SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Colestid

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains 5 g of colestipol hydrochloride.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Granules for oral suspension.

Yellow to orange colored free-flowing beads

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Colestid is indicated as adjunctive therapy to diet in the management of elevated cholesterol levels.

4.2. Posology and method of administration

Treatment for elevated serum cholesterol levels should begin with dietary therapy. A minimum of six months of dietary therapy and counseling should usually be undertaken before initiating drug therapy; shorter periods can be considered in patients with severe elevations of LDL-cholesterol (>225 mg/dl or 5.8 mmol/L) or definite Coronary Heart Disease. Drug therapy should be added to dietary therapy, and not substituted for it.
Colestipol hydrochloride granules should never be taken in dry form. Esophageal spasm or respiratory distress can result from attempting to swallow the granules dry.
Route of administration: Oral, mixed with water or other fluids.
Adults:
The recommended initial daily adult dosage of colestipol hydrochloride is 5 grams either once or twice daily.
For adults colestipol hydrochloride is recommended in doses of 5 - 30 grams taken as one dose or two divided doses. Initiation of therapy is recommended at 5 grams either once or twice daily with 5 gram increments at one month intervals. Appropriate use of lipid profiles including LDL-cholesterol and triglycerides is advised so that optimal, but not excessive doses are used to obtain the desired therapeutic effect on LDL-cholesterol level. If the desired therapeutic effect is not obtained at a dose of 5 - 30 grams/day with good compliance and acceptable side-effects, combined therapy or alternate treatment should be considered.
Patients should take other drugs at least one hour before or four hours after Colestid to minimise possible interference with their absorption. However, Colestid and Gemfibrozil may be used in the same patient when administered 2 hours apart (see Interactions).

Preparation:

Colestid Granules should always be taken mixed in a liquid such as orange or tomato juice, water, skimmed milk or non-carbonated beverage. The contents of the sachet or level scoopful should be added to 100 ml or more of the preferred aqueous vehicle and mixed thoroughly until dispersed (cholestipol hydrochloride will not dissolve in the liquid). Colestid may also be taken in soups or with cereals, pulpy fruits with a higher water content or yoghurt.

Elderly Patients:
At present there are no extensive clinical studies with colestipol in patients over the age of 65. Review of available data does not suggest that the elderly are more predisposed to side effects attributable to colestipol than the general population; however, therapy should be individualised and based on each patient's clinical characteristics and tolerance to the medication.

Children:
Dosage in children has not been established.

4.3. Contraindications

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

4.4. Special warnings and precautions for use

Warnings:
Before instituting therapy with Colestid, diseases contributing to increased blood cholesterol such as hypothyroidism, diabetes mellitus, nephrotic syndrome, dysproteinaemias and obstructive liver disease should be looked for and specifically treated.

To avoid accidental inhalation or oesophageal distress, Colestid should not be taken in its dry form.

Colestid may elevate serum triglyceride levels when used as sole therapy. This elevation is generally transient but may persist in some individuals. A significant rise in triglyceride level should be considered as an indication for dose reduction, drug discontinuation, or combined or alternate therapy.

Paediatric population
The use of Colestid in children has been limited; however, it does appear to be effective in lowering serum cholesterol in older children and young adults. Because bile acid sequestrants may interfere with the absorption of fat soluble vitamins, appropriate monitoring of growth and development is essential. Dosage and long term safety in children has not been established.

Precautions:
Effect on vitamin absorption
Because it sequesters bile acids, Colestid may interfere with normal fat absorption and may thus alter the absorption of fat soluble vitamins such as A, D, E and K. A study in humans found only one patient in whom a prolonged prothombin time was noted. Most studies did not show a decrease in vitamin A, D or E levels during the administration of Colestid; however, if Colestid is to be given for a long period these vitamin levels should be monitored and supplements given if necessary.

Both clinical usage and animal studies with Colestid have provided no evidence of drug related intestinal neoplasms. Colestid is not mutagenic in the Ames test.

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

In man, Colestid may delay or reduce the absorption of certain concomitant oral drugs (digitalis and its glycosides, propranolol and hydrochlorothiazide, tetracycline hydrochloride, penicillin G, gemfibrozil and furosemide). Studies in humans have shown that the absorption of chlorothiazide is markedly decreased even when administered 1 hour before the administration of colestipol hydrochloride. Particular caution should be taken with digitalis preparations since conflicting results have been obtained for the effect of Colestid on the availability of digoxin and digitoxin. Colestid has been shown not to interfere with the bioavailability of the respective drugs clindamycin, clofibrate, aspirin, tolbutamide, warfarin, methyldopa and phenytoin. The clinical response to concomitant medication should be closely monitored and appropriate adjustments made.

