product	Contents (all?)	Contents remaining	Observations	Cleaning of device
		16	All contents were emptied	Just under 2,5 tsp	1) Had to reduce to 2,5 ml in volume by gentle pressure on the rubber tubing	
4	Syringe 5 ml (SurgiPlus)	6	All emptied no wastage	Just over 5 ml	1) Drawing up contents from a bottle into syringe is not practical. The bottle was full during this experiment but not once the bottle is 3/4 full. 2) Volume is similar to Medi-Rite volume 3) Syringe does not reach all the way to the bottom of the bottle	1) Plunger can be removed and device cleaned 2) No special precautions
		17	All contents were emptied	2,5 ml	The is correlation between the two devices	
5	Syringe 5 ml (Pharmacist Choice)	7	All emptied no wastage	Just over 5 ml	Same comments as SurgiPlus	1) Plunger can be removed and device cleaned 2) No special precautions
			n/a	n/a	Grading is marked in increments of 0,2 ml therefore not possible to measure 2, 5 ml	
6	Teaspoon A	3 and 8	There was spillage of some of the contents. REPEAT:	1st: n/a Repeat: 1/2 tsp (2,5 ml)	1) Contents were spilled as a result of the teaspoon being at an angle. Initially the volume spilt was not measured. 2) However in the repeat to obtain volume, only 2,5 ml available in the teaspoon.	1) Is a house hold item 2) No special requirements
7	Teaspoon B	4	Not all contents (5 ml) were able to full the tsp	Just under 1 ml	Contents were poured/emptied from the Medi-Rite device into Tsp B very slow to ensure no spillage. The reminder of the contents in Medi-Rite was evaluated.	1) Is a house hold item 2) No special requirements

No	Medical Device	Order of product	Contents (all?)	Contents remaining	Observations	Cleaning of device
8	Dis-chem Med Dropper (3 ml)	9	1,5 ml	1 ml; loss of 0,5 ml	1) Repeated attempts only resulted in a maximum of 1,5 ml 2) Other comments as the 5 ml dropper are applicable	1) Practicality after use has not been evaluated; that is will the rubber continue to provide adequate suction to deliver dose
		15	n/a	n/a	It was not possible to obtain 2,5 ml	
9	Medicine dropper (FirstAid)	11	Cannot be measured		1) Product was not contained 2) Contents or product leaked from the opening from the onset 3) Volume was under 1 ml mark; appeared to be halfway thus estimate is 0,5 ml	1) Stopper can be removed 2) Dropper is glass so care needs to be exercised during cleaning
10	Syringe 3 ml	10 & 13	All emptied no wastage	Just under 3 ml mark	1) The fill was just under 3 ml 2) Based on the result of the 10 ml as well, a repeat of the volume was performed 3) The results were still the same	1) Plunger can be removed and device cleaned 2) No special precautions
					Grading is in 0,2 ml increments therefore not possible to draw 2,5 ml	
11	Syringe 10 ml	12	All contents were emptied	Just over the 10 ml mark	1) The syringe just fitted into the mouth of the product bottle 2) Same comments as SurgiPlus	Plunger can be removed and device cleaned No special precautions
		18	All contents were emptied	2,5 ml	2,5 ml: Contents of both devices yield the same volume	
		19	All contents were emptied	8 ml	7,5 ml: Contents was over by 0,5 ml in the Medi-Rite container	
12	Tablespoon	20	All contents were emptied	10 ml	Contents were transferred form the medicine measure into the tablespoon. Volume delivered is 10 ml	1) Is a house hold item 2) No special requirements

* Devices will be kept until thesis has been finalised

Package insert source summary:

No.	Proprietary name	Procurement site	Advice	Date of publication	Formulation details	Dosage; comparison	PIL	PIL: Other
1	Adco-Paracetamol Syrup	SAEPI	n/a	23 August 1989	Alcohol	n/a	no	n/a
2	Antalgic SF syrup							
3	Antalgic 500 T Tablets							
4	Austell-Paracetamol tablets							
5	Calpol Paediatric Syrup	Vitacare	n/a	April 2011	Sucrose and alcohol free	n/a	no	n/a
6	Empaped (Suppository)	Vitacare	n/a	Not available	no	n/a	no	n/a
7	Go-Pain P (syrup)	SAEPI	n/a	April 1996		Alcohol	no	n/a
8	Napamol Tablets	SAEPI	n/a	15 April 1991	no	n/a	no	n/a
9	Napamol elixir (Adco Napamol Elixir)	Dischem	n/a	15 April 1991	No	-	no	n/a
10	Painamol Syrup	Industry	n/a	Not available	no	no	no	n/a
11	Painamol Tablets	Personal	n/a	19 June 1974	Sugar content	Product examination does reveal breakline	no	n/a

No.	Proprietary name	Procurement site	Advice	Date of publication	Formulation details	Dosage; comparison	PIL	PIL: Other
12	Panado Tablets	PicknPay Family	None; off the shelf purchase	27 June 2005	Sugar free	Product description: Has breakline/scored	no	n/a
13	Panado Meltabs Sugar free	Vitacare	n/a	10 March 2005	Sugar free	n/a	No	n/a
14	Panado Capsules	PicknPay Family	None; off the shelf purchase	August 1984	Sugar free	Coincide on pack and MIMS; pack & PI reflect not for children under 9 years	No	n/a
15	Panado Infant Drops	Vitacare	n/a	August 1990	Sugar free	n/a	no	n/a
16	Panado Children Meltabs	Dischem	None; off the shelf	10 March 2005	Sugar Free	As per MIS; Carton & PI differ: 5/10 days	no	
17	Panado Paediatric Syrup Sugar and alcohol free	Vitacare	n/a	23 June 2006	Alcohol, sugar and tartrazine free	n/a	no	n/a
18	Panado Syrup (Panado Paediatric Syrup?)				Sugar and tartrazine free			
19	Panado Paediatric Syrup Strawberry	Vitacare	n/a	26 March 2002	Alcohol and sugar free	n/a	no	n/a

No.	Proprietary name	Procurement site	Advice	Date of publication	Formulation details	Dosage; comparison	PIL	PIL: Other
20	Panado Effervescent	Dischem	None, off the shelf	23 July 1992	Sugar Free	Physical examination reveals that eh tablet does not have a breakline; how can the tablet be broken in ½ as per dose instruction in the PI?	no	n/a
21	Paracet Tablets							
22	Perfalgan Solution for infusion	MDR 2012	n/a	Not listed	n/a	n/a	no	n/a
23	Perfalgan paediatric Solution for infusion	MDR 2012	n/a	Not listed	n/a	n/a	no	n/a
24	Prolief Tablets							
25	Varipan tablets							
26	Grand-Pa Paracetamol tablets	PicknPay Family	None; off the shelf purchase	23 July 2010	Sodium bicarbonate (630 mg) reflected as active Sugar free	Coincides to pack	23 July 2010; only paracetamol as active	Children over 12 specified under special care and 'how to take' section

Summary of DOSING INFORMATION of paracetamol containing products

South Africa

The following is a list of products[1] reflected in MIMS[2] [3]May 2012. The list is specific to products aimed at dosage delivery to children aged 0 to 18 years[4] containing paracetamol as a single[5] ingredient

ORAL

LIQUIDS: N = 11

Form	Strength – paracetamol per dosage unit	Age	Dosage (paracetamol quantity)	Frequency	Maximum daily dose	Preparations
Liquid	120 mg per 5 ml	3 – 12 months	2,5 ml - 5 ml (60 mg – 120 mg)	3- 4 times daily (6- 8 hourly)	Four doses (480 mg)	1. Adco-Paracetamol Syrup 2. Napamol elixir (Adco-Napamol elixir) 3. Painamol Syrup 4. Panado Paediatric Syrup Sugar and alcohol free 5. Panado Syrup
		1- 5 years	5 - 10 ml (120 mg – 240 mg)	3- 4 times daily (6- 8 hourly)	Four doses (960 mg)	
		6 – 12 years	10 – 20 ml (240 mg- 480 mg)	3- 4 times daily (6- 8 hourly)	Four doses (1 920 mg)	
		12- 18 years	Not listed	Not listed	Not applicable	
Difference		Under 3 months	10 mg/kg	4 hourly	Four doses not longer than 5 days (no quantity listed)	1. Panado Paediatric Syrup Sugar and alcohol free

