Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

SUGAR-FREE FERVEX FOR CHILDREN, granules for oral solution in sachet.

2. Qualitative and quantitative composition

Each sachet contains:

Pheniramine maleate..... 0.0100 g

Paracetamol..... 0.2800 g

Ascorbic acid (vitamin C)..... 0.1000 g

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Granules for oral solution in sachet

4. Clinical particulars

4.1. Therapeutic indications

SUGAR-FREE FERVEX FOR CHILDREN, granules for oral solution in sachet is indicated in children (over 6 years of age) to treat colds and rhinopharyngitis:

- with clear nasal discharge and lacrimation,
- with sneezing,
- with headaches and/or fever.

4.2. Posology and method of administration

Posology

Age (weight)	Dose per administration	Administration interval	Maximum daily dose
21 kg - 25 kg (approximately 6 to 10 years of age)	**1 sachet** (280 mg paracetamol 10 mg pheniramine 100 mg vitamin C)	12 hours minimum	**2 sachets** (560 mg paracetamol 20 mg pheniramine 200 mg vitamin C)
26 kg - 40 kg (approximately 10 to 12 years of age)	**1 sachet** (280 mg paracetamol 10 mg pheniramine 100 mg vitamin C)	8 hours minimum	**3 sachets** (840 mg paracetamol 30 mg pheniramine 300 mg vitamin C)
41 kg - 50 kg (approximately 12 to 15 years of age)	**1 sachet** (280 mg paracetamol 10 mg pheniramine 100 mg vitamin C)	6 hours minimum	**4 sachets** (1120 mg paracetamol 40 mg pheniramine 400 mg vitamin C)

Paediatric population

SUGAR-FREE FERVEX FOR CHILDREN, granules for oral solution in sachet is contraindicated in children under 6 years of age.

Patients with renal impairment

In cases of renal impairment and unless otherwise medically prescribed, it is recommended that the dose be reduced, and that the minimum interval between 2 doses be increased, as per the following table:

Creatinine clearance	**Minimum administration interval**
≥50 mL/min	4 hours
10-50 mL/min	6 hours
<10 mL/min	8 hours

The total dose of paracetamol should not exceed 60 mg/kg/day (no more than 3 g/day).

Special clinical situations

The lowest possible effective dose of paracetamol should be considered, without exceeding 60 mg/kg/day (and without exceeding 3000 mg/day), in the following situations:

- adults weighing less than 50 kg,
- mild to moderate hepatocellular impairment,
- chronic alcoholism,
- chronic malnutrition (low reserves of hepatic glutathione),
- dehydration.

Method of administration

Oral use.

The sachets should be taken in a sufficient quantity of hot or cold water.

Frequency of administration

Doses must be at least 4 hours apart.

Duration of treatment

The maximum duration of treatment is 3 days.

4.3. Contraindications

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

- in cases of severe hepatocellular impairment,
- if there is a risk of angle-closure glaucoma,
- if there is a risk of urinary retention related to urethroprostatic disorders,
- in children under 6 years of age,

4.4. Special warnings and precautions for use

If the fever is high or persists, signs of a superinfection occur or symptoms persist for more than 3 days, treatment should be re-evaluated.

Special warnings

The risk of essentially psychological dependence only occurs for doses

greater than those recommended and for long-term treatment.

In order to prevent the risk of overdose:

- Verify the absence of paracetamol in the composition of other medicinal products (obtained with or without a medical prescription),
- Observe the maximum recommended doses:
  - in children weighing less than 37 kg, the total dose of paracetamol should not exceed 80 mg/kg/day (see section 4.9),
  - in children weighing between 38 kg and 50 kg, the total dose of paracetamol should not exceed 3 g per day (see section 4.9),
  - in adults and children weighing over 50 kg, THE TOTAL DOSE OF PARACETAMOL SHOULD NOT EXCEED 4 GRAMS PER DAY (see section 4.9).

Very rare cases of serious cutaneous undesirable effects have been reported. Patients should be informed of the early signs of these severe skin reactions, the onset of a skin rash or any other sign of hypersensitivity that requires discontinuation of treatment.

This medicine contains an azo colouring agent (E 110) and may cause allergic reactions.

Precautions for use

Related to the presence of paracetamol:

Paracetamol is to be used with caution in patients with:
- weight <50kg,
- mild to moderate hepatocellular impairment,
- renal impairment (see table in section 4.2),
- chronic alcoholism,
- chronic malnutrition (low reserves of hepatic glutathione),
- dehydration (see section 4.2).

If acute viral hepatitis is detected, treatment should be discontinued.

Related to the presence of pheniramine maleate:

- The consumption of alcoholic beverages or sedatives (especially barbiturates) that potentiate the sedative effect of antihistamines should be avoided during treatment.

Related to vitamin C:

Vitamin C should be used with caution in patients with iron metabolism disorders and subjects deficient in Glucose-6-Phosphate Dehydrogenase.

Related to the excipients with known effect:

This medicine contains sucrose acetate isobutyrate (E444); patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicine contains an azo colouring agent (E 110), allura red AC (E129) and may cause allergic reactions.

