SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Pamol Novum 500 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 500 mg paracetamol.

Excipient with known effect:
Each film-coated tablet contains 176 mg sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

White oval shaped film-coated tablet with 'P' on one side and plain on the other side.
Tablet dimensions: 19 x 9 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of headache, toothache, menstrual pain, muscle and joint pain, rheumatic pain, fever during cold and hyperpyrexia.

4.2 Posology and method of administration

Posology

Adults and adolescents > 40 kg (age >12 years):
500 mg – 1 gram every 4-6 hours, maximum daily dose is 4 gram in 24 hours.

The recommended dose shall not be exceeded due to the risk of hepatic damage (see sections 4.4 and 4.9).

Elderly patients
Dose adjustment is generally not required in the elderly. However, in fragile elderly patients the dose may be reduced or the dosing interval prolonged (see section 4.4).

Renal insufficiency
In patients with renal insufficiency, the dose shall be reduced and the dosing interval extended to at least every 6 hours.

Impaired liver function
In patients with impaired hepatic function or Gilbert's syndrome, the dose must be reduced or the dosing interval prolonged (see sections 4.3 and 4.4).

Method of administration
To be swallowed.

4.3 Contraindications

Hypersensitivity to paracetamol or to any of the excipients listed in section 6.1.
Severe hepatic insufficiency.

4.4 Special warnings and precautions for use

Patients with suspected overdose shall be treated immediately even when the patient is feeling well due to the risk of severe liver damage, see section 4.9.

Long term intake of different types of analgesics for headache may aggravate the headache. If that occurs, or if suspected, treatment should be discontinued. Excessive use may be suspected for patients with frequent or daily headache despite (or because of) the use of analgesics.

Caution should be exercised in patients with asthma who are sensitive to acetylsalicylic acid, as mild reactions of bronchospasm have been reported with paracetamol (cross-reaction).

For patients with a glutathione deficiency, such as in sepsis, the use of paracetamol may increase the risk of metabolic acidosis.

Caution is advised in the administration of paracetamol to patients with moderate and severe renal insufficiency.

Caution in hepatic impairment. Should not be combined with other analgesics containing paracetamol (such as combination products). Higher doses than recommended result in risk of severe liver damage. Clinical signs of liver damage may generally appear after 48 hours and culminates after 4-6 days in the general case. Antidot should be administrated as early as possible. See also section 4.9 Overdose. In case of high fever, signs of secondary infection or if symptoms last for more than 3 days, the treatment shall be reevaluated. Paracetamol shall be used with special caution in patients with any of the following conditions:

- impaired liver function
- alcoholism
- Gilbert’s syndrome (familial non-hemolytic jaundice)
- dehydration
- malnutrition
- patients with low Body Mass Index
- fragile elderly
- G-6-PD deficiency (favism)
- hemolytic anaemia

The risk for severe liver damage from overdose are greater in patients with non-cirrhotic alcoholic related liver damage.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

This medicinal product contains 176 mg sodium per tablet, equivalent to 8.8 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. Maximum daily dose is equivalent to 70% of the WHO recommended maximum daily intake of sodium.
[Invented name] contains a high level of sodium. This should be noticed for patients on a salt-restricted diet e.g. patients with hypertension, cardiac- or renal impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions
Studies have shown that the effect of *warfarin* may be enhanced in treatment with paracetamol.
The effect appears to increase with the dose of paracetamol but can occur at doses of only 1.5-2.0 g paracetamol a day for at least 5-7 days. Single doses of paracetamol at normal dosage are not deemed to have any effect.

Pharmacokinetic interactions
Caution is advised when paracetamol is administered concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis, particularly in patients with risk factors (see section 4.4).

Effects of other medicinal products on the pharmacokinetics of paracetamol
In pharmacokinetic studies, enzyme-inducing medicinal products such as certain anti-epileptic drugs (*phenytoin, phenobarbital, carbamazepine*) have been shown to reduce the plasma AUC of paracetamol to approx. 60%. Other substances with enzyme-inducing properties, e.g. rifampicin and St. John's wort (hypericum) are also suspected of causing lower concentrations of paracetamol. In addition, the risk of liver damage appears to be greater for treatment with the maximum recommended dose of paracetamol in patients who are on enzyme-inducing medicinal products.

Probenecid almost halves clearance of paracetamol by inhibiting its conjugation with glucuronic acid. This should mean that the dose of paracetamol can be reduced by half in simultaneous treatment with probenecid.

The absorption rate of paracetamol may be increased by *metoclopramide*, but the substances can be administered together. The absorption of paracetamol is reduced by *cholestyramine*. Cholestyramine should not be given within an hour if the maximum analgesic effect is to be achieved.

