# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

FEBRILEX® Junior syrup

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

5 ml syrup contains:

| | |
|---|---|
| Paracetamol BP | 125 mg |
| Chlorphenamine maleate BP | 1 mg |

Excipients:
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Syrup
Brown PET bottle containing 150 ml of syrup

## 4. CLINICAL PARTICULARS

Febrilex ® Junior syrup combines several actions:
Paracetamol exercises an analgesic and antipyretic activity.
Chlorphenamine has an anti-allergic action.

### 4.1. Therapeutic indications

- Symptomatic treatment of congestive conditions in case of respiratory disorders, being irritating or allergic with headaches and/or fever.
- Acute rhinitis, allergic rhinitis, bronchial congestion, flu-like coryza.

### 4.2. Posology and method of administration

Oral route
Children from 2 to 6 years: 5 ml syrup 3 to 4 times a day
Children from 6 to 12 years: 10 ml syrup 3 to 4 times a day
Children from 12 years old and 50 kg and more: 15 ml syrup 3 to 4 times a day
Do not exceed the recommended dose.
The treatment duration should be as short as possible and should not exceed a few days (5 days maximum).

The daily dose of paracetamol should not exceed 2 g in the following situations:
Chronic alcoholism
Liver failure
Gilbert's syndrome

Kidney failure
In case of kidney failure, the dose of paracetamol should be adapted:

| Glomerular filtration | Dose |
|---|---|
| 10 - 50 mL/min | 500 mg every 6 hours |
| < 10 mL/min | 500 mg every 8 hours |

Elderly people

Based on the available pharmacokinetic data, no dose adaptation is required. Despite that, renal and liver failure are more likely to occur in those patients and is thus to be taken into account.

## 4.3. Contraindications

Hypersensitivity to one of the components
Closed-angle glaucoma
Urinary retention risk due to urethroprostatic disorders (chlorphenamine)
The use of Febrilex® Junior syrup in children under 2 years is contraindicated

## 4.4. Special warnings and precautions for use

**Warnings**

- Productive cough should be respected.
- A search for the cause of the cough should precede any antitussive treatment.

*Paracetamol*

- A frequent or time extended use is unadvised. A time extended use, unless controlled by a medical professional, can harm the health.
- The maximal dose should not be exceeded. In order to prevent the risk of overdose, no other medical product containing paracetamol should be taken simultaneously.
- Taking at once a dose corresponding to several times the daily dose can seriously damage the liver; there might not be any conscious loss. Despite, it is recommended to call a doctor in regard to the risk of irreversible liver damage.
- Caution should be given if the following risk factors, lowering the liver toxicity threshold, are present: liver failure (including Gilbert's syndrome), acute hepatitis, kidney failure, chronic alcoholism and very meagre adults (< 50 kg). In those cases, the posology should be adapted (see 4.2).
- A concomitant treatment with drugs influencing the liver function, dehydration, chronic malnutrition (low glutathione liver stock) are as well regarded as risk factors for the emergence of liver toxicity and that can lower the liver toxicity threshold. The maximal daily dose should certainly not be exceeded in these patients.
- Caution should be given in case of paracetamol administration to patients with glucose-6-phosphate dehydrogenase deficiency and with haemolytic anaemia.
- In case of acute fever, signs of secondary infection or persistency of the complaints, the patients should be referred to the doctor.

**Precautions for use**

FEBRILEX JUNIOR contains sucrose. Patients with hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.
FEBRILEX JUNIOR contains propylene glycol. Concommitant administration with any substrate of alcohol deshydrogenase as ethanol may induce serious undesirable effects in new-born children.

*Due to paracetamol:* monitor by principle the renal function, in case of prolonged administration or renal impairment, though no nephrotoxicity due to paracetamol has been proven in humans in normal conditions of use.

*Due to an antihistamine (chlorphenamine maleate):*

The concomitant use of drugs with sedative effects, such as alcohol or sedatives (especially barbiturates should be avoided during Febrilex Junior syrup treatment.

## 4.5. Interaction with other medicinal products and other forms of interactions

*Due to paracetamol;*

Paracetamol is fully metabolized in the liver. Some of its metabolites are toxic to the liver, a concomitant administration of potent enzymes inducers (rifampicin, certain anti-convulsants) can lead to liver-toxic reactions, especially with high doses of paracetamol.

