SCHEDULING STATUS

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1 NAME OF THE MEDICINE

PANADO CAPSULES, 500 mg, Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 500 mg paracetamol.

Sugar free

Potassium sorbate 0,12 % *m/m* (preservative)

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules.

A hard gelatin capsule, size No. 0, opaque white body and cap, with "Panado 500" printed in red on cap and body.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For 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

Adults: One or two capsules repeated every 3 to 4 hours if necessary, but not more than 8 capsules to be taken in any 24 hour period.

Paediatric population

Children 9 to 12 years: One capsule repeated every 3 to 4 hours if necessary, but not more than 4 doses in any 24 hour period.

Children under 9 years: Not recommended.

Method of administration

For oral use.

The capsule should be swallowed with a glass of water.

4.3 Contraindications

- Hypersensitivity to paracetamol or to any of the excipients of PANADO CAPSULES listed in section 6.1.
- Severe liver function impairment.

4.4 Special warnings and precautions for use

PANADO CAPSULES contain 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.
Prolonged or frequent use is discouraged. Do not use continuously for more than 10 days without consulting a doctor.

Patients should be advised not to take other paracetamol containing medicines concurrently.
Consult a doctor if no relief is obtained from the recommended dosage or in cases of high fever, signs of a secondary infection, or persistence of the symptoms for more than three days.

Patients suffering from liver or kidney disease should take PANADO CAPSULES under medical supervision. Caution is advised in the administration of PANADO CAPSULES to patients with acute hepatitis, concomitant treatment with medicines affecting hepatic functions, glucose-6-phosphatedehydrogenase deficiency, haemolytic anaemia, alcohol abuse, chronic dehydration and malnutrition.

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. Alcohol must not be used during treatment period. The daily dose should not exceed 2 grams in such case.

After prolonged use (> 3 months) of analgesics intake every day or more often, headaches may occur or worsen. Headaches caused by overuse of analgesics should not be handled by increasing the dose. In

those cases, the use of analgesics should be taken after consulting a doctor.

Caution is advised in asthmatic patients sensitive to aspirin (acetylsalicylic acid), because light reaction bronchospasm with paracetamol (cross-reaction) has been reported.

Self-medication with paracetamol should be limited when taking anticonvulsants because with the concomitant use of both, liver toxicity is potentiated and the bioavailability of paracetamol is reduced, especially when using high-doses of paracetamol (see section 4.5).

Caution is advised if PANADO CAPSULES 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.

Severe cutaneous adverse reactions (SCARs):

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

Paediatric population

Children under 9 years: Not recommended (see section 4.2).

4.5 Interaction with other medicines and other forms of interaction

Hepatotoxic medicines: Increased risk of hepatotoxicity of paracetamol, as contained in PANADO CAPSULES.

Metoclopramide and domperidone: Absorption of PANADO CAPSULES may be accelerated.

Cholestyramine: Absorption of PANADO CAPSULES is reduced if given within one hour of cholestyramine.

Salicylates: Salicylamide may prolong the elimination t ½ of paracetamol.

Prolonged concurrent use of PANADO CAPSULES with salicylates increases the risk of adverse renal effects.

Warfarin and anticoagulants: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol (e.g., PANADO CAPSULES) with increased risk of bleeding; occasional doses have no significant effect.

Concurrent, chronic, high-dose administration of PANADO CAPSULES may increase the anticoagulant effect.

Paracetamol, as contained in PANADO CAPSULES, is recommended as the general analgesic and antipyretic of choice in patients on oral anticoagulant therapy. However, caution is needed since, although it has no effect on the gastric mucosa or on platelet function, some studies (with warfarin, anisindione, dicoumarol, or phenprocoumon) and isolated reports have found an increased risk of bleeding in patients taking regular doses of paracetamol while on an oral anticoagulant. An increase in INR has also been reported in controlled studies of the use of paracetamol in patients stabilised on warfarin. Increased monitoring of anticoagulant therapy may be appropriate for those also taking paracetamol, as contained in PANADO CAPSULES, regularly.

Enzyme-inducing medicines: Increased risk of hepatotoxicity of paracetamol, as contained in PANADO CAPSULES. Possible decrease in therapeutic effects of PANADO CAPSULES.

Paracetamol (i.e., PANADO CAPSULES) is extensively metabolised in the liver and can therefore interact with medicines with the same metabolic pathway or induce/inhibit the same metabolic pathway.

Chronic use of alcohol or medicines which induce liver enzymes, such as rifampicin, barbiturates, some anti-epileptic medicines (e.g., carbamazepine, fosphenytoin, phenytoin, phenobarbital, primidone), tricyclic antidepressants and St. John's wort can increase the hepatotoxicity of PANADO CAPSULES as a result of an increased and fast formation of toxic metabolites. Caution is therefore necessary with concomitant use of enzyme-inducing medicines.