[1] Pharmacological classification: Analgesic (3), Analgesics and antipyretics (3.2)

[2] Listing is based on fee; hence not all registered products will be reflected

[3] Monthly publication that has abbreviated product labelling information

[4] As per definition in the National Health Act

[5] Multicomponent preparation are not a component of this review

Form	Strength – paracetamol per dosage unit	Age	Dosage (paracetamol quantity)	Frequency	Maximum daily dose	Preparations
Liquid	120 mg per 5 ml	Under 3 months	Not recommended	Not applicable	Not applicable	1. Calpol Paediatric Syrup
		3 – 12 months	2,5 ml at four hourly intervals (60 mg)	3- 4 times daily (6 – 8 hourly)	Not listed	
		1 – 2 years	5 ml at four hourly intervals (120 mg	3 – 4 times daily (6 – 8 hourly)	Not listed	
		3 – 6 years	10 ml at four hourly intervals (240 mg)	3 – 4 times daily (6 – 8 hourly)	Not listed	
		6 – 12 years	Not listed	Not listed	Not applicable	
		12- 18 years	Not listed	Not listed	Not applicable	
Liquid	120 mg per 5 ml	3 – 12 months	2,5 ml – 5 ml (60 mg – 120 mg)	4 – 6 hourly (4- 6 times)	Four doses in 24 hours (480 mg)	1. Panado Paediatric Syrup Strawberry
		1 - 5 years	5 ml – 10 ml (120 mg – 240 mg)	4 – 6 hourly (4- 6 times)	Four doses in 24 hours (960 mg)	
		6 – 12 years	10 ml – 20 ml (240 mg – 480 mg)	4 – 6 hourly (4- 6 times)	Four doses in 24 hours (1 920 mg)	
		12 – 18 years	Not listed	Not applicable	Not applicable	
Liquid	120 mg per 5 ml	3 – 12 months	2,5 ml (60 mg)	6 - 8 hourly	Four doses (240 mg)	1. Go-Pain (syrup)
		1- 6 years	5 – 10 ml (120 mg – 240 mg)	6 – 8 hourly	Four doses (960 mg)	
		7 – 12 years	10 - 20 ml (240 – 480 mg)	6 – 8 hourly	Four doses (1 920 mg)	
		12 – 18 years	Not listed	Not applicable	Not applicable	

Form	Strength – paracetamol per dosage unit	Age	Dosage (paracetamol quantity)	Frequency	Maximum daily dose	Preparations
Liquid	120 mg per 5 ml	3 – 12 months	2,5 ml (60 mg)	4 hourly (6 times)	Four doses (240 mg)	1. Antalgesic Syrup
		1- 6 years	5 ml (120 mg)	4 hourly (6 times)	Four doses (480 mg)	
		7 – 12 years	5 – 10 ml (120 mg- 240 mg)	4 hourly (6 times)	Four doses (960 mg)	
		12- 18 years	Not listed	Not listed	Not applicable	
Liquid	120 mg per 5 ml	3 – 12 months	2,5 ml (60 mg)	3- 4 times daily (6 – 8 hourly)	Four doses per day (240 mg)	1. Woodward's Paracetamol Syrup
		1 – 4 years	2,5 – 5 ml (60 – 120 mg)	3- 4 times daily (6 – 8 hourly)	Four doses per day (480 mg)	
		5- 8 years	5 – 10 ml (120 – 240 mg)	3- 4 times daily (6 – 8 hourly)	Four doses per day (960 mg)	
		9 – 12 years	10 - 15 ml (240 – 360 mg)	3- 4 times daily (6 – 8 hourly)	Four doses per day (1 440 mg)	
		12 – 18 years	Not listed	Not listed	Not applicable	
Liquid	60 mg per 0,6 ml	3 – 12 months	0,6 ml – 1,2 ml (60 mg – 120 mg)	4 hours (6 times)	Four doses in 24 hours (480 mg)	1. Panado Infant Drops