- Anticoagulants: the weak bonding of paracetamol to plasmatic proteins allows its association with anticoagulants. However, prolonged administration of paracetamol can increase the risk of bleeding. In that case, regular monitoring of the INR (International Normalized Ratio) is recommended.
- Metoclopramide: paracetamol absorption can be increased when associated with metoclopramide.
- Chloramphenicol: paracetamol increases chloramphenicol clearance.
- Colestyramine: colestyramine may decrease the intestinal absorption of paracetamol. While using concomitantly paracetamol and colestyramine, paracetamol should be administered 1 hour prior or 4 hours after the administration of colestyramine.
- Probenecid: probenecid can decrease by almost half the clearance of paracetamol by the inhibition of the conjugation with glucuronic acid. A reduction in the dose of paracetamol should therefore be considered if concomitant treatment with probenecid.
- Zidovudine: concomitant administration of paracetamol and zidovudine can lead to neutropenia and liver toxicity. The chronic/frequent use of paracetamol in patients treated with zidovudine should be avoided. If required, white blood cells and liver function should be monitored, especially in undernourished patients.
- Vitamin K antagonists: a stronger effect of the vitamin K antagonists can arise, especially if paracetamol is taken often and in high doses. In this case, a frequent monitoring of the International Normalised Ratio (INR) is recommended.
- Lamotrigine: a decreased bioavailability of lamotrigine, with possible reduced therapeutic effect can appear because of likely induction in the metabolism of lamotrigine by paracetamol.
- Metoclopramide and domperidone: accelerated intestinal resorption of paracetamol can arise due to the accelerated stomach emptying.
- Diagnosis tests: paracetamol can interfere with the determination of blood uric acid by the phosphotungstic acid method and with the determination of blood glucose by the glucose oxydase-peroxydase method.

*Due to chlorphenamine;*

Potentiation of the central nervous system depressants (hypnotics, anaesthetics ...).
Take the potentiation of the central atropinic effects into account in case of association with other anticholinergics (other antihistamines, antidepressants, imipramines, phenothiazine neuroleptics, anticholinergic antiparkinsonians, atropinic antispasmodics, disopyramide).

## 4.6. Pregnancy and lactation

As a preventing measure, this medicine will not be administered to pregnant women nor to women with childbearing potential. The use during lactation is not recommended.

## 4.7. Effects on ability to drive and use machines

Due to the antihistamine, drivers and machine operators should be aware that this medicine induces somnolence risks.

## 4.8. Undesirable effects

*Paracetamol*

- Haematological and lymphatic system disorders:

Very rare (<1/10,000): thrombocytopenia, leucopenia, pancytopenia, neutropenia, haemolytic anaemia, agranulocytosis,
Undetermined frequency: anaemia.µ

- Immune system disorders:

Rare (≥1/10,000, < 1/1,000): allergic reactions
Very rare (< 1/10,000): allergic reaction requiring stopping the treatment,
Undetermined frequency: anaphylactic shock.

- Nervous system disorders:

Rare (≥1/10,000, < 1/1,000): headaches

- Gastro-intestinal disorders:

Rare (≥1/10,000, < 1/1,000): abdominal pain, diarrhoea, nausea, vomiting, constipation.

- Hepatic disorders:

Rare (≥1/10,000, < 1/1,000): troubled liver function, liver failure, liver necrosis, icterus,
Very rare (<1/10,000): liver-toxicity,
Undetermined frequency: hepatitis.

- Skin and subcutaneous tissue disorders:

Rare (≥1/10,000, < 1/1,000): pruritus, rash, sweating, angioedema, hives,
Very rare (< 1/10,000): very rare cases of severe skin reactions have been reported.

- Kidney and urinary disorders:

Very rare (< 1/10,000): sterile pyuria (cloudy urines),
Undetermined frequency: nephropathy (interstitial, nephritis, tubular necrosis) following the extended use of high doses.

- General disorders and administration site conditions:

Rare (≥1/10,000, <1/1,000): dizziness, unease

- Injuries, intoxication, procedural complication:

Rare (≥1/10,000, <1/1,000): overdose and intoxication

*Chlorphenamine*

Atropinic effects such as dry mouth, accommodation disorders, dysuria, mental confusion or excitation in elderly patients
These disorders progressively disappear when interrupting the treatment.

