Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Micromol 1000 1000mg BP Effervescent Tablet

2. Qualitative and quantitative composition

Each effervescent tablet contains 1000 mg of paracetamol BP.

Excipients with known effects: Aspartame, sodium, and sodium benzoate

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Effervescent tablet.

4. Clinical particulars

4.1 Therapeutic indications

Symptomatic treatment of mild to moderate pain and/or fever in adults and adolescents aged 16 years and above.

4.2 Posology and method of administration

Posology

This presentation is reserved for use in adults and in adolescents aged 16 years and above.

Paediatric population

The product is not recommended for children under the age of 16 as the tablet is not divisible.

Adolescents of 16 to 18 years and weighing more than 50 kg are referred to as adults in the context of the use of this product.

Adults

For adults and adolescents (aged 16 years and older) weighing more than 50 kg, the usual single dose is 1 tablet at a time, to be repeated every 6 hours as needed, the maximum being 4 tablets per day (paracetamol 4000 mg per 24 hours).

The product is not recommended for adults and adolescents (aged 16 years and older) and weighing less than 50 kg**.**

Renal impairment

In patients with renal insufficiency, the dose should be reduced.

Hepatic impairment
In patients with impaired hepatic function or Gilbert´s syndrome, the dose must be reduced or the dosing interval prolonged.

Method of administration

Oral use. Place the tablets in a full tumbler of water and allow to dissolve completely before swallowing.

After dissolving the tablets, a slightly opalescent solution will be produced.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Prolonged or frequent use is discouraged. Patients should be advised not to take other paracetamol-containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such a case, unconsciousness does not occur. However, medical assistance should be sought immediately. Prolonged use except under medical supervision may be harmful. In adolescents treated with 60mg/kg daily of paracetamol, the combination with another antipyretic is not justified except in the case of ineffectiveness.

Renal and hepatic impairment

Caution is advised in the administration of paracetamol to patients with moderate and severe renal insufficiency, mild to moderate hepatic insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (child-Pugh>9), acute hepatitis, concomitant treatment with medicinal products affecting hepatic functions, glucose-6-phosphatedehydrogenase deficiency, hemolytic anemia, alcohol abuse dehydration and chronic malnutrition.

Alcohol usage

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2000 mg in such a case. Alcohol should not be used during the treatment with paracetamol.

“Caution is advised in asthmatic patients sensitive to aspirin (acetylsalicylic acid), because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested.”

Other medications and withdrawal:

Abrupt discontinuation of long-term use of high-dose analgesics, taken not as directed, may cause headache, tiredness, muscular pain, nervousness, and vegetative symptoms. The withdrawal symptoms subside within a few days. Patients should be advised to consult their doctor if headaches become persistent.

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 the underlying cause of HAGMA in patients with multiple risk factors.

This medicinal product contains sodium. WHO recommended maximum daily intake of sodium for an adult is 2gm.

This product also contains aspartame, a source of phenylalanine. It may be harmful for people with phenylketonuria.

Do not exceed the stated dose.

If symptoms persist, consult a doctor.

Treatment with an antidote is advised if an overdose is suspected. Immediate medical advice should be sought in the event of overdosage, even if the patient feels well, because of the risk of delayed serious liver damage.

This product should not be used for more than 10 consecutive days without a prescription. Liver and kidney damage cannot be excluded with prolonged use or excessive doses (more than 2 grams per day).

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions:

The anticoagulant effect of warfarin and other coumarins may be enhanced by regular use of paracetamol, with increased risk of bleeding. The effect may occur already at daily doses of 2000 mg after 3 days. Occasional doses have no significant effect on bleeding tendency. Increased monitoring of INR values should be done during the duration of the combination and after its discontinuation.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin, as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risk factors.

Pharmacokinetic interactions:

Use of substances that induce liver enzymes, such as carbamazepine, phenytoin, phenobarbital, rifampicin, and St John's wort (Hypericum perforatum), can increase the hepatotoxicity of paracetamol due to increased and more rapid formation of toxic metabolites. Therefore, caution should be taken in case of concomitant use of enzyme-inducing substances.

Probenecid nearly halves the clearance of paracetamol by inhibiting its conjugation with glucuronic acid. This probably means that the dose of paracetamol can be halved when being given at the same time as probenecid.

