Applicant: Oethmaan Biosims (Pty) Ltd	**SAHPRA approval date:** 28 February 2022
Product: OBIDENT 500 TABLETS	**Dosage form and strength:** Each tablet contains: 500 mg Paracetamol

SCHEDULING STATUS:

S0 Pack of 20 tablets

S1 Pack of 100 and 5000 tablets

1. NAME OF THE MEDICINE:

OBIDENT 500 TABLETS, tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each tablet contains 500 mg paracetamol.

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Green, round, flat, beveled edge tablets, plain on one side and break line on the other side.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications

The relief of mild to moderate pain and fever such as headaches, toothache and pain associated with colds and flu.

4.2 Posology and method of administration

DO NOT EXCEED THE RECOMMENDED DOSE

Posology

Children 6 – 12 years: ½ - 1 tablet every 6 hours. Not more than 4 doses to be taken in any 24-hour period.

Children over 12 years: 1 tablet every 4 – 6 hours. Not more than 4 tablets to be taken in any 24-hour period.

Adults: 1 – 2 tablets every 4 – 6 hours. Not more than 8 tablets to be taken in any 24-hour period.

Paediatric population:

Children under 6 years: Not recommended.

Method of administration

OBIDENT 500 TABLETS should be taken orally. The tablets should be swallowed with liquid and should not be chewed.

4.3 Contraindications

OBIDENT 500 TABLETS is contraindicated in the following:

- Hypersensitivity to paracetamol, or any of the other ingredients in OBIDENT 500 TABLETS (see section 6.1).
- Severe liver function impairment (see section 4.4).

4.4 Special warnings and precautions for use

OBIDENT 500 TABLETS contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Centre must be contacted immediately.

- Dosages in excess of those recommended may cause severe liver damage.
- Consult a doctor or pharmacist if pain or fever persists or gets worse at the recommended dosage, or if new symptoms occur.
- Do not use OBIDENT 500 TABLETS continuously without consulting a medical practitioner:

  Pain – for more than 7 days in adults (5 days for children); and

Fever – for more than 3 days.

- Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease should not take excessive quantities of OBIDENT 500 TABLETS.
- Caution is recommended in patients with moderate renal failure and patients on dialysis, as plasma concentrations of OBIDENT 500 TABLETS and its conjugates are increased.
- Use with caution in renal impairment, chronic malnutrition or dehydration.
- Caution should be exercised in patients with glutathione depleted states, as the use of paracetamol may increase the risk of metabolic acidosis.
- Use with caution in patients with glutathione depletion due to metabolic deficiencies.

4.5 Interaction with other medicines and other forms of interaction

Hepatotoxic medicines (e.g. rifampicin and isoniazid): Increased risk of hepatotoxicity.

Enzyme-inducing medicines (e.g. carbamazepine): Increased risk of hepatotoxicity and possible decrease in therapeutic effects of OBIDENT 500 TABLETS.

Metoclopramide: Absorption of OBIDENT 500 TABLETS may be accelerated.

Probenecid: Pre-treatment with probenecid can decrease OBIDENT 500 TABLETS clearance, and increase its half-life.

Cholestyramine: Absorption of OBIDENT 500 TABLETS is reduced if given within one hour of cholestyramine.

Salicylates (e.g. aspirin): Prolonged concurrent use of OBIDENT 500 TABLETS with salicylates increases the risk of adverse renal effects.

Antibiotics: Chronic use of isoniazid, an antibiotic medicine often prescribed for tuberculosis, may increase the risk of liver damage when combined with OBIDENT 500 TABLETS, even at recommended doses.

Warfarin: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Fertility, pregnancy and lactation

Pregnancy

OBIDENT 500 TABLETS is generally considered safe for use in pregnant patients, if used infrequently (not daily or on most days).

Breastfeeding

OBIDENT 500 TABLETS is distributed into breastmilk, in amounts too small to be considered harmful to a breastfed infant. No significant adverse effects have been seen in breastfed infants whose mothers received paracetamol.

Fertility

There is no data on adverse effects on male or female fertility.

4.7 Effects on ability to drive and use machines

OBIDENT 500 TABLETS is expected to have no or negligible influence.

