PRODUCT: STOPKOF SYRUP
(COUGH SYRUP ADULT)

MODULE 2 COMMON TECHNICAL DOCUMENT SUMMARIES
SECTION 1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

SUB SECTION

1.3.1 Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Stopkof syrup 100 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains Diphenhydramine Hydrochloride 13.5 mg Ammonium chloride 131.5 mg

Sr. No	Ingredients	Quantity (mg/ 5 ml)	Function of Ingredients
1	Diphenhydramine Hydrochloride	13.50	Active
2	Ammonium chloride	131.50	Active
3	Sugar	742.50	Sweetening agent / syrup base
4	Sodium Benzoate	25.00	Preservative
5	Sodium Saccharine	15.00	Sweetening agent
6	Sodium citrate	57.665	pH adjustment
7	Glycerin	0.156 ml	Demulcent
8	Liquid glucose	2.494	Anti-crystallizing agent
9	Menthol	0.550	Flavouring agent
10	Propylene glycol	0.259 ml	Vehicle
11	Citric acid anhydrous (For pH adjustment)	q.s	pH adjustment
12	Trisodium citrate dihydrate(For pH adjustment)	q.s	pH adjustment
13	Soluble Essence cherry	0.010 ml	Flavour
14	Purified water	q.s to 5 ml	Vehicle

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3. PHARMACEUTICAL FORM

Colourless to pale yellow syrupy liquid with pleasant odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

Stopkof syrup is indicated for the relief of cough and associated congestive symptoms.

4.2 Posology and Method of Administration

For oral use

Adults and Children aged 12 years and over:

Adults and children aged 12 years and above 5-10 ml of syrup every 4 hours

Children aged 6-12 years - 5 ml of syrup 4 times a day.

Children under 12 years:

Not recommended for children under 6 years.

Route of Administration: Oral

4.3 Contraindications

Stopkof syrup is contraindicated in individuals with known hypersensitivity to the product or any of its constituents.

Stopkof syrup is contraindicated in individuals with chronic or persistent cough, such as occurs with asthma, or where cough is accompanied by excessive secretions, unless directed by the physician.

Stopkof syrup should not be administered to patients currently receiving monoamine oxidase inhibitors (MAOI) or those patients who have received treatment with MAOIs within the last two weeks.

Not recommended for children below 6 years of age.

4.4 Special warnings and precautions for use

This product may cause drowsiness. If affected individuals should not drive or operate machinery.

Subjects with moderate to severe renal or hepatic dysfunction or urinary retention should exercise caution when using this product (see Pharmacokinetics - Renal/Hepatic Dysfunction).

This product contains Diphenhydramine and therefore should not be taken by individuals with narrow-angle glaucoma or symptomatic prostatic hypertrophy.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine

4.5 Interaction with other medicinal products and other forms of interaction

This product contains Diphenhydramine and therefore may potentiate the effects of alcohol, codeine, antihistamines and other CNS depressants.

As Diphenhydramine possesses some anticholinergic activity, the effects of anticholinergics (eg. some psychotropic drugs and atropine) may be potentiated by this product. This may result in tachycardia, dry mouth, gastrointestinal disturbances (eg, colic), urinary retention and headache.

4.6 Fertility, pregnancy and lactation

Although Diphenhydramine has been in widespread use for many years without ill consequence, it is known to cross the placenta and has been detected in breast milk. Stopkof Syrup should therefore only be used when the potential benefit of treatment to the mother exceeds any possible hazards to the developing foetus or suckling infant.

4.7 Effects on ability to drive and use machines

This product may cause drowsiness. If affected, the patient should not drive or operate machinery.

4.8 Undesirable effects

Side effects associated with the use of Stopkof syrup are uncommon.

Diphenhydramine may cause drowsiness; dizziness; gastrointestinal disturbance; dry mouth; nose and throat; difficulty in urination or blurred vision.

Less frequently it may cause palpitations, tremor, convulsions or parasthesia.

Hypersensitivity reactions have been reported, in particular, skin rashes, erythema, urticaria and angiodema.

Adverse reactions to menthol at the low concentration present in Stopkof Syrup are not anticipated.