TABLETS: N = 13 (11 + 1 =1)

Form	Strength – paracetamol per dosage unit	Age	Dosage (paracetamol quantity)	Frequency	Maximum daily dose	Preparations
Tablet	500 mg per tablet	Children under 6	Not recommended	Not applicable	Not applicable	1. Antalgesic 500 T Tablets 2. Austell-Paracetamol tablets 3. Painamol tablets 4. Napamol tablets
		6 – 12 years	½ - 1 tablet (250 – 500 mg)	4- 6 hourly (4 – 6 times)	4 tablets in 24 hours (2 g)	
		12 – 18 years	Not listed	Not applicable	Not applicable	
		Adult Assumption: 12-18 years	1 – 2 tablets (500 mg – 1 g)	4- 6 hourly (4 – 6 times)	8 tablets in 24 hours (4 g)	
Tablet	500 mg per tablet	Children under 6	Not recommended	Not applicable	Not applicable	1. Panado tablets
		6 – 12 years	½ - 1 tablet (250 – 500 mg)	4 hourly	Four doses for no longer than 5 days (2 g)	
		12 – 18 years	Not listed	Not applicable	Not applicable	
		Adult Assumption: 12-18 years	*1 tablet, or* 1 – 2 tablets (500 mg – 1 g)	*3 hours,* or 4- 6 hourly	4 g in 24 hours	
Tablet	500 mg per tablet	Not for children under 6 years	Not applicable	Not applicable	Not applicable	1. Paracet Tablets
		6- 12 years	½ - 1 tablet (250 mg – 500 mg)	4 hourly (six times)	Not listed	
		Children over 12 years	1 – 2 tablets (500 mg – 1 g)	4 hourly (six times)	Not listed	
Tablet	500 mg per tablet	Children under 6	Not listed	Not applicable	Not applicable	1. Prolief tablets
		6 – 12 years	½ - 1 tablet (250 – 500 mg)	4 hourly (six times)	4 tablets in 24 hours (2 g)	
		Adults; assumption 12 – 18 years	1 – 2 tablets (500 mg – 1 g)	4 hourly (six times)	8 tablets in 24 hours (4 g)	

Form	Strength – paracetamol per dosage unit	Age	Dosage (paracetamol quantity)	Frequency	Maximum daily dose	Preparations
Tablet	500 mg per tablet	Children under six years	Not listed	Not applicable	Not applicable	1. Varipan tablets
		6- 12 years	½ - 1 tablet (250 – 500 mg)	6 - 8 hourly	4 tablets in 24 hours (2 g)	
		Adult assumption 12 – 18years	1 – 2 tablet (500 mg – 1 g)	6 – 8 hourly	8 tablets in 24 hours (4 g)	
Tablet	500 mg per tablet	Not recommended for children under 12 years	Not applicable	Not applicable	Not applicable	1. Grand-Pa Paracetamol tablets
		Adults assumption 12 – 18 years	1 – 2 tablets (500 mg – 1 g)	4- 6 hourly	4 g	
Difference		-	-	-	No maximum	1. Napamol tablets
Difference		12 years and older	1 tablet (500 mg)	4 – 6 hourly	8 tablets in 24 hours (4 g)	2. Painamol tablets
Meltab	500 mg per tablet	*Adult Assumption: 12-18 years*	1 – 2 tablets (500 mg – 1 g)	4- 6 hourly	8 tablets in 24 hours (4 g)	1. Panado Meltabs
Effervescent tablet	500 mg per tablet	Not for children under 6 years	Not applicable	Not applicable	Not applicable	1. Panado Effervescent tablet
		6 – 12 years	½ - 1 tablet dissolved in water (250 – 500 mg)	Min interval is 4 hours	Four doses in 24 hours (2 g)	
		Adult assumption 12 - 18 years	2 tablets dissolved in water (1 g)	Four times daily	Not listed	