4.8 Undesirable effects

System Organ Class	Adverse reaction	Frequency
Blood and lymphatic system disorders	Neutropenia, pancytopenia, leucopenia, thrombocytopenia, agranulocytosis, anaemia.	Less frequent
Immune system disorders	Anaphylaxis. Hypersensitivity reactions (characterised by urticaria, dyspnoea and hypotension). Angioedema.	Less frequent
Respiratory, thoracic and mediastinal disorders	Bronchospasm - more likely in asthmatics sensitive to aspirin or other NSAIDS.	Less frequent
Gastrointestinal disorders	Pancreatitis.	Less frequent
Hepatobiliary disorders:	Hepatitis, hepatic dysfunction.	Less frequent
Renal and urinary disorders	Renal colic, renal failure, sterile pyuria.	Less frequent
Skin and subcutaneous tissue disorder	Skin rashes. Skin rashes are usually erythematous or urticarial, but sometimes more serious and may be accompanied by fever and mucosal lesions. Dermatitis.	Less frequent

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Medicine Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose:

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. A delay in starting treatment may mean that the antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 – 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning, do not reflect the potential seriousness of the overdosage.

Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.

Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

After maternal overdosage during pregnancy, foetal metabolism of paracetamol that crosses the placenta can produce hepatotoxic metabolites, causing foetal hepatotoxicity.

Treatment for paracetamol overdosage:

Although evidence is limited it is recommended that any adult person who has ingested 5 - 10 grams or more of paracetamol (or a child who has had more than 140 mg/kg) within the preceding four hours, should have the stomach emptied by lavage (emesis may be adequate for children) and a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning (see above). In patients who are stuperose or comatose endotracheal intubation should precede gastric lavage in order to avoid aspiration.

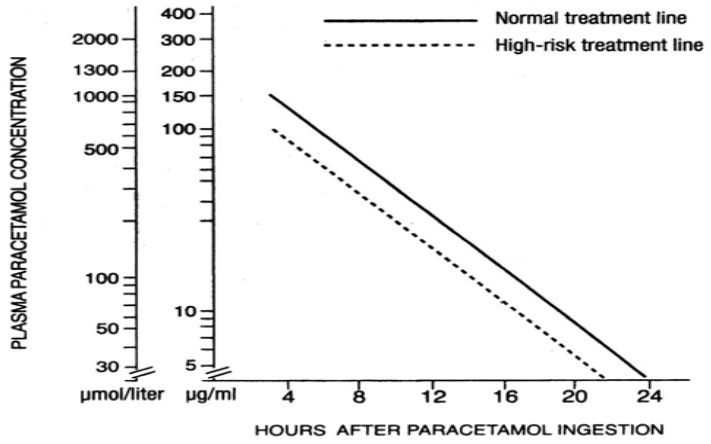
N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken.

IV: An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given **intravenously** over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next sixteen hours. **The volume of intravenous fluid should be modified for children.**

Oral: Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours may be misleading.

Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below.



** Nomogram reproduced from the Guidelines for the Management of Acute Paracetamol Overdose produced by the Medicines Information Centre, UCT.*

The nomogram should be used only in relation to a single acute ingestion. Those, whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations are above the “high risk treatment line” (*refer to paracetamol nomogram above)*. Prothrombin index correlates best with survival.

Monitor all patients with significant ingestions for at least ninety-six hours.

Hepatic tests must be carried out at the beginning of treatment and repeated every 24 hours. In most cases hepatic transaminases return to normal in one to two weeks with full restitution of the liver function. In very severe cases, however, liver transplantation may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 2.7 Antipyretics or antipyretic and anti-inflammatory analgesics

ATC Code: N02BE01

Paracetamol has analgesic and antipyretic activity.

5.2 Pharmacokinetic properties

Absorption:

Paracetamol is readily absorbed from the gastrointestinal tract, with peak plasma concentrations occurring approximately 10 – 60 minutes after oral doses.

Distribution:

Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk.

Biotransformation:

Paracetamol is mainly metabolised in the liver, following two major hepatic pathways: glucuronic acid conjugation and sulphuric acid conjugation.

Elimination:

The metabolites of paracetamol are mainly excreted in the urine. Less than 5 % is excreted as unchanged paracetamol.

The elimination half-life of paracetamol varies from about 1 – 3 hours.

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica, dioctyl sodium sulphosuccinate, magnesium stearate, maize starch, polyvinylpyrrolidone.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store at or below 30 °C.

Protect from light and moisture.

Store in the original package/container.

Keep the blister in the carton until required for use.

6.5 Nature and contents of container

OBIDENT 500 TABLETS is packed in a blister comprising of plain aluminium foil with VMCH coating and clear transparent PVC film and placed in a preprinted carton along with a patient information leaflet. Pack sizes: 20 and 100 tablets.

White polypropylene container with a white polypropylene lid containing 5000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Oethmaan Biosims (Pty) Ltd

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Greenacres Office Park

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Victory Park

Johannesburg

2195

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8 REGISTRATION NUMBER(S):

47/2.7/0931

9 DATE OF FIRST AUTHORISATION

Date of registration: 28 February 2022

10 DATE OF REVISION OF THE TEXT

Not applicable