1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

PYNSPAS 150 mg/500 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of PYNSPAS contains 150 mg mephenesin and 500 mg paracetamol.

Sugar free.

Sodium 1,31 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

PYNSPAS is a round, white to off-white, flat bevelled edged, bisected uncoated tablet debossed with 'F' and '41' on either side of bisect and plain on the other side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

PYNSPAS tablets are indicated for generalised pain associated with tension.

4.2. Posology and method of administration

Posology

DO NOT EXCEED THE RECOMMENDED DOSE

Adults (18 years and older):

Take one to two tablets every four hours. The maximum dosage is eight tablets per day, for 10 days.

The lowest effective dose for the shortest possible duration of treatment should be used.

Do not use continuously for more than 10 days.

Paediatric population

No data are available on the use of PYNSPAS in children and adolescents.

Method of administration

For oral administration.

4.3. Contraindications

PYNSPAS is contraindicated in:

- Patients with hypersensitivity to mephenesin, paracetamol or to any excipients in PYNSPAS (see section 6.1).
- Impaired kidney and liver function.
- Pregnancy and lactation as safety has not been proven (see section 4.6).

4.4. Special warnings and precautions for use

PYNSPAS 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 (see section 4.9).

Dosage in excess of those recommended may cause severe liver damage.

Concomitant use with other paracetamol-containing products, such as PYNSPAS, should be avoided as there may be an increased risk of serious adverse effects (see section 4.8).

Mephenesin, as contained in PYNSPAS, may cause drowsiness; patients that are affected should not drive or operate machinery (see sections 4.7 and 4.8).

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines, like PYNSPAS (see section 4.8). If a patient develops SCAR, treatment with PYNSPAS must immediately be discontinued and appropriate treatment instituted.

Patients should be advised to consult a doctor if they suffer from non-serious arthritis and need to take painkillers every day.

Paediatric population

See section 4.2.

PYNSPAS contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodiumfree’.

4.5. Interaction with other medicines and other forms of interaction

Mephenesin

Mephenesin may enhance the effects of barbiturates and opioids.

Paracetamol

Alcohol

Alcohol reduces liver capacity to deal with paracetamol.

Warfarin

Chronic use of paracetamol as contained in PYNSPAS enhances effect of warfarin with increased risk of bleeding; occasional doses have no significant effect.

Colestyramine

Colestyramine reduces absorption of paracetamol as contained in PYNSPAS. Therefore, the colestyramine should not be taken within one hour if maximal analgesia is required.

Metoclopramide and domperidone

Metoclopramide and domperidone accelerate absorption of paracetamol as contained in PYNSPAS. Concurrent use need not be avoided.

Chloramphenicol

May interact with chloramphenicol causing increased plasma levels of chloramphenicol.

Flucloxacillin

Caution is advised if paracetamol, as contained in PYNSPAS, is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily

doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

4.6. Fertility, pregnancy and lactation

The use of PYNSPAS is contraindicated in pregnancy and lactation (see section 4.3).

4.7. Effects on ability to drive and use machines

PYNSPAS has moderate influence on the ability to drive and use machinery. PYNSPAS can cause drowsiness (see sections 4.4 and 4.8).

Patients who experience drowsiness should avoid driving or using machinery.

4.8. Undesirable effects

a) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Blood and the lymphatic system disorders			Leucopoenia, thrombocytopenia, neutropenia, pancytopenia, agranulocytosis, anaemia
Immune system disorders			Hypersensitivity, anaphylactic shock, angioedema, allergic reactions
Nervous system disorders			Drowsiness
Cardiac disorders			Tachycardia, low blood pressure
Respiratory, thoracic and mediastinal disorders			Bronchospasm
Gastrointestinal disorders			Anorexia, nausea, vomiting, acute pancreatitis, abdominal pain
Hepatobiliary disorders			Hepatic dysfunction

Skin and subcutaneous tissue disorders			Skin rashes and other allergic reactions. The rash is usually erythematous or urticarial but sometimes more serious and may be accompanied by fever and mucosal lesions. Severe cutaneous adverse reactions (SCARs) such as Toxic Epidermal Necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS), fixed drug eruption (FDE), facial oedema, pruritus, dyspnea, general oedema without skin eruption, cutaneous eruptions like contact dermatitis and erythema multiform like eruptions (see section 4.4)
General disorders and administrative site conditions			Lassitude, fever

b) Description of selected adverse reactions

There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Post marketing data for paracetamol, as contained in PYNSPAS, has reported Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) as an undesirable effect with unknown frequency (see section 4.4).