Form	Strength – paracetamol per dosage unit	Age	Dosage (paracetamol quantity)	Frequency	Maximum daily dose	Preparations
Capsules	500 mg per capsule	Not recommended for children under 9 years	Not applicable	Not applicable	Not applicable	1. Panado Capsules
		9 – 12 years	1 capsule (500 mg)	Not specified	4 doses in 24 hours (2 g)	
		Adult: assumption 12 – 18 years	1 – 2 capsules (500 mg – 1 g)	4 hourly	8 capsules in 24 hours (4 g)	
Meltab	125 mg per tablet	1 – 5 years	1 – 2 tablets (125 mg – 250 mg)	4 hours	Four doses in 24 hours maximum of 5 days (1 g)	1. Panado Children Meltabs
		Older than 5 years	Not listed	Not applicable	Not applicable	

RECTAL: N = 1

Form	*Strength*	*Age*	*Dosage (paracetamol quantity)*	*Frequency*	*Maximum daily dose*	*Preparations*
Suppository	125 mg or 250 mg	3 – 12 months	125 mg	3 - 4 times daily	500 mg	1. Empaped 125 mg and 250 mg (suppository)
		1- 5 years	250 mg	3- 4 times daily	1 000 mg	
		Alternate: 10 mg/kg	Not applicable	3 – 4 times daily	Not listed	
		If jaundices: 5 mg/kg	Not applicable	3 – 4 times daily	Not listed	

INTRAVENOUS: N = 2

Form	Strength	Age	Dosage (paracetamol quantity)	Frequency	Maximum daily dose	Preparations
IV Solution	1 g per 100 ml	Children between 33 – 50 kg	15 mg/kg (1,5 ml/kg) over 15 minutes	4 times daily with min of 4 hours between doses	60 mg/kg not exceeding 4 g	1. Perfalgan Solution for infusion
		Adolescent over 50 kg	1 g	4 times daily with min of 4 hours between doses	4 g	
IV Solution	10 mg per 1 ml	1 year and older with weight less than 33 kg (approximately 11 years)	15 mg/kg	4 times daily with min of 4 hours between doses	60 mg/kg	1. Perfalgan Paediatric Solution for infusion
		Children up to the age of years	Not listed	Not applicable	Not applicable	

Summary of overdose information of paracetamol containing products

South Africa

Number	Component in package insert	MCC Package inserts for human use	Product
7	Yes	Yes	1. Calpol Paediatric Syrup 2. Grand-Pa Paracetamol tablets 3. Panado Children meltabs 4. Panado Meltabs 5. Panado Paediatric Syrup 6. Panado Paediatric Syrup Alcohol and sugar free 7. Panado tablets
13	Yes	No	1. Adco Paracetamol Syrup 2. Adco-Napamol Elixir 3. Empaped 4. Go-Pain Syrup 5. Napamol Tablets 6. Painamol Syrup 7. Painamol Tablets 8. Panado Capsules 9. Panado Effervescent Tablets 10. Panado Infants Drops 11. Panado Paediatric Syrup Strawberry 12. Perfalgan 13. Perfalgan paediatric 14. Woodward's Paracetamol Syrup
unknown	Product labelling could not be obtained; MIMS information is abbreviated and summarised		1. Austell Paracetamol 2. Prolief Tablets 3. Varipan tablets
	No longer listed in MIMS (08/2013)		1. Antalgesic Syrup 2. Antalgesic T Tablets 3. Paracet tablets
21 evaluated			27

