Colpermin®

Herbal Medicine

Peppermint oil 187 mg capsules

Tillotts Pharma AG

Therapeutic Indications

For the treatment of symptoms of discomfort abdominal colic and distension following irritable bowel syndrome.

Composition

Active substance:

Peppermint oil (Menthae x piperita L., aetheroleum)

*Excipient*s:

Capsule content: refined arachis oil, white beeswax, colloidal anhydrous silica,

Capsule shell: gelatin, methacrylic acid-ethyl acrylate copolymer (1:1), triethyl citrate, water, methacrylic acid-methyl methacrylate copolymer (1:2), titanium dioxide (E 171), glycerol monostearate 40-55, talc, macrogol 4000, indigotine (E 132).

Pharmaceutical form and quantity of active substance per unit

1 hard capsule contains 187 mg (= 0.2 mL) peppermint oil.

Dosage / Administration

Adults from 18 years:

1 capsule three times daily, in case of severe symptoms the dosage may be increased to 2 capsules three times daily (equivalent to 0.6 – 1.2 mL peppermint oil).

Adolescents:

Adolescents aged 15 to 17 years:

1 capsule three times daily (equivalent to 0.6 mL peppermint oil).

Colpermin is intended for use in adults and adolescents aged 15 years and over.

Duration of treatment

Treatment should be continued until symptoms resolve, usually within 1 or 2 weeks, and no longer than 3 months.

Mode of administration

The capsules must be taken whole with some liquid at least 2 hours before or after meals. The capsules must not be broken or chewed.

Contraindications

Hypersensitivity to the active substance or to any excipient listed in the composition.
Achlorhydria.
Colpermin must not be taken in cases of biliary strictures, cholecystitis or liver disease.
Colpermin contains refined arachis oil. Colpermin must not be taken in cases of known hypersensitivity to peanuts and/or soya (cross-allergy).
Children under 15 years of age.

Warnings and precautions

Colpermin should not be taken with food or with medicinal products used to reduce stomach acid. This may result in premature dissolution of the capsule and cause pyrosis as a result of the release of peppermint oil.

If patients suffer from heartburn (including when caused by a diaphragmatic hernia), the condition sometimes worsens after taking peppermint oil. These patients should stop taking this medicine.

Interactions

Simultaneous use of food or antacids could cause premature release of peppermint oil. This assumption is based on in vitro data on the pH-dependent dissolution of Colpermin capsules. Colpermin capsules release their content from pH 6.8 onwards. Antacids and food intake can increase the gastric pH value temporarily.

Pregnancy, lactation

Pregnancy
There exist no or only a limited amount of data concerning the use of peppermint oil in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see preclinical data). The potential risk to humans is unknown. Colpermin is not recommended during pregnancy except when it is clearly indicated. Administration of Colpermin is not recommended in women of childbearing potential who are not using contraception.

Lactation
It is unknown whether peppermint constituents / metabolites are excreted in human milk. A risk to the newborn/infants cannot be excluded. Colpermin should not be used during breastfeeding.

Fertility
No data on the effects of peppermint oil on fertility are available.

Effect on the ability to drive and use machines
No corresponding studies have been conducted in this matter.

Undesirable effects
Summary of the safety profile
Heartburn can occur following administration on a full stomach or in patients with achlorhydria. In patients suffering from haemorrhoids, perianal irritation can occur during treatment with Colpermin. In very rare cases, patients may have an allergic reaction to the active substance or its main component, menthol. The observed reactions, however, were always transient and harmless. In such cases, the medicinal product must be discontinued immediately.

List of adverse reactions

The adverse reactions should be arranged according to MedDRA system organ classes and the conventional frequencies as follows:
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)

Eye disorders
Uncommon: Blurred vision

Renal and urinary disorders
Very rare: Dysuria

Disorders of the blood and the lymph system
Isolated: basophilic leukopenia

Gastro-intestinal disorders
Common: Perianal-irritation (4.2%), heartburn (2.5%), nausea, vomiting
Uncommon: Bleeding of the stomach

Immune system disorders

Uncommon: allergic reactions with skin rash

Very rare*: a*naphylactic reactions

Cardiac disorders

Very rare: bradycardia.

Neurological disorders

Common: headache.

On concomitant intake of alcohol, tremor and impaired motor coordination.

Skin and subcutaneous tissue disorders

Uncommon: Pruritus

Very rare: Erythematous rash, balanitis.

