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	Doc No. BML/PCM/S008	Date rev 06/2020	Next rev date: 05/2025

Summary of Product Characteristics

For

Biomedical Paracetamol syrup

1. Name of Medicinal Product

Biomedical Paracetamol syrup

2. QUALITATIVE AND QUANTITATIVE DESCRIPTION

Each 5ml of the syrup contains
Paracetamol BP 120mg

3. PHARMACEUTICAL FORM

Pink-colored non-viscous liquid oral preparation presented as sugar-based syrup and flavored in 60ml amber-colored bottle with dose measurement cap to facilitate easy dosing

4. Clinical Particulars

4.1 Therapeutic indications

Mild to moderate pain and reduction of fever.

4.2 Posology and method of administration

Post-immunization pyrexia:60mg followed by a second dose if necessary 4-6 hour later.

Under 1yr	2.5ml-5mlthree or four times daily
1-5yrs	5-10mlthree or four times daily
6-12yrs	10-20mlthree or four times daily

Or as directed by the physician

4.3 Contraindications

Hypersensitivity to paracetamol or to any of the excipients

4.4 Special warnings and precautions for use

Paracetamol should be given with care in patient with impaired kidney or renal function.it should be given with care to patient with alcohol dependence. Paracemol should not be taken than it is prescribed. should not be given to babies less than 2

months of age. For infants 2-3months no more than 2 doses should be given. Do not give more than 4 doses in any 24 periods. Leave at least 4 hours between doses.do not give this medicine to your child for more than 3 days without speaking to your pharmacist or doctor. Seek immediate medical advice in case of overdose.

4.5 Interaction with other medicinal products and other forms of interaction
Paracetamol is hepatotoxic when overdose is taken. Drugs, such as barbiturates, tricyclic antidepressants and alcohol which induce liver microsomal enzymes may increase the toxicity. Chronic alcoholic intake may also increase the toxicity.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.

Regular use of paracetamol possibly reduces metabolism of Zidovudine.

4.6 Pregnancy and lactation

Pregnancy

Paracetamol is generally considered to be the analgesic of choice in pregnant patients. However, the frequent use of paracetamol (defined as most days or daily use) in late pregnancy may be associated with an increased risk of persistent wheezing in the infant. The authors emphasized that the number of pregnant women taking frequent doses was very small and they recommended that infrequent paracetamol should remain the analgesic of choice in pregnancy.

Breastfeeding.

No adverse effects have been observed in breast-feeding infants whose mothers were receiving paracetamol, and the American Academy of Pediatrics considers that it is therefore usually compatible with breast feeding. The British National Formulary also considers that the amount of paracetamol distributed into breast milk is too small to be harmful to a breast-fed infant.

Pharmacokinetic studies in 12 nursing mothers given a single dose of paracetamol showed that peak paracetamol concentrations in breast milk of 10 to 15 micrograms/mL were achieved in 1 to 2 hours. Plasma concentrations were

determined in 2 mothers; a breast milk/plasma ratio of about 1 was reported. Similar findings have been reported from other studies.

4.7 Undesirable effects

Side-effects of paracetamol are rare and usually mild, although hematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia, and agranulocytosis have been reported. Skin rashes, and other hypersensitivity reactions occur occasionally.

Over dosage with paracetamol can result in severe liver damage and sometimes acute renal tubular necrosis. Prompt treatment with acetylcysteine or methionine is essential and is discussed under Overdosage

4.8 Overdose

Acute overdosage with paracetamol, whether accidental or deliberate, is relatively common and can be extremely serious because of the narrow margin between therapeutic and toxic doses. Ingestion of as little as 10 to 15 g of paracetamol by adults may cause severe hepatocellular necrosis and, less often, renal tubular necrosis. Patients should be considered at risk of severe liver damage if they have ingested more than 150 mg/kg of paracetamol or 12 g or more in total, whichever is the smaller. The risk of severe toxicity after acute paracetamol overdose appears to be less in children than in adults at comparable doses; however, chronic use of supratherapeutic doses in children has resulted in unintentional overdoses and severe hepatotoxicity.

Management of Paracetamol Overdose.

Prompt treatment is essential, even when there are no obvious symptoms, and all patients should be admitted to hospital; full supportive measures should also be instituted.