PROFESSIONAL SURVEY: PARACETAMOL IN CHILDREN 12 YEARS AND UNDER

	Respondent	1	2	3	4	5	No.	Percentage
	Response							
1		Do you PRESCRIBE paracetamol as first line treatment						
	Yes	x	x	x	x	x	5	100
	No	n/a	n/a	n/a	n/a	n/a	0	0
2		What is the dose that you recommend						
	Open question	2 yr / 6 yr	As per package insert	6 yr/ 12 yr	2 yr / 6 yr	As per package insert		0
		1 tsp / not syrup		5 ml / 10 ml	5 ml / 10 ml			0
		1/2 tablet child swallow						
3		What is the frequency of the dose						
	4 hours	n/a	n/a	n/a	n/a	As prescribed by doctor	0	0
	6 hours	x	x	x	x		4	80
	8 hours	n/a	n/a	n/a	n/a		0	0
							1	20
4		Do you look at the package insert of the product that						
	Yes	x	x	n/a	x	x	4	80
	No	n/a	n/a	x	n/a	n/a	1	20
5		When last have you looked at the package insert						
	Last month	n/a	x	n/a	n/a	x	2	40
	Last 3 months	x	n/a	n/a	n/a	n/a	1	20
	Last 12 months	n/a	n/a	x	x	n/a	2	40
	> 12 months ago	n/a	n/a	n/a	n/a	n/a	0	0
6		Do you hand out a medicine measure						
	No	x	x	n/a	n/a	x	3	60
	Yes	n/a	n/a	x	x	n/a	2	40
7		Do you ask if the caregiver has an adequate dispensing device (medicine measure) to dose the child						
	Yes	x	x	x	x	n/a	4	80
	No	n/a	n/a	n/a	n/a	x	1	20
		Comments shared						
		Syrup not effective for 6 yr for pain As soon child swallow prefer solid dosage form	Baby hand out syringe always.	Prefer to give syrup. Product as advertised on TV		Doctor tend prescribe 4 to 6 hourly		

Aadila Patel

		Not effective for migraine	devices need to procured as a separate item			Sometimes ask about device and hands out		

CAREGIVER SURVEY: PARACETAMOL IN CHILDREN 12 YEARS AND UNDER

	Respondent	1	2	3	4	5	6	7	8	9	10	No.	Percentage
	Response												
1		Why do you give your child (or child under your care) paracetamol?											
	Pain	x	x	x	x	x	x	x	x	x	x	10	100
	Fever	x	x	x	x	x	x	x	x	x	x	10	100
	Other	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0	0
2		Do you use paracetamol as first line of treatment											
	Yes	x	x	x	x	x	x	x	x	x	x	10	100
	No	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a		0
3		What is the dose that you give to the child											
	Open question	4 yr / 10 yr	All ages	2 year	2 year	All ages	2 year	6 yr / 8 yr	3, 5 years	2 year	5 yr /10 yr		
		1 tsp / 2 tsp	As per directions	Pharma-cist recommend ation	1 tsp	5 ml	5 ml	7,5 ml / 10 ml	1 tsp	5 ml	1 tsp / 10 ml		
4		How often do you give the child paracetamol											
	4 hours	x	n/a	n/a	n/a	n/a	n/a	n/a	x	x	n/a	3	30
	6 hours	n/a	x	x	n/a	x	n/a	x	n/a	n/a	n/a	4	40
	8 hours	n/a	n/a	n/a	x	n/a	x	n/a	n/a	n/a	x	3	30
5		Do you look at the package insert of the product before giving the paracetamol syrup											
	Yes	x	x	x	x	n/a	n/a	x	x	x	x	8	80
	No	n/a	n/a	n/a	n/a	x	x	n/a	n/a	n/a	n/a	2	20
6		When last have you looked at the package insert											
	Last month	n/a	x	x	x	n/a	n/a	x	x	x	x	7	70
	Last 3 months	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0	0
	Last 12 months	x	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1	10
	> 12 months ago	n/a	n/a	n/a	n/a	x	x	n/a	n/a	n/a	n/a	2	20

Aadila Patel

7		How do you give the child paracetamol											
	Teaspoon	x	n/a	n/a	x	n/a	x	n/a	x	x	x	6	60
	Tablespoon	n/a	x	n/a	n/a	x	n/a	x	n/a	n/a	n/a	3	30
	Medicine measure	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0	0
	Syringe	n/a	n/a	x	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1	10
8		Do you tell the pharmacist or doctor if you think that the product is not working											
	Yes	n/a	x	n/a	x	x	n/a	n/a	n/a	n/a	n/a	3	30
	No	n/a	n/a	x	n/a	n/a	x	x	x	x	x	6	60
												1	10
9		For how long do you use paracetamol before you go to seek the advice of your pharmacist or											
	3 - 5 days	x		x	x	x	x	x	x	x	x	9	90
	10 days	n/a		n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0	0
	Other	n/a	After 24 hrs	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1	10
		Comments shared											
		works all the time					Grow up with originator				works all the time		

Abbreviations:
tsp : teaspoon
yr: year
hrs: hours