Repeated doses of Colestid given prior to a single-dose of propranolol in human trials have been reported to decrease propranolol absorption. However, in a follow-up study in normal subjects, single dose administration of Colestid and propranolol or multiple-dose administration of both agents did not affect the extent of propranolol absorption. Effects on the absorption of other beta-blockers have not been determined. Patients on propranolol should be observed when Colestid is either added or deleted from a therapeutic regimen.

A study has shown that cholestyramine binds bile acids and reduces mycophenolic acid exposure. As colestipol also binds bile acids, colestipol may reduce mycophenolic acid exposure and potentially reduce efficacy of mycophenolate mofetil.

4.6. Fertility, pregnancy and lactation

Pregnancy
No clinical data are available on the use of colestipol hydrochloride in pregnant women. Though animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3), caution should be exercised when prescribing to pregnant women.
The use of Colestid in pregnancy or lactation or by women of childbearing age requires that the potential benefits of treatment be weighed against the possible hazards to the mother and child.

Breast-feeding
The safety of colestipol hydrochloride has not been established in breast-feeding women. Caution should be exercised when prescribing to breast-feeding women.

Fertility
There are no data on the effect of colestipol hydrochloride on fertility in humans. A study conducted in rats did not result in any differences in reproductive parameters that might imply reproductive effects attributable to colestipol hydrochloride.

4.7. Effects on ability to drive and use machines

No adverse effect has been reported.

4.8. Undesirable Effects

Adverse events are described by system organ class and frequency (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) in the table below:

MedDRA System Organ Class	**Frequency**	**Undesirable Effects**
Metabolism and nutrition disorders	Uncommon	Decreased appetite
Psychiatric disorders	Uncommon	Insomnia

Nervous system disorders	Very common	Migraine, Sinus headache, Headache
	Uncommon	Dizziness
Cardiac disorders	Uncommon	Angina pectoris, Tachycardia
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea
Gastrointestinal disorders	Very common	Constipation, Abdominal pain, Abdominal discomfort
	Common	Haematochezia, Haemorrhoidal haemorrhage, Abdominal distention, Dyspepsia, Nausea, Vomiting, Diarrhoea, Flatulence, Eructation
	Uncommon	Peptic ulcer and bleeding, Haemorrhoids, Impaction
Hepatobiliary disorders	Uncommon	Cholecystitis, Cholelithiasis
Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Urticaria, Dermatitis
Musculoskeletal and connective tissue disorders	Common	Arthritis, Arthralgia, Back pain, Musculoskeletal pain, Pain in extremity
General disorders and administration site conditions	Common	Fatigue
	Uncommon	Chest pain, Oedema peripheral, Asthenia
Investigations	Uncommon	Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood alkaline phosphatase increased

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/

4.9. Overdose

No toxic effects due to overdosage have been reported. Should overdosage occur, obstruction of the gastro-intestinal tract would be expected to occur. Treatment would be determined by the location and degree of obstruction.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: bile acid sequestrants, ATC code: C10AC02

Ion exchange resin which lowers plasma cholesterol through binding with bile acids in the intestinal lumen

5.2 Pharmacokinetic properties

Colestid is not absorbed; its action is limited to the lumen of the gastro-intestinal tract, and it is passed in the faeces. It binds bile acids in the intestinal lumen and causes them to be excreted in the faeces together with the polymer. When the enterohepatic circulation of bile acids is

interrupted, cholesterol conversion to bile acids is enhanced and plasma cholesterol levels are thereby lowered.

5.3. Preclinical safety data

Both clinical and animal studies with Colestid have provided no evidence of drug related intestinal neospasms. Colestid is not mutagenic in the Ames test.

Reproduction and teratologic studies in animals gave no evidence of drug toxicity in parents or offspring.

6. PHARMACUETICAL PARTICULARS

6.1. List of excipients

Colloidal anhydrous silica

6.2. Incompatibilities

Not applicable

6.3. Shelf life

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

6.4. Special precautions for storage

store below 25°C

6.5. Nature and contents of container

Paper/polyethylene /aluminium sachet of 5 g X 50.

6.6. Special precautions for disposal and other handling

No special requirements for disposal.

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

7. MARKETING AUTHORISATION HOLDER

Pfizer PFE Pharmaceuticals Israel Ltd 9 Shenkar St Herzliya Pituach

8. MARKETING AUTHORISATION NUMBER

044-74-23527

9. MANUFACTURER

Farmea, France

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