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 providers are asked to report any suspected adverse reactions to:

SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Mephenesin

Symptoms

Overdosage may produce nystagmus, blurred vision and motor in-coordination; in gross overdosage there may be hypotonia, a fall in blood pressure and respiratory paralysis.

Treatment

Treatment is symptomatic and supportive.

Paracetamol

Symptoms

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 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 to 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 dysrhythmias have been reported.

Treatment

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. 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.**

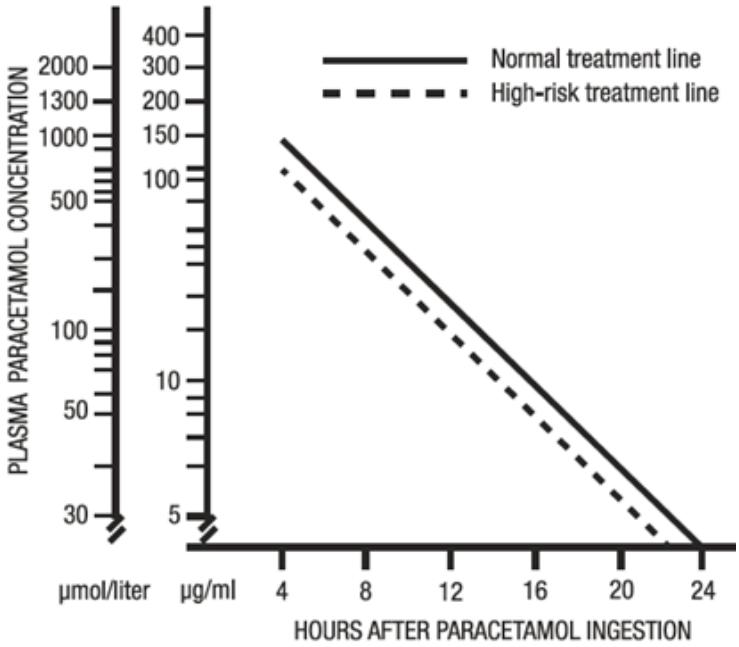
Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

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. 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”. Prothrombin index correlates best with survival.

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



5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A 2.8 Analgesic combinations

Pharmacotherapeutic group: Other analgesics

ATC Code: N02BG other analgesics and antipyretics

Mechanism of action

Combination of the analgesic and antipyretic properties of paracetamol with the skeletal muscle relaxant effect of mephenesin.

Mephenesin

Mephenesin is a skeletal muscle relaxant.

Paracetamol

Paracetamol is an effective analgesic and antipyretic medicine but has only weak anti-inflammatory properties. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system and to a lesser extent, through a peripheral action by blocking pain-impulse generation. This inhibition appears to be on a selective basis.
The peripheral action may also be due to inhibition of prostaglandin synthesis or to the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.
Antipyretic- paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulation centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss.
The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

5.2. Pharmacokinetic properties

Mephenesin

No data.

Paracetamol

Absorption

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring in 30 to 60 minutes.

Distribution

Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of the medicine to plasma proteins is variable; 20 to 30 % may be bound at the concentrations encountered during acute intoxication.

Biotransformation and Elimination

The elimination half-life varies from about 1 to 4 hours after therapeutic doses. Following therapeutic doses 90 to 100 % of the medicine may be recovered in the urine within the first day. However, practically no paracetamol is excreted unchanged and the bulk is excreted after hepatic conjugation.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Calcium hydrogen phosphate anhydrous, carmellose sodium (sodium carboxymethyl cellulose), colloidal anhydrous silica (aerosil 200), maize starch B, magnesium stearate, purified talc, sodium starch glycolate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store or at below 25 °C.

Keep in original packaging until required for use.

6.5. Nature and contents of container

24 tablets (3 x 8’s or 2 x 12's) are packed in a clear rigid PVC film coated with PVdC and plain aluminium foil. Blister strips are packed in an outer cardboard carton.

100 tablets are packed in a white HDPE bottle with a screw cap with induction wad.

Not all packs or pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

56/2.8/0309

9. DATE OF FIRST AUTHORISATION

12 March 2024

10. DATE OF REVISION OF TEXT

12 March 2024

Die Afrikaanse Professionele Inligting is op versoek beskikbaar.

Mediese Blitslyn: 0800 118 088.

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