Effects of paracetamol on the pharmacokinetics of other medicinal products
Paracetamol can affect the pharmacokinetics of *chloramphenicol*. Analysis of plasma chloramphenicol is therefore recommended during combination therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy
A large amount of data from pregnant women indicates neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurological development in children exposed to paracetamol in utero show inconclusive results. If clinically justified, paracetamol can be used during pregnancy however it shall be used in the lowest effective dose for the shortest time possible and at the lowest possible frequency.

Breast-feeding
Paracetamol is excreted in human milk, however, risk for negative effects in children seem unlikely with therapeutic doses.

4.7 Effects on ability to drive and use machines

Paracetamol has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Side effects caused by paracetamol are generally rare. The most common side effects are skin reactions and elevated liver transaminase.

Side effects reported after very long experience of paracetamol are reported in below table according to system organ classes and frequency. Adverse reactions frequency is specified as follows:

Very common (≥1/10); Common (≥ 1/100, < 1/10); Uncommon (≥ 1/1 000, < 1/100); Rare (≥ 1/10 000, <1/1 000); Very rare (< 1/10 000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders Very rare (< 1/10 000)	Thrombocytopenia, neutropenia, leukopenia and hemolytic anemia
Immune system disorders Very rare (< 1/10 000)	Anaphylaxis
Metabolism and nutrition disorders Not known (cannot be estimated from the available data)	High anion gap metabolic acidosis (HAGMA)
Respiratory, thoracic and mediastinal disorders Very rare (< 1/10 000)	Bronchospasm in patients sensitive for acetylsalicylic acid or other NSAID
Renal and urinary disorders Very rare (< 1/10 000)	Renal side effects, sterile pyuria (cloudy urine)
Skin and subcutaneous disorders Rare (≥ 1/10 000 to <1/1 000) Very rare (< 1/10 000)	Exanthema, urticaria, angioedema Allergic dermatitis, rash, itch, sweating, redness. Toxic epidermal necrolysis (TEN), drug induced dermatitis, Stevens-Johnson syndrome, acute generalised exanthematous pustulosis.
Hepatobiliary disorders Rare (≥ 1/10 000 to <1/1 000) Very rare (< 1/10 000)	Increased liver transaminases. Liver damage.

Description of selected adverse reactions

High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Liver damage

Liver damage with paracetamol has occurred in conjunction with alcohol abuse.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

At excess doses the conjugation capacity in the liver may be reduced after which a large part of the dose is metabolised by oxidation. If stores of glutathione are depleted the reactive intermediate metabolites bind irreversibly to liver macromolecules. Clinical symptoms of liver damage generally only appear after a few

days. It is therefore crucial to start treatment with an antidote as soon as possible in order to prevent or minimise liver damage after toxic doses.

Toxicity
See below under Treatment for information on toxic plasma concentrations.
Even a small overdose can cause liver damage if the patient is exposed to other risk factors that can cause low glutathione stores like starvation, eating disorders, cystic fibrosis, HIV infection, dehydration or cachexia, or long-term treatment with medication with enzyme-inducing agents (phenytoin, phenobarbital, carbamazepine), rifampicin, primidone, St. John's wort (hypericum) or chronic high alcohol consumption.

5 g over 24 hours for 3½ year-old, 15-20 g for adults and10 g to an alcoholic patient produced lethal intoxication. A toxic dose for adults is generally 140 mg/kg. A toxic dose for children is approx. 175 mg/kg. Even sub-acute "therapeutic" overdose has led to severe intoxication with doses varying from 6 g/day for a week, 20 g for 2-3 days, etc.

Symptoms
Symptoms of paracetamol overdosage appearing in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain.
Symptoms of liver damage may become apparent 12 to 48 hours after overdose ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death.
The patients symptoms may at first be limited to nausea and vomiting which do not always reflect the severity of the poisoning and the risk of organ damage.
Kidney damage (renal failure with acute tubular necrosis, with symptoms like severe back pain, hematuria and proteinuria) can be be present without liver damage. Pancreatitis and toxic myocardial damage with arrhythmia and heart failure have been reported. At extremely high concentrations there have been reports of loss of consciousness combined with acidosis and hyperglycemia. Pancytopenia.