4.9 Overdose

Symptoms and signs

The symptoms and signs of Stopkof syrup overdose may include drowsiness, hyperpyrexia and anticholinergic effects. With higher doses, and particularly in children, symptoms of CNS excitation including hallucinations and convulsions may appear; with massive doses, coma or cardiovascular collapse may follow.

Treatment

Treatment of overdose should be symptomatic and supportive. Measures to promote rapid gastric emptying (with Syrup of Ipecac-induced emesis or gastric lavage) and, in cases of acute poisoning, the use of activated charcoal may be useful. Seizures may be controlled with Diazepam or Thiopental Sodium. The intravenous use of Physostigmine may be efficacious in antagonizing severe antichlolinergic symptoms

5. Pharmacological properties

5.1 Pharmacodynamic properties

Diphenhydramine possesses antitussive, antihistaminic and anticholinergic properties. Experiments have shown that the antitussive effect (resulting from an action on the brainstem) is discrete from its antihistaminic effect.

The duration of activity of Diphenhydramine is between 4 and 8 hours.

Menthol has mild local anaesthetic and decongestant properties.

5.2 Pharmacokinetic properties

Absorption

Diphenhydramine and menthol are well absorbed from the gut following oral administration. Peak serum levels of Diphenhydramine following a 50 mg oral dose are reached at between 2 and 2.5 hours.

Distribution

Diphenhydramine is widely distributed throughout the body, including the CNS. Following a 50 mg oral dose of Diphenhydramine, the volume of distribution is in the range 3.3 - 6.8 l/kg, and it is some 78% bound to plasma proteins.

Metabolism and Elimination

Diphenhydramine undergoes extensive first pass metabolism. Two successive N-demethylations occur, with the resultant amine being oxidised to a carboxylic acid. Values for plasma clearance of a 50 mg oral dose of Diphenhydramine lie in the range 600-1300 ml/min and the terminal elimination half-life lies in the range 3.4 - 9.3 hours. Little unchanged drug is excreted in the urine. Menthol is hydroxylated in the liver by microsomal enzymes to p-methane-3,8 diol. This is then conjugated with glucuronide and excreted both in urine and bile as the Glucuronide

The Elderly

Pharmacokinetic studies indicate no major differences in distribution or elimination of Diphenhydramine compared to younger adults.

Renal Dysfunction

The results of a review on the use of Diphenhydramine in renal failure suggest that in moderate to severe renal failure, the dose interval should be extended by a period dependent on Glomerular filtration rate (GFR).

Hepatic Dysfunction

After intravenous administration of 0.8 mg/kg Diphenhydramine, a prolonged half-life was noted in patients with chronic **liver disease** which correlated with the severity of the disease. However, the mean plasma clearance and apparent volume of distribution were not significantly affected.

5.3 Preclinical safety data

Mutagenicity

The results of a range of tests suggest that neither Diphenhydramine nor menthol have mutagenic potential.

Carcinogenicity

There is insufficient information to determine the carcinogenic potential of Diphenhydramine or menthol, although such effects have not been associated with these drugs in animal studies.

Teratogenicity

The results of a number of studies suggest that the administration of either Diphenhydramine or menthol does not produce any statistically significant teratogenic effects in rats, rabbits and mice.

Fertility

There is insufficient information to determine whether Diphenhydramine has the potential to impair fertility, although a diminished fertility rate has been observed in mice in one study.

6. Pharmaceutical particulars

6.1 List of excipients

Sugar

Sodium Benzoate

Sodium Saccharine

Sodium citrate

Glycerin

Liquid glucose

Menthol

Propylene glycol

Citric acid anhydrous (For pH adjustment)

Trisodium citrate dihydrate (For pH adjustment)

Soluble Essence cherry

Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C, protected from light.

6.5 Nature and contents of container

100 ml amber glass bottle sealed with plastic caps having PE wads.

6.6 Special precautions for disposal and other handling

No special requirements for storage.

7. Marketing authorization holder

National Pharmaceutical Industries Co. (SAOG)

P.O Box 120, Road No.15

Postal Code 124

Rusayl, Sultanate of Oman