Alcohol: Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have

contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

Antiepileptics and oral contraceptives: The use of medicines that induce hepatic microsomal enzymes such as anticonvulsants and oral contraceptives may increase the extent of metabolism of paracetamol, as contained in PANADO CAPSULES, resulting in reduced plasma concentrations of paracetamol and a faster elimination rate. The plasma-paracetamol concentrations considered an indication for antidote treatment, should be halved in patients receiving enzyme inducing medicines such as carbamazepine, phenobarbital, phenytoin, or primidone.

Paracetamol, as contained in PANADO CAPSULES, may decrease the bioavailability of lamotrigine, with possible reduction of its effect, due to a possible induction of its metabolism in the liver.

Probenecid: Probenecid blocks the binding of paracetamol to glucuronic acid reducing paracetamol clearance by a factor of about 2 and increase its plasma half-life. Although urinary excretion of the sulphate and glucuronide conjugates of paracetamol are reduced, that of paracetamol is unchanged. If probenecid is taken concurrently, the PANADO CAPSULES dose should be reduced.

Antibacterials: The plasma-paracetamol concentrations considered an indication for antidote treatment should be halved in patients receiving enzyme-inducing medicines such as rifampicin.

Isoniazid reduces the paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibition of its metabolism in the liver. Severe hepatotoxicity at therapeutic doses or moderate overdoses of paracetamol has been reported in patients receiving isoniazid, alone or with other medicines for tuberculosis.

PANADO CAPSULES can increase the plasma concentration of chloramphenicol.

Caution should be taken when paracetamol, as contained in PANADO CAPSULES, is used concomitantly with flucloxacillin, as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risk factors (see section 4.4).

Antivirals: With chronic concomitant use of PANADO CAPSULES and zidovudine, neutropenia often occurs and is probably due to the reduced metabolism of zidovudine.

Severe hepatotoxicity has occurred after use of paracetamol in a patient taking zidovudine and co-trimoxazole. However, neither short-term nor long-term studies (the latter also in an individual patient) have shown any alteration of zidovudine elimination in patients taking zidovudine and paracetamol.

Paracetamol, as contained in PANADO CAPSULES, has also been found to enhance the antiviral effect of interferon alfa.

Interference with laboratory tests

Paracetamol, as contained in PANADO CAPSULES, may affect uric acid tests by wolframato phosphoric acid and blood sugar tests by glucose-oxydase-peroxydase.

4.6 Fertility, pregnancy and lactation

Pregnancy
Safety in pregnancy has not been established.

Breastfeeding
Safety in breastfeeding has not been established.

Fertility
No data available.

4.7 Effects on ability to drive and use machines
PANADO CAPSULES has no influence on the ability to drive and use machines.

4.8 Undesirable effects
Tabulated list of adverse reactions

System Organ Class	Frequency	Undesirable effect
Blood and lymphatic system disorders	*Less frequent*	Agranulocytosis (long-term use), thrombocytopenia, **thrombocytopenic** purpura, leukopenia, haemolytic anaemia, platelet disorders, stem cell disorders, pancytopenia, neutropenia, anaemia.

Immune system disorders	*Less frequent*	Hypersensitivity (excluding angioedema), hypersensitivity reaction, requiring discontinuation of treatment (angioedema, ventilation difficulty, hyperhidrosis, nausea, hypotension, shock, anaphylactic reaction).
	Frequency unknown	Drug-induced hypersensitivity syndrome (DIHS), hypersensitivity reactions characterised by urticaria, dyspnoea, and hypotension * (see section 4.4).
Metabolism and nutrition disorders	*Less frequent*	Hypoglycemia.
Psychiatric disorders	*Less frequent*	Depression NOS*, confusion, hallucinations.
Nervous system disorders	*Less frequent*	Tremor NOS, headache NOS.
Eye disorders	*Less frequent*	Abnormal vision.
Cardiac disorders	*Less frequent*	Oedema.
Respiratory, thoracic and mediastinal disorders	*Less frequent*	Bronchospasm in patients sensitive to aspirin and other NSAIDS.
Gastrointestinal disorders	*Less frequent*	Haemorrhage NOS, abdominal pain NOS, diarrhoea NOS, nausea, vomiting, pancreatitis.
Hepato-biliary disorders	*Less frequent*	Abnormal hepatic function, hepatic failure, hepatic necrosis**, jaundice, hepatotoxicity, hepatitis.
Skin and subcutaneous tissue disorders	*Less frequent*	Dermatitis, skin rashes, sweating, purpura, angioedema, urticaria and other allergic reactions. The rash is usually erythematous or urticarial but sometimes more serious and accompanied by fever and mucosal lesions.
	Frequency unknown	Acute generalised exanthematous pustulosis (AGEP), toxic epidermal necrolysis (TEN), drug-induced dermatosis, Stevens-Johnson syndrome (SJS), fixed drug eruptions (FDE) (see section 4.4).
Renal and urinary disorders	*Less frequent*	Sterile pyuria (cloudy urine) and renal side effects (severe renal impairment, nephrite interstitial, haematuria, enuresis).
General disorders and administration site conditions	*Less frequent*	Dizziness (excluding vertigo), malaise, pyrexia, sedation, medicine interaction NOS.