Treatment
Despite a lack of significant early symptoms of overdose, patients shall be referred to the emergency room for immediate medical attention.
If necessary, gastric irrigation and activated charcoal. S-paracetamol concentration is to be measured at 4 hours or later after ingestion, acute response. False lows may occur if acetylcysteine has already been administered. If an antimotility agent has been taken a new sample should be taken 2 hours after the first (delayed peak concentration). Treatment with acetylcysteine initiated within 8-10 hours provides complete protection from liver damage, but thereafter the effect diminishes. Acetylcysteine is used when the paracetamol concentration in plasma is above the following levels at respective measuring points: 1000 micromol/l at 4 hours, 700 micromol/l at 6 hours and 450 micromol/l at 9 hours after exposure. In cases of concomitant alcoholism, starvation, dehydration, impaired liver function or medication with enzyme-inducing drugs there may be grounds for setting the threshold for antidote therapy at about ¾ the listed levels. The method of administration is adapted to the circumstances (level of consciousness, tendency to vomiting etc.): however, intravenously administered acetylcysteine is deemed more effective and safer.
Dosage of acetylcysteine: *Intravenously* initially 150 mg/kg in 200-300 ml isotonic infusion solution over 15 minutes, then 50 mg/kg in 500 ml of 50 mg/ml glucose over 4 hours and then 6.25 mg/kg/hour over 16 hours (75 mg/kg dissolved in 500 ml of isotonic glucose solution and administered over 12 hours). Fluid volumes can be reduced, if necessary. Contact the National (local) Poisons Information Centre for a specific schedule. (In exceptional cases, acetylcysteine may be administered orally if the intravenous route is not available. Contact the National (local) Poisons Information Centre for information).
Acetylcysteine may provide some protection even after 10 hours, but in such cases prolonged treatment should be administered. Acetylcysteine also reduces mortality in the event of manifest paracetamol-induced liver failure (please discuss with the Poisons Information Centre). Close monitoring of hepatic and renal function, coagulation status, fluid and electrolyte status. Liver and kidney failure therapy is often required in cases where the deadline for effective antidote treatment has passed and there are toxic concentrations present. Haemoperfusion may be indicated in special circumstances. In extreme cases a liver transplant may be required.

High doses of sodium hydrogencarbonate can lead to gastrointestinal symptoms like burps and nausea. High doses of sodium hydrogencarbonate can delay the gastric emptying and thereby possibly slow down the absorption of paracetamol. Since high doses of sodium hydrogencarbonate can cause hypernatremia the electrolyte balance should be monitored closely and patients treated accordingly.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesic, antipyretic, ATC code: N02BE01

Paracetamol is an aniline derivative with analgesic and antipyretic effects corresponding to those of acetylsalicylic acid. However, paracetamol does not cause gastrointestinal irritation and is also well tolerated by patients with ulcers. Paracetamol does not affect thrombocyte aggregation or bleeding time. Paracetamol is generally well tolerated by patients who are hypersensitive to acetylsalicylic acid.

The antipyretic effect is achieved by influencing the heat-regulation centre in CNS, whereby heat dissipation is increased.

The latency time for the analgesic effect is approx. 15-20 minutes regardless of food intake. The peak effect is achieved within 1-2 hours and lasts for 4-5 hours. The antipyretic effect is somewhat slower; thus the latency time is about ½-1 hour, maximum fever reduction is obtained after 2-3 hours and the duration of effect is about 8 hours.

[Invented name] contains sodium hydrogen carbonate. Sodium hydrogen carbonate promotes gastric emptying and release of the tablet, thereby promoting the absorption of paracetamol from [Invented name]. Clinical data has shown that paracetamol in a formulation including sodium hydrogen carbonate provides faster pain relief than regular paracetamol tablets.

5.2 Pharmacokinetic properties

Absorption
Paracetamol is absorbed well when administered orally. Peak plasma concentration of paracetamol after intake is achieved after approx. 30 minutes regardless of food intake. The plasma half-life of paracetamol is approx. 2 hours.

Biotransformation
Paracetamol is metabolised in the liver primarily by conjugation with glucuronide acid and sulphate. A small amount (about 3-10% of a therapeutic dose) is metabolised by oxidation by cytochrome P450 to a liver toxic intermediate metabolite. This metabolite is then conjugated to the liver glutathione and excreted as cysteine and mercapturic acid conjugates.

Elimination
Paracetamol and its metabolites are excreted via the kidneys. Approx. 2-3% of a therapeutic dose is excreted as unchanged paracetamol, approx. 80-90% as glucuronide and sulphate and a smaller amount as cysteine and mercapturic acid derivatives.

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

Tablet core:
Sodium hydrogen carbonate
Maize starch
Maize starch, pregelatinised
Povidone
Potassium sorbate (E 202)
Talc (E 553b)
Croscarmellose sodium
Stearic acid

Film-coating:
Titanium dioxide (E 171)
Polydextrose (E 1200)
Hypromellose (E 464)
Triacetin (E 1518)
Macrogol
Carnauba wax (E 903)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister packs (PVC/aluminium): 10, 20, 100, 300 film-coated tablets.
Bottles (HDPE) with a screw cap: 100, 300 film-coated tablets.
The bottle contains a pouch of silica gel desiccant, it must not be removed from the bottle.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2026-04-10