This medicine contains 0.28 mg benzyl alcohol in each sachet. Benzyl alcohol may cause allergic reactions.
This medicine contains trace amounts (0.0036 mg) of alcohol (ethanol), less

than 100 mg per sachet. This medicine contains 0.0036 mg sodium benzoate (E 202) in each sachet.

This medicine contains less than 1 mmol sodium (23 mg) per sachet, that is to say essentially 'sodium-free'.

4.5. Interaction with other medicinal products and other forms of interaction

Related to the presence of paracetamol:

Combinations requiring precautions for use

- **VITAMIN K ANTAGONISTS**

Risk of increased oral anticoagulant effect and of haemorrhage if paracetamol is taken at maximum doses (4 g/day) for at least 4 days.

The INR should be regularly monitored. Potential adjustment of the oral anticoagulant posology during treatment with paracetamol and after its discontinuation.

Interactions with paraclinical examinations

Administration of paracetamol may distort the results of blood glucose assays using the glucose oxidase-peroxidase method in the case of abnormally high concentrations.

Administration of paracetamol may distort the results of blood uric acid assays using the phosphotungstic acid method.

Related to the presence of pheniramine maleate:

Inadvisable combinations

- **Alcohol (beverage or excipient):**

Increased sedative effect of the H1 antihistamine via alcohol. Impaired alertness may make driving vehicles and using machines dangerous.

The consumption of alcoholic beverages or medicinal products containing alcohol should be avoided.

+ Sodium oxybate

Increased CNS depression. Impaired alertness may make driving vehicles and using machines dangerous.

Combinations to take into account

+ Other sedatives (related to the presence of pheniramine): morphine derivatives (analgesics, antitussives and substitute treatments), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1 antihistamines, centrally-acting antihypertensives, baclofen and thalidomide.

Increased CNS depression. Impaired alertness may make driving vehicles and using machines dangerous.

+ Other atropinic medicines (related to the presence of pheniramine): imipramine antidepressants, most atropinic H1 antihistamines,

anticholinergic antiparkinsonian agents, atropinic antispasmodics, disopyramide, phenothiazine neuroleptics and clozapine.

Addition of atropinic undesirable effects, such as urinary retention, constipation, dry mouth.

+ Anticholinesterases

Risk of reduced efficacy of anticholinesterases via acetylcholine receptor antagonism due to the atropinic medicine.

+ Opioids

Significant risk of colic akinesia, with severe constipation.

4.6. Fertility, pregnancy and lactation

Pregnancy

RELATED TO PARACETAMOL:

Animal studies are insufficient with respect to reproductive toxicity. Extensive data on pregnant women has not indicated any malformative risk or neonatal or foetal toxicity associated with the use of paracetamol. Epidemiological studies on the neurodevelopment of children exposed to paracetamol in utero show conflicting results.

RELATED TO THE COMBINATION PARACETAMOL/PHENIRAMINE/VITAMIN C:

There are no available clinical data on the use of paracetamol combined with vitamin C and pheniramine.

Therefore, as a precaution, SUGAR-FREE FERVEX FOR CHILDREN is not recommended in pregnant women.

Breast-feeding

Due to the lack of animal studies and clinical data in humans, the risk to breast-fed children is not known. Therefore, SUGAR-FREE FERVEX FOR CHILDREN is not recommended during breast-feeding.

Fertility

Due to the potential mechanism of action on cyclooxygenase and prostaglandin synthesis, paracetamol may impair fertility in women, affecting ovulation. This is reversible upon discontinuation of treatment. Its use is not recommended in women who wish to become pregnant.

Effects on male fertility were observed in one animal study. The relevance of these effects in humans is not known.

4.7. Effects on ability to drive and use machines

SUGAR-FREE FERVEX FOR CHILDREN, granules for oral solution in sachet has major influence on the ability to drive and use machines.

Attention is drawn, especially for those who drive or use a machine, to the risk of drowsiness related to this medicinal product, especially at the start of treatment.

This effect is increased by the consumption of alcoholic beverages, medicinal

products containing alcohol or sedative medicinal products.

4.8. Undesirable effects

Related to the presence of paracetamol:

Immune system disorders

- Rare: hypersensitivity reactions such as anaphylactic shock, angioedema, erythema, urticaria, skin rash have been reported. Their occurrence requires permanent discontinuation of this medicinal product and related medicinal products.

Skin and subcutaneous tissue disorders

- Very rare: Serious skin reactions. Their occurrence requires discontinuation of treatment.

Blood and lymphatic system disorders

- Very rare: thrombocytopenia, leukopenia and neutropenia.

Related to the presence of pheniramine maleate:

The pharmacological characteristics of this drug substance cause undesirable effects that vary in severity and may or may not be dose-dependent (see section 5.1).

