Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT (FPP)

HACTOSEC

Levodropropizine

1.1. Strength

6 mg/ml

1.2. Pharmaceutical form

Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1. Qualitative declaration

Levodropropizine

For the full list of excipients, see section 6.1

2.2. Quantitative declaration

Each ml of syrup contains 6 mg of levodropropizine

Excipients with known effect:

- Sucrose 500 mg/ml
- Methyl parahydroxybenzoate 0.6 mg/ml
- Propyl parahydroxybenzoate 0.25 mg/ml

3. PHARMACEUTICAL FORM

Syrup

Liquid preparation for oral use, clear colourless to pale yellow, aqueous solution

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Symptomatic treatment of dry cough (non-productive, disturbing cough).

4.2. Posology and mode of administration

4.2.1. Posology

Adults and children from 12 years and older

- Maximum 60 mg levodroprozine (10 ml syrup), three times daily. The time between administrations should be at least 6 hours.

4.2.2. Special populations

- In elderly patients, levodropropizine is used with caution; a risk of changed pharmacokinetics linked to age can be present.
- In case of severe renal (creatin clearance below 35ml/min) or in case of severe hepatic failure, the benefit-risk ratio should be taken into consideration.

4.2.3. Pediatric population

Children 6 to 12 years

- 12 mg to maximum 30 mg levodropropizine (2 ml to maximum 5 ml syrup) three times daily. The time between administrations should be at least 6 hours.

Children 2 to 6 years

- 12 mg to 18 mg levodropropizine (2 ml to 3 ml syrup), maximum three times daily. The time between administrations should be at least 6 hours. It is important to follow the advice of the health professional. The usual dose is 1 mg to 2 mg per kg of bodyweight (eq. with 0.15 ml to 0.3 ml of syrup).

Hactosec syrup is contraindicated in children below 2 years.

4.2.4. Method of administration

Oral use, administration via a dosing device.
Preferably, the syrup will be taken away from meals with an interval of at least 6 hours between administrations. The period of treatment should remain brief; treatment should be discontinued as soon as the symptoms have disappeared.

4.3. Contraindications

- Known hypersensitivity to the active substance or to any of the excipients (see section 6.1).
- Bronchorrhoea or disturbed muco-ciliary function (Kartagener syndrome, bronchial dyskinesia).

- Rare hereditary problems of fructose intolerance, glucose galactose malabsorption or sucrose-isomaltase insufficiency.
- Pregnancy and lactation.
- Children below 2 years.

4.4. Special warning and precautions for use

4.4.1. General information

- Before starting treatment with a cough syrup, cough-underlying causes requiring a specific treatment should be investigated. It is not coherent to administer a cough preparation combined with mucolytics or expectorants.
- In elderly patients, levodropropizine is used with caution; a risk of changed pharmacokinetics linked to age can be present.
- In case of severe renal (creatin clearance below 35ml/min) or in case of severe hepatic failure, the benefit-risk ratio should be taken into consideration.
- The syrup contains preservative ingredients belonging to the category of parabens (methyl parahydroxybenzoate E218 and propyl parahydroxybenzoate E216). These ingredients may cause allergic reaction (possibly delayed).
- The syrup contains 500 mg sucrose per ml (eq. 5 g sucrose in 10 ml). Diabetic patients should take it into account. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- In the absence of studies to determine the influence of food on the absorption of levodropropizine, advice is given to take the syrup away from meals.

4.4.2. Pediatric population

Hactosec syrup is contraindicated in children below 2 years.

Caution is advised when administering the syrup to children below the age of 6 years.

4.5. Interactions with other medicinal products and other forms of interactions

4.5.1. General information

- Clinical studies have not revealed interactions following simultaneous administration of medicines used to treat bronchopulmonary diseases.
- Patients sensitive to sedative medication should be careful when using these medicines combined with levodropropizine.

4.5.2. Additional information on special populations

None

4.5.3. Pediatric population

None

4.6. Pregnancy, lactation and fertility

4.6.1. Pregnancy

There are not enough clinical data studying the use of levodropropizine during pregnancy to evaluate the potential toxicity. Hactosec syrup is contra-indicated during pregnancy.

4.6.2. Lactation

In animal studies it was demonstrated that levodropropzine is excreted in maternal milk. Therefore, Hactosec syrup is contra-indicated during breast feeding.

4.6.3. Fertility

There are no data available.