Concurrent intake of medicinal products that accelerate gastric emptying, such as metoclopramide or domperidone, accelerates the absorption and onset of effect of paracetamol.

The absorption of paracetamol is reduced by cholestyramine. Cholestyramine should not be given within one hour if the maximum analgesic effect is to be obtained.

Isoniazid affects the pharmacokinetics of paracetamol with possible potentiation of liver toxicity.

Paracetamol may affect the pharmacokinetics of chloramphenicol. Therefore, an analysis of chloramphenicol in plasma is recommended in the event of combination treatment with chloramphenicol for injection.

Interference with laboratory tests:

Paracetamol may affect uric acid tests by wolframato phosphoric acid, and blood sugar tests by glucose-oxidase-peroxidase.

4.6 Pregnancy and Lactation

Pregnancy

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

Lactation

Paracetamol/ metabolites are excreted in human milk, but at therapeutic doses of Paracetamol 1000 mg Effervescent Tablets, no effects on the breastfed newborns/infants are anticipated.
Paracetamol 1000 mg Effervescent Tablets can be used during breastfeeding.

Fertility

There is no or limited amount of data on the influence of Paracetamol 1000 mg Effervescent Tablets on fertility.

4.7 Effects on the ability to drive and use machines

Paracetamol does not influence the ability to drive and use machines.

4.8 Undesirable effects

The frequency using the following convention should be: very common (≥1/10); common (≥1/100 to < 1/10); uncommon (≥1/1,000 to < 1/100); rare (≥1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequency	System	Symptoms
Rare >1/10000 - < 1/1000	Blood and lymphatic system disorders	Platelet disorders, stem cell disorders, agranulocytosis, leucopenia, thrombocytopenia, haemolytic anaemia, pancytopenia, methemoglobinaemia
	Immune system disorders	Allergies (excluding angioedema).
	Psychiatric disorders	Depression NOS, confusion, hallucinations.
	Nervous system disorders	Tremor NOS, headache NOS.

	Eye disorders	Abnormal vision.
	Cardiac disorders	Oedema.
	Gastrointestinal disorders	Haemorrhage NOS, abdominal pain NOS, diarrhoea NOS, nausea, vomiting.
	Hepato-biliary disorders	Abnormal Hepatic function, hepatic failure, hepatic necrosis, jaundice.
	Skin and subcutaneous tissue disorders	Pruritus, rash, sweating, purpura, angioedema, urticaria
	General disorders and administration site conditions	Dizziness (excluding vertigo), malaise, pyrexia, sedation, drug interaction NOS.
	Injury, poisoning and procedural complications	Overdose and poisoning
Very Rare (< 10,000)	Respiratory, thoracic and mediastinal disorders	Bronchospasm
	Hepato-biliary disorders	hepatotoxicity
	General disorders and administration site conditions	hypersensitivity reaction (requiring discontinuation of treatment)
	Metabolism and nutrition disorders	Hypoglycemia
	Renal and urinary disorders	Sterile pyuria (cloudy urine) and renal side effects
	Skin and subcutaneous disorders	Very rare cases of serious skin reactions have been reported.
Not known (cannot be estimated from the available data)	Metabolism and nutrition disorders	High anion gap metabolic acidosis

Interstitial nephritis has been reported incidentally after prolonged use of high doses. Some cases of epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, edema of the larynx, anaphylactic shock, anemia, liver alteration and hepatitis, renal alteration (severe renal impairment, haematuria, anuresis), gastrointestinal effects, and vertigo have been reported.

Description of selected adverse reactions

High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors who use paracetamol. Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

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 Yellow Card Scheme at Website: https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store, or through the PPB reporting portal through https://pv.pharmacyboardkenya.org/

4.9 Overdose

There is a risk of poisoning, particularly in elderly subjects, in young adolescents, in patients with liver disease, in cases of chronic alcoholism, and in patients with chronic malnutrition. An overdose of Micromol 1000 is potentially fatal in all populations.

Liver damage (liver necrosis) is possible in adults who have taken 10g or more of paracetamol or 150mg/kg body weight. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors.

