SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

[SE:]
Paracetamol/Phenylephrine Orifarm 1000 mg/10 mg powder for oral solution in sachets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 sachet contains:

Paracetamol	1000 mg
Phenylephrine hydrochloride	12.2 mg (equivalent to phenylephrine 10.0 mg)

Excipients with known effect
Sucrose 3.8 g
Aspartame (E951) 35 mg
Sorbitol (E420) 1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution in sachet
White powder

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of the symptoms of colds and influenza, including the relief of aches and pains, sore throat, headache, nasal congestion and lowering of temperature.

4.2 Posology and method of administration

Posology

Adults and Adolescents over 16 years of age who weigh more than 50 kg
One sachet.The dose may be repeated in 4-6 hours.
No more than three doses should be taken in 24 hours.

Children and adolescents under 16 years of age
[Invented name] is not recommended for use in children and adolescents below the age of 16 without medical advice.

Elderly
There is no indication that dosage needs to be modified in the elderly.

Method of administration

For oral use after dissolution in hot water.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Severe coronary heart disease
- Hypertension
- Glaucoma
- Hyperthyroidism
- Use in patients taking tricyclic antidepressants
- Use in patients who are currently taking or have taken monoamine oxidase inhibitors (MAOis) within the last 2 weeks

4.4 Special warnings and precautions for use

Use with caution in patients with

- Raynaud's phenomenon
- Diabetes
- Moderate and severe renal insufficiency
- Liver function disorders
  mild to moderate hepatocellular insufficiency (including Gilbert’s syndrome), severe hepatic insufficiency (Child-Pugh >9), acute hepatitis and concomitant treatment with medicinal products affecting hepatic functions
- haemolytic anaemia
- dehydration
- alcohol abuse
- chronic malnutrition
- glutathione depletion due to metabolic deficiencies

This medicinal product should not be combined with other medicinal products that contain paracetamol. Higher doses than recommended may lead to severe liver damage. Clinical signs of liver damage normally become evident 2 days after ingestion. Antidote should be given as soon as possible. See also section 4.9.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as 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.

Each sachet contains approximately 3.9 g of carbohydrates. This should be taken into account in patients with diabetes mellitus.

Contains sucrose and sorbitol (E420). Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Contains aspartame (E951), a source of phenylalanine. May be harmful for people with phenylketonuria.

Medical supervision is recommended if symptoms are not relieved or deteriorate within 3 days of therapy with [Invented name].

Aspirin-hypersensitive asthmatics may also be hypersensitive to [Invented name].

4.5 Interaction with other medicinal products and other forms of interaction

Paracetamol
Medicinal products which induce hepatic microsomal enzymes, such as alcohol, barbiturates, anticonvulsants such as phenytoine, phenobarbital, methylphenobarbital and primidone, rifampicin, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol, particularly after overdosage.
The speed of absorption of paracetamol may be decreased by anticholinergic medicinal products (e.g., glycopyrronium, propantheline), and increased by metoclopramide or domperidone and absorption reduced by cholestyramine. Isoniazide reduces paracetamol clearance with possible potentiation of its action and/or toxicity, by inhibition of its metabolism in the liver. 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. Probenecid reduces clearance of paracetamol by inhibiting conjugation with glucoronic acid.

Regular use of paracetamol possibly reduces metabolism of zidovudine (increased risk of neutropenia).

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 risks factors (see section 4.4).

Phenylephrine
Phenylephrine may adversely interact with other sympathomimetics, vasodilators and beta-blockers and other antihypertensives.
The vasopressor effects of phenylephrine can be potentiated by digoxin, MAO inhibitors, tricyclic antidepressants such as amitryptiline, amoxapine, clomipramine, desipramine and doxepine or tetracyclics such as maprotiline; antidepressants such as phenelzine, isocarboxylic acid, nialamide, tranylcipromine, moclobemide; Parkinson's disease medicinal products such as selegiline, and others such as furazolidone.

Contraindicated for patients currently receiving or within two weeks of stopping therapy with monoamine oxidase inhibitors.

4.6 Pregnancy and lactation

Pregnancy

Paracetamol
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.

Phenylephrine
There are limited data on the use of phenylephrine in pregnant women. Vasoconstriction of uterine vessels and reduced uterine blood flow associated with use of phenylephrine may result in fetal hypoxia. Until more information is available, use of phenylephrine should be avoided during pregnancy.

Lactation

Paracetamol
Paracetamol is excreted in breastmilk, but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

Phenylephrine
There are no data available on whether phenylephrine is released into breast milk and no reports on the effects of phenylephrine on the nursing infant. Until more data are available, use of phenylephrine should be avoided in lactating woman.

In summary, [Invented name] is not recommended during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. No such effects have been described to date.