Activated charcoal may be used to reduce gastrointestinal absorption, if it can be given within 1 hour of the overdose, and if more than 150 mg/kg of paracetamol has been ingested. However, if acetylcysteine or methionine is to be given by mouth the charcoal is best cleared from the stomach to prevent it reducing the absorption of the antidote

There is little evidence that gastric lavage is of benefit in those who have overdosed solely with paracetamol

The plasma-paracetamol concentration should be determined as soon as possible, but not within 4 hours of ingestion, to ensure that peak concentrations are recorded. The risk of liver damage is determined by comparison with a nomogram reference line on a plot of plasma-paracetamol concentration against hours after ingestion. A semi-logarithmic plot or a linear plot may be used. Generally, antidote treatment is required if the patient's plasma-paracetamol concentration is higher than the appropriate line (but see below)

Patients receiving enzyme-inducing drugs such as carbamazepine, phenytoin, phenobarbital, rifampicin, and hypericum, or those with malnutrition or a history of alcohol abuse, are considered at high risk, and should receive an antidote even if their plasma-paracetamol concentrations are up to 50% below the standard reference line

Plasma-paracetamol concentrations measured more than 15 hours after ingestion are not reliable indicators of hepatic toxicity. Furthermore, the nomogram may not be suitable for use when patients have taken modified-release preparations of paracetamol.

Plasma-paracetamol concentrations are also of little value in patients who have taken several overdoses of paracetamol over a short period of time: such patients should be considered as at serious risk and given antidote treatment

Deaths from liver failure have occurred in patients presenting with plasmaparacetamol concentrations below the treatment line: suggested explanations include inadequate patient histories and a need for a lower treatment threshold.

If there is any doubt about timing or the need to treat, then a patient should be treated with an antidote. In some centres, patients who have ingested 150 mg/kg or more of paracetamol are treated regardless of plasma-paracetamol concentrations.

Antidote treatment should be started as soon as possible after suspected paracetamol ingestion and should not be delayed while awaiting the results of plasma assays. Once the results become available, treatment may be stopped if the initial concentration was below the nomogram reference line. However, if the initial concentration is above the reference line, the full course of antidote must be given and should not be stopped when subsequent plasma concentrations fall below the reference line.

Choice of antidote. Acetylcysteine is usually the antidote of choice but the route of administration varies, and the best protocol has yet to be determined. Intravenous use has been associated with anaphylactic reactions but is the preferred route in the UK

Methionine, like acetylcysteine, is most effective when given as early as possible following paracetamol overdosage. However, it is not as effective if treatment is delayed.

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and hepatic damage is more frequent and severe if treatment with methionine is started more than 10 hours after ingestion; it may also precipitate hepatic encephalopathy.5

The usual dose of methionine in adults and children over 6 years is 2.5 g by mouth every 4 hours for 4 doses starting less than 10 to 12 hours after ingestion of the paracetamol and provided the patient is not vomiting. Children under 6 years should be given 1 g every 4 hours for 4 doses. It has also been given intravenously

5. PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

the mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system and to a lesser extent through the peripheral action by blocking pain impulse generation. Paracetamol also produces antipyretic by acting on the hypothalamic heat regulating center to produce peripheral vasodilation resulting in increased blood flow through the skin sweating and heat loss.

Pharmacokinetics

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. The elimination half-life of paracetamol varies from about 1 to 3 hours.

Paracetamol is metabolized predominantly in the liver and excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. A minor hydroxylated metabolite (N-acetyl-pbenzoquinoneimine), is usually produced in very small amounts by cytochrome P450 isoenzymes (mainly CYP2E1 and CYP3A4) in the liver and kidney. It is usually detoxified by conjugation with glutathione but may accumulate following paracetamol overdosage and cause tissue damage.

Absorption.

Absorption of paracetamol was slow and incomplete in vegetarian subjects compared with non-vegetarian subjects.

6. Pharmaceutical Particulars

6.1. List of Excipients

Ethanol 96%BP, Sodium carboxyl methyl cellulose BP, Sucrose BP, Sodium benzoate BP, Strawberry flavor BP, Propylene glycol BP, Allura red BP

6.2 Incompatibilities

None

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in temperature not more than 30^{o}C.

Replace cap after use and store away from light.

6.5 Nature and contents of container

60ml pack size amber plastic bottle

7. Marketing Authorization Holder

Biomedical Limited

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