This leaflet format has been determined by the Ministry of Health and the content thereof has been checked and approved on October 2017

Summary of Product Characteristics

1. Name of the medicinal product

Bronchiclear

Film-coated tablets

2. Qualitative and quantitative composition

1 film-coated tablet contains:
60 mg of dry extract of primula root (6-7 : 1); extracting agent: ethanol 47.4% (V/V)
160 mg of dry extract of thyme herb (6-10 : 1); extracting agent: ethanol 70% (V/V).

Excipients:

Glycose syrup	34 mg
Lactose monohydrate	50 mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablets

Green, round, biconvex film-coated tablets with semi-matte surface

4. Clinical particulars

4.1 Therapeutic indications

For the relief of symptoms in acute bronchitis with coughs and colds associated with viscous mucus in children from 12 years of age, adolescents and adults.

4.2 Posology and method of administration

Adolescents, children from the age of 12 years and adults take 1 film-coated tablet 3 times a day. The film-coated tablets should be swallowed unchewed, with sufficient liquid (preferably a glass of water) before meals.
Do not chew, split or crush the film-coated tablet.

The duration of treatment depends on the course of the disease. In each case, please note the information given in the first paragraph under “Special warnings and precautions for use" and the information under “Undesirable effects".

4.3 Contraindications

Bronchiclear must not be used in case of known hypersensitivity to the active substances or other labiates (*Lamiaceae*), birch, mugwort, celeriac or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

If complaints persist for longer than 10 days or if shortness of breath, fever and purulent or bloody expectoration occur, a doctor should be consulted immediately.

Caution should be exercised in patients with gastritis or gastric ulcer. In such patients Bronchiclear should be taken after meals with sufficient liquid (preferably a glass of water).

Patients with rare hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take Bronchiclear.

Children

Since there are insufficient studies on the use of this medicinal product in children, Bronchiclear should not be administered to children under 12 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with other medicinal products are not known to date.

Studies with Bronchiclear to investigate potential interactions with other concomitantly used medicinal products are not available.

4.6 Fertility, pregnancy and lactation

Pregnancy and breast-feeding

Due to insufficient studies, Bronchiclear should not be used during pregnancy and breast-feeding.

Fertility
There are no human data on the effect of the medicinal product on fertility. In animal studies no effects on fertility have been observed.

4.7 Effects on ability to drive and use machines

No special precautions are required.

4.8 Undesirable effects

Like all medicinal products, Bronchiclear can cause side effects.

The following frequency categories are used for the evaluation of undesirable effects:
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 (frequency cannot be estimated from the available data)

Gastrointestinal symptoms such as cramps, nausea, vomiting and diarrhoea may occur in uncommon cases.

Very rarely, hypersensitivity reactions such as dyspnoea, skin rash, hives and swelling of the face, mouth and/or pharynx may occur.

In the package leaflet, the patient is advised as follows:
If any side effects occur, discontinue use of the medicine and contact a doctor. He/she will decide on their severity and any further measures required.

At the first signs of a hypersensitivity reaction Bronchiclear must not be taken again.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:

http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

4.9 Overdose

No cases of intoxication with preparations from thyme herb and primula root have been reported to date. In case of overdose gastrointestinal complaints, vomiting and possibly diarrhoea may occur.

In the package leaflet, the patient is advised to inform a doctor in this case.

Treatment of intoxications:

If signs and symptoms of intoxication and overdose occur, symptomatic treatment should be initiated.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: herbal medicinal products for the treatment of respiratory disorders caused by colds

ATC code: R05CA

Thyme extracts are capable of increasing mucociliary clearance; for primula root extracts, a reflex increase in bronchial secretion as an expectorant mechanism of action is under discussion.

Bronchodilatory effects have also been shown for both extracts *in vivo* and *in vitro*.

Antitussive activity has been demonstrated for Bronchiclear in a cough model in the guinea pig.

A number of *in vitro* and *in vivo* studies have found significant anti-inflammatory properties for Bronchiclear and its individual extracts. The underlying mechanisms of action are varied.

Furthermore, *in vitro* studies on Bronchiclear have brought to light antibacterial and antiviral properties against respiratory tract-related bacterial (e.g. *S. pneumoniae and S. pyogenes*) and viral strains (influenza A, respiratory syncytial virus, human rhinovirus).

5.2 Pharmacokinetic properties

Thymol, a main lipophilic component of essential thyme oil, is absorbed in the intestine and can be detected in human plasma as thymol sulphate. The oral administration of a Bronchiclear film-coated tablet to healthy volunteers resulted in geometric mean values of C_{max}= 90 ng/mL and $AUC_{0\text{-}tlast}$= 794 h*ng/mL for thymol sulphate. The median of the T_{max} value was 2 hours, that of the elimination half-life ($t_{1/2}$) 10 hours. The thymol metabolites, especially thymol sulphate and glucuronide, are excreted renally.

No data is available on the pharmacokinetics and bioavailability of the primula root extract.

5.3 Preclinical safety data

Acute toxicity

The acute toxicity of Bronchiclear dry extract has been investigated after a single oral administration to rats and mice at dosages up to 5,000 mg/kg of body weight (BW). For male animals, the LD_{50} was not reached, whereas in female animals an LD_{50} of 4,564 mg/kg BW was calculated.

Subacute toxicity

Bronchiclear dry extract was investigated as part of a four-week study after repeated oral administration to rats (up to 1,500 mg/kg BW) and dogs (up to 1,250 mg/kg BW). The No Observed Adverse Effect Level (NOAEL) in rats was 1,500 mg/kg BW and in dogs 500 mg/kg BW. Relative to the recommended human dose equivalent, this corresponds to a 22-fold and 25-fold safety margin for the rat and dog respectively.

Chronic toxicity

No preclinical data is available for the chronic toxicity of Bronchiclear..

Mutagenicity

Bronchiclear dry extract was tested *in vitro* (Ames test, mouse lymphoma test) and *in vivo* (micronucleus test) for mutagenicity. No mutagenic potential was ascertained within the framework of these investigations.

Reproductive toxicity

In reproductive toxicology studies involving rats (segment I and segment II), no negative influences of Bronchip dry extract were found on fertility or embryofoetal development up to the highest tested dose (1,500 mg/kg BW).

Carcinogenicity

No preclinical data is available for the carcinogenicity of Bronchiclear.

Safety pharmacology

In preclinical *in vivo* studies on neuropharmacological, cardiovascular and respiratory safety, no safety-relevant findings occurred after the administration of Bronchiclear dry extract.

6. Pharmaceutical particulars

6.1 List of excipients

Chlorophyllin preparation (25% copper chlorophyllin, 75% dextrose) (E141), crospovidone, dimethicone, glucose liquid spray-dried, colloidal anhydrous silica, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, peppermint flavour, polyacrylate dispersion 30%, povidone K25, propylene glycol, riboflavin (E101), saccharin sodium, talc, titanium dioxide (E171).

Note for diabetics:

One Bronchiclear film-coated tablet contains approximately 0.2 gr carbohydrates.

6.2 Incompatibilities

None known.

6.3 Shelf life

The shelf life is 3 years.

Do not use this medicinal product after the expiry date.

6.4 Special precautions for storage

Do not store above 25° C.

6.5 Nature and contents of container

Pack of 20 film-coated tablets

6.6 Special precautions for disposal

No special requirements.

7. Israeli Marketing authorisation holder

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8. Marketing authorisation number

159-49-34894-00

9. Date of first authorisation

October 2017

10. Date of revision of the text

October 2017

11. General classification for supply

Only for sale in pharmacies, Over the counter (OTC)