## 4.9. OVERDOSE

Paracetamol

A risk of acute hepatotoxicity exists particularly in elderly people, young children, in case of liver or kidney failure, of chronic alcoholism, of chronic malnutrition, in case of use of enzyme inducing agents and in very meagre adults (> 50 kg).
Pre-existing hepatic impairment and chronic alcohol consumption can lower the toxicity threshold. It has to be kept in mind that a massive overdose due to a glutathione depletion exceeding 70 % (which theoretically requires an absorption of 15 g paracetamol in adults and a child a dose equal or higher than 150 mg/kg body weight) leads to the formation of increased quantity of the reactive metabolite which, as it cannot be detoxified, causes hepatic

cytolysis potentially leading to a complete and irreversible necrosis. Paracetamol accumulation due to metabolism impairment has not been observed at therapeutic doses. Glutathione depletion, which could increase the toxicity risk, does not usually occur.

Symptoms:
Early symptoms, that can occur only 12 hours after ingestion of a potentially toxic dose, may include: nausea, vomiting, anorexia, abdominal pain and sweating. Clinical and biological signs of liver disorders can appear later (48 to 72 hours).
As a consequence, in case of any suspicion of paracetamol overdose, the patient should be immediately hospitalized and serum levels should be determined at the earliest from the $4^{th}$ hour post-ingestion on.
Values exceeding 200 µg/ml at the $4^{th}$ hour or 50 µg/ml at the $12^{th}$ hour are the signs of a high risk of hepatic necrosis. The usual liver function tests should be performed as early as possible and repeated on a regular basis (every 24 hours).

Treatment:
The overdose treatment in a specialized environment includes the administration at the earliest of the N-acetylcysteine antidote.
Early treatment can result in a total functional recovery.
N-acetylcysteine proposed posology: initial dose 150 mg/kg in 30 minutes, then 50 mg/kg in 4 hours and 100 mg/kg during the following 16 hours. A close monitoring of hepatic function is recommended (every 24 hours).

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamics properties

Pharmacological classification: COUGH AND COLD PREPARATIONS
**ATC code:** R05 (R Respiratory system)
Paracetamol - Analgesic / Antipyretic
Chlorphenamine maleate - Histamine $H_1$ - receptor antagonist

### 5.2. Pharmacokinetics properties

Paracetamol is quickly and totally absorbed. It is not much bonded to plasmatic proteins (20 to 50 %) and its diffusion is quick.
Paracetamol is metabolised in the liver and follows two major metabolic routes. It is excreted via the urine under glucuronoconjugated (60 to 80 %) and sulfoconjugated (20 to 40 %) forms. A small fraction (less than 4 %) is transformed with the intervention of cytochrome P450 into a metabolite formed by oxidative process and which would have been involved in the hepatotoxicity of paracetamol at high doses; indeed, at therapeutic doses, this metabolite is eliminated by conjugation with glutathione. The conjugation ability is not changed in elderly patients and the kinetics is linear for doses until 7 g. In case of massive intoxication, the conjugation ability is exceeded, and the hepatotoxic metabolite quantity is increased.
At therapeutic doses, the half-life lasts for about 3 hours.

Chlorphenamine maleate is quickly and almost totally absorbed by the gastrointestinal tract. The average plasmatic half-life is about 20 hours in adults (huge differences have been recorded); in children, it is much shorter. In vitro studies have shown a binding to plasmatic proteins of around 70 %. Chlorphenamine is metabolized in the liver and excreted in the urine, mainly under the form of demethylchlorphenamine and didesmethylchlorphenamine.

## 6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Propyleneglycol, sodium methyl parahydroxybenzoate (E219), sodium propyl parahydroxybenzoate (E217), aspartame (E951), citric acid, sucrose, xanthan gum, cherry flavour, ponceau 4R (E124) colour, purified water.

6.2. Incompatibilities

None reported to this day.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Keep away from heat, light and moisture.
Store below 30°C.

6.5. Nature and contents of container

Plastic bottle made of polyethylene terephthalate for (non parenteral) pharmaceutical use.

6.6. Special precautions for disposal and other handling

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

## 7. CATEGORY OF DISTRIBUTION

☒ OTC (over-the-counter) ☐ POM (Prescription only medicine)

## 8. MARKETING AUTORISATION HOLDER

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**10. DATE OF REVISION OF THE TEXT**

01/2019