- **Neurovegetative effects:**
  - sedation or drowsiness, more significant at the start of treatment,
  - anticholinergic effects such as dry mucous membranes, constipation, accommodation disorders, mydriasis, palpitations, risk of urinary retention,
  - orthostatic hypotension,
  - balance disorders, dizziness, impaired memory or concentration, more common in elderly subjects,
  - motor incoordination, tremor,
  - mental confusion, hallucinations,
  - in rarer cases, excitatory effects: agitation, nervousness, insomnia.
- **Hypersensitivity reactions (rare):**
  - erythema, pruritus, eczema, purpura, urticaria,
  - oedema, in rarer cases angioedema,
  - anaphylactic shock.
- **Blood disorders:**
  - leukopenia, neutropenia,
  - thrombocytopenia,
  - haemolytic anaemia.

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 relevant national regulatory authority pharmacovigilance.

4.9. Overdose

Related to the presence of paracetamol:

The risk of severe intoxication (therapeutic overdose or accidental intoxication) may be particularly high in elderly subjects, young children, patients with hepatic impairment, cases of chronic alcoholism, and patients suffering from chronic malnutrition. In these cases, intoxication can be fatal.

Symptoms

Nausea, vomiting, anorexia, pallor, abdominal pains usually appearing within the first 24 hours.

An overdose causes hepatic cytolysis that is likely to develop into complete and irreversible necrosis characterised by hepatocellular impairment, metabolic acidosis and encephalopathy that may lead to a coma and death.

At the same time, an increase in hepatic transaminases, lactic dehydrogenase and bilirubin, and a decrease in the prothrombin level may occur 12 to 48 hours after ingestion.

Emergency procedure

- Discontinue treatment.
- Immediate transfer to hospital.
- A tube of blood should be collected to measure the initial paracetamol plasma concentration
- Rapid elimination of the ingested product by gastric lavage.
- The treatment of paracetamol overdose typically includes administration of the antidote N-acetyl cysteine intravenously or orally as early as possible, preferably before the tenth hour.
- Symptomatic treatment.

Related to the presence of pheniramine:

Pheniramine overdose may cause: seizures (especially in children), loss of consciousness, coma.

Related to the presence of vitamin C:

Vitamin C overdose may cause gastrointestinal disorders (heartburn, diarrhoea, abdominal pain).

At doses of vitamin C greater than 1 g/day, there is a risk of haemolysis in subjects with G6PD deficiency.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: OTHER COLD PREPARATIONS, ATC code: R05X

SUGAR-FREE FERVEX FOR CHILDREN, granules for oral solution in sachet has 3 pharmacological actions:

- antihistamine action which reduces rhinorrhoea and often associated lacrimation and also reduces spasmodic phenomena such as episodes of sneezing.
- antipyretic analgesic action, which allows sedation for fever and pain (headache, myalgia).

- compensation of ascorbic acid in the body.

5.2. Pharmacokinetic properties

Paracetamol

Absorption

The absorption of paracetamol for oral use is complete and fast. Maximum plasma concentrations are reached 30 to 60 minutes after ingestion.

Distribution

Paracetamol is distributed rapidly throughout all tissues. The concentrations are comparable in the blood, saliva and plasma. Plasma protein binding is low.

Biotransformation

Paracetamol is metabolised primarily by the liver. The two major metabolic routes are conjugation with glucuronic acid and sulphate. The latter route can be rapidly saturated at posologies that exceed the therapeutic doses. A minor pathway, catalysed by cytochrome P450, is the formation of a reactive intermediate (N-acetyl-p-benzoquinone imine), which, under normal conditions of use, is quickly detoxified by reduced glutathione and eliminated in urine after conjugation with cysteine and mercapturic acid. In contrast, during massive intoxications, the quantity of this toxic metabolite is increased.

Elimination

Elimination is primarily urinary. 90% of the ingested dose is eliminated by the kidneys within 24 hours, mostly in glucuro-conjugated (60 to 80%) and sulfo-conjugated (20 to 30%) forms.

Less than 5% is eliminated unchanged. The elimination half-life is around 2 hours.

Physiopathological variations

- Renal impairment: in cases of severe renal impairment (creatinine clearance lower than 10 mL/min) see section 4.2, the elimination of paracetamol and its metabolites is delayed.
- Elderly subjects: conjugation capacity is not changed.

Pheniramine maleate

Pheniramine maleate is well absorbed from the gastrointestinal tract. Its plasma half-life is approximately 1 hour to 1 hour 30 minutes. It has a high tissue affinity and is eliminated primarily by the kidneys.

Ascorbic acid

Gastrointestinal absorption is good. When intake exceeds requirements, the excess is eliminated in urine.

5.3. Preclinical safety data

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

Mannitol (E 421), anhydrous citric acid, povidone, anhydrous magnesium citrate, acesulfame potassium, sodium benzoate (E 202), raspberry flavouring containing sunset yellow FCF (E 110) , allura red AC (E129), benzyl alcohol, sodium benzoate, ethanol, sucrose acetate isobutyrate (E444).

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

No special storage conditions.

6.5. Nature and contents of container

3 g in sachet (Paper/Aluminium/ Polyethylene).

Box of 8, 12 or 16 sachets. 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

UPSA SAS

8. Marketing authorisation number(s)

H2024/CTD10806/22541

9. Date of first authorisation/renewal of the authorisation

2024 October 24

10. Date of revision of the text

2024 October 24