Risk factors

If the patient,

- Is on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort, or other drugs that induce liver enzymes.
- Or regularly consumes ethanol above recommended amounts.
- Or is likely to be glutathione depleted, e.g., eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms generally appear within the first 24 hours and comprise: nausea, vomiting, anorexia, pallor, and abdominal pain. Immediate emergency measures are necessary in case of paracetamol overdose, even when no symptoms are present.

Liver damage may become apparent 12 to 48 hours after 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. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria, and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase, and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

Management

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to the hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required, the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside a hospital.

High doses of sodium bicarbonate may be expected to induce gastrointestinal symptoms, including belching and nausea. In addition, high doses of sodium bicarbonate may cause hypernatraemia; electrolytes should be monitored and patients managed accordingly.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics; anilides
ATC code: N02BE01
Paracetamol has analgesic and antipyretic properties, but it has no useful anti-inflammatory properties.
Paracetamol's effects are thought to be related to inhibition of prostaglandin synthesis.

5.2 Pharmacokinetic properties

Absorption

The absorption of paracetamol by the oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes following ingestion.

Distribution

Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood. saliva and plasma. Protein binding is low.

Metabolism

Paracetamol is metabolized mainly in the liver following two major metabolic pathways: glucuronic acid and sulfuric acid conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dose. A minor route, catalyzed 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 and mercaptopuric acid. Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

Elimination

Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours. principally as glucuronide (60 to 80%) and sulphate conjugates (20 to 30%). Less than 5% is eliminated in unchanged form.

Elimination half-life is about 2 hours.

<u>Special patient groups</u>

Renal impairment

In cases of severe renal insufficiency (creatinine clearance lower than 10 ml/min), the elimination of paracetamol and its metabolites is delayed.

Elderly

The capacity for conjugation is not modified.

5.3 Preclinical safety data

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

There are no pre-clinical data of relevance to the prescriber that are additional to those already included in other sections of the SmPC.

6. Pharmaceutical Particulars

6.1 List of Excipients

Sr No	Material	Grade	Qty/tablet mg	% Overages added	Qty/tablet mg with Overages	Selection
PART-I						
1.	Citric acid (Anhydrous)	BP	1261.000	10	1387.100	Effervescent System
2.	Sodium bicarbonate (Anhydrous)	BP	898.000	10	987.800	Effervescent System
3.	Sodium saccharin	BP	8.000	0	8.000	Sweetening agent
4.	PVP-K 30	USP	72.000	0	72.000	Binder
5.	Purified water	BP	0.04 ml	0	0.04ml	Solvent
PART-II						
6.	Sodium Bicarbonate	BP	300.000	0	300.000	Effervescent System
7.	Simethicone	BP	10.000	0	10.000	Antiflatulent Agent
8.	Tween-80	BP	1.000	0	1.000	Emulsifier
9.	Isopropyl Alcohol	BP	0.020 ml	0	0.020 ml	Solvent
LUBRICATION						
10	Sodium Carbonate	BP	145.000	0	145.000	Effervescent System
11	Aspartame	USP	35.000	0	35.000	Sweetening agent
12	Sodium Benzoate	BP	30.000	0	30.000	Lubricating Agent
13	Flavour Orange	IH	40.000	0	40.000	Flavouring Agent
TOTAL			2800.00			

* The overages of anhydrous citric acid and anhydrous sodium bicarbonate (10% each) cater for reaction loss in the manufacturing process.

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

36 months.

The solution is stable up to 8 hours below 25°C after dissolving the tablet.

6.4 Special precautions for storage

Do not store above 30°C. Store in a dry place. Protect from direct sunlight.

Store in the original package to protect from light and moisture.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

KEEP MEDICINES OUT OF REACH OF CHILDREN.

6.5 Nature and content of the container

A strip pack containing 2 rows with 4 tablets each.

6.6 Special precautions for disposal and other handling

After dissolving the tablets, a slightly opalescent solution will be produced.

There are no special requirements for the handling of the product.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

NATIONAL PHARMACY LTD,
P.O. BOX 17843-00500,
NAIROBI, KENYA

8. Marketing Authorization Number

CTD9143

9. Date of first authorization/renewal of the authorization

03/02/2023

10. Date of revision of the text

08/05/2025