4.8 Undesirable effects

The frequency of occurrence of undesirable effects is classified according to the following frequency convention:
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)

Paracetamol

System organ class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Rare	Blood dyscrasias including platelet disorders, agranulocytosis, leucopenia, thrombocytopenia, haemolytic anaemia, pancytopenia
Immune system disorders	Rare	Allergic or hypersensitivity reactions including skin rashes, urticaria, anaphylaxis, bronchospasm
Metabolism and nutrition disorders	Not known	High anion gap metabolic acidosis
Gastrointestinal disorders	Very rare	Acute pancreatitis
Hepatobiliary disorders	Rare	Abnormal hepatic function (increase in hepatic transaminases), hepatic failure, hepatic necrosis, jaundice
Skin and subcutaneous tissue disorders	Rare Very rare	Hypersensitivity including skin rash and urticaria, pruritus, sweating, purpura, angioedema Serious skin reactions (Drug induced Stevens-Johnson syndrome-SJS, toxic epidermal necrolysis-TEN, acute generalised exanthematous pustulosis-AGEP)
Renal and urinary disorders	Very rare	Intersticial nephritis after prolonged use of high doses of paracetamol, sterile pyuria (cloudy urine)

Isolated cases of 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 using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Phenylephrine

System organ class	Frequency	Undesirable effects
Immune system disorders	Rare	Allergic or hypersensitivity reactions including skin rashes, urticaria, anaphylaxis, bronchospasm
Nervous system disorders	Very rare	Insomnia, nervousness, tremor, anxiety, restlessness, confusion, irritability, dizziness, headache
Cardiac disorders	Rare	Tachycardia, palpitation
Vascular disorders	Rare	Blood pressure increase
Gastrointestinal disorders	Common	Anorexia, nausea, vomiting

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

Liver damage is possible in adults who have taken a single dose of 10 g or more of paracetamol. Ingestion of a single dose of 5 g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk Factors
If the patient:
(a) Is on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St. John's Wort or other medicinal products that induce liver enzymes.
Or
(b) Regularly consumes ethanol in excess of recommended amounts.
Or
(c) Is likely to be glutathione deplete, e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.
Or
(d) is a young child.
Or
(e) has a liver disease.

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. 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.

After prolonged use of high doses of paracetamol hypokalemia may develop.

Management
Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to 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 hospital. Management of patients who present with serious hepatic dysfunction beyond 24 hours from ingestion should be discussed with the specialised services or a liver unit.

Hypertensive effects may be treated with an i.v. alpha-receptor blocking agent.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: paracetamol combinations excl. psycholeptics, ATC code: N02BE51

Paracetamol: Paracetamol has both analgesic and antipyretic activity which is believed to be mediated principally through its inhibition of prostaglandin synthesis within the central nervous system.

Phenylephrine: Phenylephrine is a post-synaptic alpha-receptor agonist with low cardioselective beta-receptor affinity and minimal central stimulant activity. It is a recognised decongestant and acts by vasoconstriction to reduce oedema and nasal swelling.

5.2 Pharmacokinetic properties

Paracetamol: Paracetamol is absorbed rapidly and completely mainly from the small intestine and, depending on the formulation, produces peak plasma levels after 30 minutes to 2 hours following oral dosing. The systemic availability is subject to first-pass metabolism and varies with dose between 70% and 90%. The substance is rapidly and widely distributed throughout the body and is eliminated from plasma with a $t_{½}$ of approximately 2 hours. Plasma protein binding is about 10%. The major metabolites are glucuronide and sulphate conjugates (>80%) which are excreted in urine.

Phenylephrine: Phenylephrine is absorbed from the gastrointestinal tract but has reduced bioavailability by the oral route due to first-pass metabolism. It retains activity as a nasal decongestant when given orally, the substance distributing through the systemic circulation to the vascular bed of nasal mucosa. When taken by mouth as a nasal decongestant phenylephrine is usually given at intervals of 4-6 hours.

5.3 Preclinical safety data

Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not already been mentioned elsewhere in this SmPC.

Paracetamol
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

Ascorbic acid, sucrose, aspartame (E951), lemon flavour (containing: natural lemon oils and natural and nature identical flavouring substances, maltodextrin, mannitol, gluconolactone, acacia, sorbitol (E420), α-tocopherol (E307) and silica, colloidal anhydrous), saccharin sodium, silica, colloidal anhydrous, citric acid, sodium citrate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years
The reconstituted solution in hot water is stable for 60 min at room temperature.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

The sachet foil is composed of paper, glue or polyethylene, aluminium and ethylene methacrylic acid copolymer.
5, 8, 10 or 12 sachets in a cardboard carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

10 February 2026