1.3 Product Information
1.3.1 Summary of product characteristics (SmPC)
1. 3.1.1 Name of the medicinal product:

COCOFF
(Chlorphenamine Maleate & Phenylephrine Hydrochloride Capsules)

1.3. 1.2 Qualitative and quantitative composition:
Each Capsule Contains:
- Chlorphenamine Maleate (In pellets form) (4 mg)
- Phenylephrine Hydrochloride (In pellets form) (2.5 mg)
- Approved Colours are Used in Pellets and Empty Capsule Shell. (-)

Sr. No.	Ingredients	Specifi-cation	Label Claim / Capsule (In mg)	Over ages added (In %)	Qty. / Capsule (In mg)	Reason for Function
1.	Chlorphenamine Maleate 4 mg & Phenylephrine Hydrochloride 2.5 mg Pellets	IHS	Chlorphenamine Maleate (In pellets form) (4 mg) Phenylephrine Hydrochloride (In pellets form) (2.5 mg)	NA	Pellets of Chlorphenamine Maleate and Phenylephrine Hydrochloride260.00mg equivalent to Chlorphenamine Maleate 4mg and Phenylephrine Hydrochloride 2.5mg	Medicament
2.	EHG Capsule Size`2` Cap-Pink Body-Clear Transparent	IHS	NA	NA	1 Capsule = 63 mg	Capsule Shell
	Net Content/Capsule (In mg)				**260.00**	
	Weight of Empty Hard Gelatin Capsule Shell (In mg)				**63.00**	
	Average Weight of Filled Capsule (In mg)				**323.00**	

1.3 Pharmaceutical form: Hard Gelatin Capsules
Description: Pink coloured Cap and Clear Transparent body of capsules size 2 containing white, pink and yellow pellets.

1.4 Clinical Particulars

1.4.1 Therapeutic indications

COCOFF (Chlorphenamine Maleate 4 mg & Phenylephrine Hydrochloride 2.5 mg Capsules) is indicated for effective relief from Nasal congestion, running nose, sneezing, rhinitis, upper respiratory congestion associated
with influenza & common cold

1.4.2 Posology and method of administration

Route: Oral
1 capsules 3 to 4 times a day or as directed by the physician.

1.4.3 Contraindications

COCOFF (Chlorphenamine Maleate 4 mg & Phenylephrine Hydrochloride 2.5 mg Capsules) is contraindicated in the following patients:
-Severe coronary heart disease and cardiovascular disorders.
-Hypertension.
-Hyperthyroidism.
-Contraindicated in patients currently receiving or within two weeks of stopping therapy with monoamine oxidase inhibitors
- The anticholinergic properties of Chlorphenamine are intensified by monoamine oxidase inhibitors (MAOIs). The tablets are therefore contraindicated in patients who have been treated with MAOIs within the last fourteen days.

1.4.4 Special warnings and precautions for use

Chlorphenamine in common with other drugs having anticholinergic effects, should be used with caution in epilepsy, raised intra-ocular pressure including glaucoma, prostatic hypertrophy; severe hypertension or cardiovascular disease; bronchitis, bronchiectasis and asthma; hepatic impairment; renal impairment. Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness). Avoid use in elderly patients with confusion.
The anticholinergic properties of Chlorphenamine may cause drowsiness, dizziness, blurred vision and psychomotor impairment in some patients which may seriously affect ability to drive and use machinery.
Concurrent use with drugs which cause sedation such as anxiolytics and hypnotics may cause an increase in sedative effects, therefore medical advice should be sought before taking Chlorphenamine concurrently with these medicines.
The effects of alcohol may be increased and therefore concurrent use should be avoided.
Should not be used with other antihistamine containing products, including antihistamine containing cough and cold medicines
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. Keep out of the sight and reach of children.
Use with caution in patients with Raynaud's phenomenon or diabetes mellitus.
Patients with prostatic hypertrophy may have increased difficulty with micturition.
Phenylephrine should be used with care in patients with closed angle glaucoma and prostatic enlargement.