Injury, poisoning and procedural complications	*Less frequent*	Overdose and poisoning

* NOS: Not otherwise specified

** Administration of 6 grams of paracetamol may already lead to hepatic damage (in children: more than 140 mg/kg); higher doses cause irreversible hepatic necrosis.

Post-marketing experience:

The following side effects have been reported and frequencies are unknown: Fixed drug eruptions (FDE) and drug-induced hypersensitivity syndrome (DIHS) (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. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

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

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain (see section 4.8). 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.

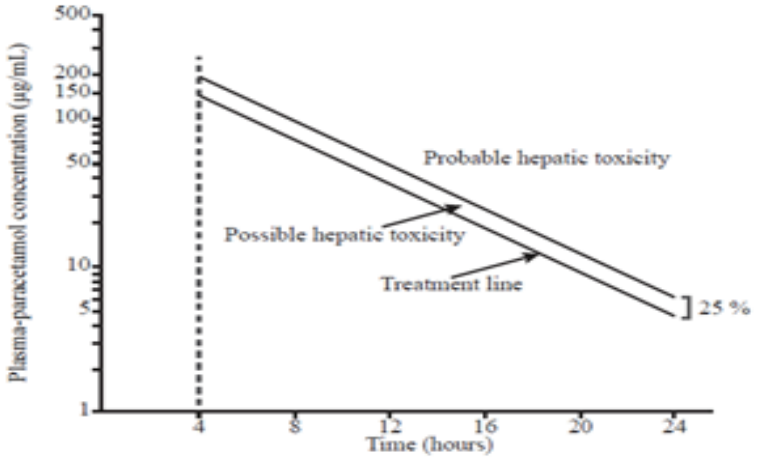
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac dysrhythmias have been reported.

Management

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.



Source: Martindale: The Complete Drug Reference -37th Edition.

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

Class of the medicine: A 2.7 Antipyretics or antipyretic and anti-inflammatory analgesics.
ATC code: N02 BE01, Other analgesics and antipyretics.
Paracetamol has analgesic and antipyretic actions.

5.2 Pharmacokinetic properties

Absorption
After oral administration, paracetamol is rapidly and almost completely absorbed. Peak plasma concentrations are reached after 30 minutes to 2 hours.

Distribution
Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood, saliva and plasma.

The volume of distribution of Paracetamol is approximately 1 L/kg bodyweight. At therapeutic doses, protein binding is negligible.

Metabolism

In adults, paracetamol is conjugated in the liver with glucuronic acid (~60 %), and sulphate (~35 %) conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dose. A minor route, catalysed by the cytochrome P450, results in the formation of an intermediate reagent (N acetyl-p-benzoquinoneimine) which under normal conditions of use is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cysteine (~3 %) and mercaptopuric acid.

In neonates and children <12 years sulphate conjugation is the main elimination route and glucuronidation is lower than in adults. Total elimination in children is comparable to that in adults, due to an increased capacity for sulphate conjugation.

Elimination

Elimination of Paracetamol is essentially through the urine. 90 % of the ingested dose is eliminated via the kidneys within 24 hours, predominantly as the glucuronide (60 to 80 %) and the sulphate (20 to 30 %) conjugates. Less than 5 % is eliminated in unchanged form. The elimination half-life is about 2 hours.

In cases of renal or hepatic insufficiency, after overdose, and in neonates the elimination half-life of paracetamol is delayed. The maximum effect is equivalent with plasma concentrations. For elderly patients, the capacity for conjugation is not modified.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silica
Magnesium stearate
Maize starch
Potassium sorbate
Capsule components:
Gelatin
Sodium lauryl sulphate
Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C in a well-closed container protected from light. Exposure to air should be kept to a minimum.

6.5 Nature and contents of container

Blister packs of 20 sealed capsules.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road, Erand Gardens,
Midrand, 1685
Customer Care: 0860 ADCOCK/232625

8 REGISTRATION NUMBER

S/2.8/0057

9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

12 December 1984

10 DATE OF REVISION OF THE TEXT

06 October 2025

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