4.7. Effects on the ability to drive and use machines

In exceptional cases, somnolence and vertigo have been reported. Caution is advised when driving or operating a machine.

4.8. Undesirable effects

Frequencies are defined as: Very common (≥ 1 /10), common (≥ 1 /100 to <1 /10), uncommon (≥ 1/1.000 to <1/ 100), rare (≥ 1/10.000 to <1 / 1000), very rare (< 1/10.000).

During controlled clinical trials, common (≥ 1 /100 to <1 /10) effects have been reported. Post –marketing experience: some very rare (< 1/10.000) undesirable effects have been reported following the use of levodropropizine syrups.

System organ class	**Common (≥ 1 /100 to <1 /10)**	**Very rare (<1/10 000)**
Cardiac disorders	palpitations	tachycardia
Gastro-intestinal disorders	nausea, pyrosis, dyspepsia, diarrhea, vomiting	abdominal pain, stomach pain
Skin and subcutaneous disorders	cutaneous allergic reactions	urticaria, erythema, exanthema, pruritis, angio-edema
Nervous system disorders	-----	tremor, paresthesia
Respiratory, thoracic and mediastinal disorders	-----	dyspnea, cough, bronchial edema
Muscoskeletal and connective tissue disorders	---	weakness of the internal membranes
Vascular disorders	----	hypotension
General disorders	----	discomfort, feeling of weakness
Immune system disorders	----	anaphylactic reaction
Psychiatric disorders	----	depersonalisation

4.9. Overdose

Significant undesirable effects have not been observed following ingestion of a single dose up to 240 mg or following ingestion of multiple 120 mg doses, 3 times daily for 8 consecutive days.

In case of an overdose, a temporary transitional tachycardia can be expected.

General measures for treating a drug overdose apply (gastric lavage, activated charcoal, giving parenteral fluid,…).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Cough and cold preparations, cough suppressant excluding combinations with expectorans: other cough suppressant.
ATC code: R05D B27

Levodropropizine is a peripherally acting antitussive working at tracheobronchial level. The peripheral action has been demonstrated in animal studies.

Its mechanism provides this drug antitussive properties against cough associated to different lung pathologies, but without relevant central side effects.

Levodropropizine inhibits bronchospasms induced by histamine, serotonin and bradykinin. Levodropropizine exerts its antitussive effect through an inhibitory action at the level of the airway sensory nerves involving modulation of sensitive C-fibers and release of neuropeptides.

5.2. Pharmacokinetic properties

Absorption

Following oral administration, levodropropizine is quickly absorbed showing a bioavailability of more than 75% in humans.

Distribution

Levodropropizine is distributed throughout the body after oral administration. Binding of levodropropizine to plasma proteins is low (11–14%).

Metabolism and biotransformation

Levodropropizine is quickly absorbed and extensively metabolised. Identified metabolites are conjugated levodropropizine, free para-hydroxy-levodropropizine and conjugated para-hydroxy-levodropropizine.

Elimination and excretion

The half-life of levodropropzine is about one to two hours. The main excretion route is through the kidney, with a renal excretion of 35%. Urinary excretion is done in unchanged form and via conjugated metabolites.

5.3. Preclinical safety data

The toxicity tests after repeated oral doses (4-26 weeks) have revealed that the dose devoid of toxic effects is the dose of 24mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Sucrose (500 mg/ml**)**
- Glycerol
- Methyl parahydroxbenzoate (E218)
- Propyl parahydroxybenzoate (E216)
- Coffee flavour
- Cocoa flavour
- Citric acid monohydrate
- Purified water

6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store below 30^{o}C in the original bottle pack, protect from light.

6.5. Nature and contents of container

Cardboard box including 150 ml of syrup in an amber coloured glass bottle closed with a plastic screw cap, a leaflet and a plastic dosing device.

6.6. Special precautions for disposal and other handlings

No special requirements. Dispose in line with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

7.1. Marketing Authorisation Holder

Dafra Pharma GmbH, Mühlenberg 7, 4052 Basel, Switzerland

7.2. Manufacturer

Bilim Pharmaceuticals, GOSB 41480 Gebze, Koaceli, Turkey

8. MARKETING AUHORISATION NUMBER

See list of countries

9. DATE OF FIRST REGISTRATION

See list of countries

10. DATE OF REVISION OF TEXT

April 2019