1.4.5 Interaction with other medicinal products and other forms of interaction

Concurrent use of chlorphenamine and hypnotics or anxiolytics may cause an increase in sedative effects, therefore medical advice should be sought before taking chlorphenamine concurrently with these medicines.

Chlorphenamine inhibits phenytoin metabolism and can lead to phenytoin toxicity.
The anticholinergic effects of chlorphenamine are intensified by MAOIs
Monoamine oxidase inhibitors (including moclobemide): hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors
Sympathomimetic amines: concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects.

Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa): phenylephrine may reduce the efficacy of beta-blockers and antihypertensives. The risk of hypertension and other cardiovascular side effects may be increased.

Tricyclic antidepressants (e.g. amitriptyline): may increase the risk of cardiovascular side effects with phenylephrine.

Digoxin and cardiac glycosides: concomitant use of phenylephrine may increase the risk of irregular heartbeat or heart attack.

1.4.6 Pregnancy and Lactation

Pregnancy
There is no adequate data from the use of chlorphenamine maleate in pregnant women. The potential risk for humans is unknown. Use during the third trimester may result in reactions in the newborn or premature neonates. Not to be used during pregnancy unless considered essentially by a physician.

Due to the vasoconstrictive properties of phenylephrine the product should not be used in patients with a history of pre-eclampsia. Phenylephrine may reduce placental perfusion. There is no information on use in lactation. The safety of this medicine during pregnancy and lactation has not been established but in view of a possible association of foetal abnormalities with first trimester exposure to phenylephrine, the use of the product during pregnancy should be avoided. emature neonates. Not to be used during pregnancy unless considered essentially by a physician.

Breast-feeding
Chlorphenamine maleate and other antihistamine may inhibit lactation and may be secreted in breast milk. Not to be used during lactation unless considered essential by a physician.

1.4.7 Effects on ability to drive and use machines

The anticholinergic properties of chlorphenamine may cause drowsiness, dizziness, blurred vision and psychomotor impairment which can seriously hamper the patient's ability to drive and use machinery.
If affected, patients should not drive or operate machinery.

1.4.8 Undesirable effects

Phenylephrine hydrochloride
High blood pressure with headache, vomiting, probably only in overdosage. Rarely, palpitations. Also, rare reports of allergic reactions and occasionally urinary retention in males.
Adverse reactions identified during post-marketing use with chlorphenamine are listed below. As these reactions are reported voluntarily from a population of uncertain size, the frequency of some reactions is unknown but likely to be rare or very rare

System Organ Class	Adverse Reaction	Frequency
Nervous system disorders	Sedation, somnolence	Very common
	Disturbance in attention,	Common

	abnormal co-ordination, dizziness, headache	
Eye disorders	Blurred vision	Common
Gastrointestinal disorders	Nausea, dry mouth	Common
	Vomiting, abdominal pain, diarrhoea, dyspepsia	Unknown
Immune system disorders	Allergic reaction, angioedema, anaphylactic reactions	Unknown
Metabolism and nutritional disorders	Anorexia	Unknown
Blood and lymphatic system disorders	Haemolytic anaemia, blood dyscrasias	Unknown
Musculoskeletal and connective tissue disorders	Muscle twitching, muscle weakness	Unknown
Psychiatric disorders	Confusion, excitation, irritability, nightmares, depression	Unknown
Renal and urinary disorders	Urinary retention	Unknown
Skin and subcutaneous disorders	Exfoliative dermatitis, rash, urticaria, photosensitivity	Unknown
Respiratory, thoracic and mediastinal disorders	Thickening of bronchial secretions	Unknown
Vascular disorders	Hypotension	Unknown
Hepatobiliary disorders	Hepatitis, including jaundice	Unknown
Ear and labyrinth disorders	Tinnitus	Unknown
Cardiac disorders	Palpitations, tachycardia, arrhythmia	Unknown
General disorders and administration site conditions	Fatigue	Common
	Chest tightness	Unknown

1.4.9 Overdose

Symptoms and signs

The estimated lethal dose of Chlorphenamine is 25 to 50mg/kg body weight. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, apnoea, convulsions, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias.