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

https://sideeffects.health.gov.il/

Overdose

Signs and symptoms

Overdose may cause severe gastro-intestinal symptoms, diarrhoea, nausea, rectal ulceration, epileptic convulsions, loss of consciousness, apnoea, disturbances in cardiac rhythms, ataxia and other CNS problems. Literature attributes these to the component menthol.

Treatment

Vomiting should not be induced due to danger of aspiration. Sufficient amounts of liquids should be given (no milk, no alcohol, in order to prevent additional absorption of the essential oil). After ingestion of large amounts or in case of severe clinical symptoms, gastric lavage following endotracheal intubation and the administration of medicinal charcoal are indicated.

Properties/Effects

ATC-Code: A03AX15

Various alimentary tract and metabolism products.

Mechanism of action

Colpermin has a relaxant and antispasmodic effect on the intestinal muscles in intestinal hyper-excitability, particularly in irritable bowel. Colpermin prevents irritation of the stomach, through which the capsule passes undissolved. Menthol (from peppermint oil) is released within about 20 minutes but not until it reaches the alkaline environment of the intestine, where it acts as a local intestinal therapeutic agent, particularly in the colon.

Pharmacodynamics

Peppermint oil exerts a local, dose-dependent muscle relaxant effect and thus results in a reduction of intestinal wall tension. The effect is attributed to an interaction of menthol with voltage-dependent calcium channels.

Clinical efficacy

The clinical efficacy was studied in 404 patients with irritable bowel. Six studies were placebo-controlled, in two studies anticholinergics were used, and in one study psychotherapy was used as a control. Of the six placebo-controlled studies, four achieved a statistically significant result in favour of peppermint oil.

Pharmacokinetics

Absorption

After ingestion of peppermint oil (Colpermin), the active substance, menthol, reaches the small and large sections of the intestine unchanged. The active substance is released continuously from the hydrophobic paste formulation. The absorption of peppermint was measured in 13 healthy subjects on the basis of renal elimination of the main component, menthol. After administration of three capsules of Colpermin, 95.5 mg of menthol (as glucuronide) were eliminated in the urine over a 24-hour period. With an average menthol content of peppermint oil of 44%, a mean absorption of 39% can be deduced. The lag-time was 1.07 hours and a T_{max} of 5 hours was determined.

Distribution

No distribution studies are available.

Metabolism

Menthol, as the main ingredient of peppermint oil, is eliminated predominantly as glucuronide. Animal studies have shown that menthol is also excreted in the form of sulphate.

Elimination

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Colpermin, 95.5 mg of menthol (as glucuronide) were eliminated in the urine over a 24-hour period.

Kinetics of special patient groups

The kinetics of special patient groups (e.g. in patients with hepatic and renal insufficiency, genetic polymorphism) has not been studied.

Preclinical data

Preclinical data concerning repeated dose toxicity are incomplete and therefore of limited informative value. Based on its long-standing clinical use, the safety of the usage of peppermint oil in the given dosage (up to 1.2 mL daily) in humans is sufficiently established.

A standard battery of genotoxicity studies (in-vitro bacterial reverse mutation assay, in-vitro mouse lymphoma assay, in-vivo bone marrow micronucleus assay) showed that Colpermin peppermint oil has no genotoxic potential.

Tests on reproductive toxicity and carcinogenicity have not been performed.
As of 2012, the European Pharmacopoeia has limited the concentration of pulegon (abortifacient) in peppermint oil to 3%, thereby minimising the risk of reproductive toxicity. The highest recommended daily dose is 1.2 mL of peppermint oil, i.e., 1,122 mg of peppermint oil, which, at the most, contains 37.03 mg of pulegone + menthofuran. For a person weighing 50 kg, this would correspond to a daily intake of 0.74 mg/kg body weight. No cases of liver damage caused by peppermint oil or mint oil were reported under that dosage.

Other information

Shelf Life

The expiry date of the product is indicated on the packaging materials.

Special precautions for storage

Keep this medicine out of reach of children.
Store below 25°C.
Store in the original packaging in order to protect the contents from light and moisture.

Instructions for handling

Remove the capsules from the blisters carefully.

Licence number

1090726971

Packs

20, 30, 50, 100 capsules. Not all sizes are marketed.

Licence holder

Tradis Gat Ltd.

32 Shacham St. Petach Tikva

Manufacturer

Tillotts Pharma AG, Baslerstrasse 15, 4310 Rheinfelden Switzerland.

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