Features of severe overdosage of phenylephrine include haemodynamic changes and cardiovascular collapse with respiratory depression. Treatment includes early gastric lavage and symptomatic and supportive measures. Hypertensive effects may be treated with an i.v. alpha-receptor blocking agent.

Phenylephrine overdose is likely to result in: nervousness, headache, dizziness, insomnia, increased blood pressure, nausea, vomiting, mydriasis, acute angle closure glaucoma (most likely to occur in those with closed angle glaucoma), tachycardia, palpitations, allergic reactions (e.g. rash, urticaria, allergic dermatitis), dysuria, urinary retention (most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy). Additional symptoms may include, hypertension, and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may

occur. However, the amount required to produce serious phenylephrine toxicity would be greater than that required to cause paracetamol-related liver toxicity.

Treatment
Management should be as clinically indicated or as recommended by the national poisons centres where available.
Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions, and fluid and electrolyte balance. Severe hypertension may need to be treated with alpha blocking medicinal products such as phentolamine.
If overdosage is by the oral route, treatment with activated charcoal should be considered provided there are no contraindications for use and the overdose has been taken recently (treatment is most effective if given within an hour of ingestion).
Treat hypotension and arrhythmias vigorously; CNS convulsions may be treated with I.V. diazepam.
Haemoperfusion may be used in severe cases

1.5 Pharmacological properties

5.1 Pharmacodynamic properties
ATC Code: R06AB04
Chlorphenamine is a potent antihistamine (H1-antagoonist). Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine H1-receptor sites on tissues. Chlorphenamine also has anticholinergic activity.
Antihistamines act to prevent the release of histamine, prostaglandins and leukotrienes and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenamine include inhibition of histamine on smooth muscle, capillary permeability and hence reduction of oedema and wheal in hypersensitivity reactions such as allergy and anaphylaxis.

Phenylephrine: phenylephrine is a post-synaptic alpha-receptor agonist with low cardioselective beta-receptor affinity and minimal central stimulant activity. It is a recognised decongestant and acts by vasoconstriction to reduce oedema and nasal swelling.

5.2 Pharmacokinetic properties
Chlorphenamine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours.

There is significant plasma protein binding. The drug is largely inactivated in the liver and excreted as metabolites in the urine. Chlorphenamine is metabolised to the monodesmethyl and didesmethyl derivative. About 22% of an oral dose is excreted unchanged in the urine. Only trace amounts have been found in the faeces.
Phenylephrine: Phenylephrine is absorbed from the gastro-intestinal tract, but has reduced bioavailability by the oral route due to first-pass metabolism. It retains activity as a nasal decongestant when given orally, the drug distributing through the systemic circulation to the vascular bed of nasal mucosa. When taken by mouth as a nasal decongestant, phenylephrine is usually given at intervals of 4-6 hours.

5.3 Preclinical safety data
None stated.

1.3.1.6 Pharmaceutical particulars

1.3.1.6.1 List of excipients

There are no excipients used in the formulation. Ready Pellets Chlorphenamine Maleate 4 mg & Phenylephrine Hydrochloride 2.5 mg are directly used for encapsulation in the formulation of **COCOFF** (Chlorphenamine Maleate 4 mg & Phenylephrine Hydrochloride 2.5 mg Capsules)

1.3.1.6.2 Incompatibilities

Not applicable

1.3.1.6.3 Shelf life

36 months

1.3.1.6.4 Special precautions for storage

Store below 30˚C in dry and dark place.
Keep all medicines out of reach of children.

1.3.1.6.5 Nature and contents of container

Packing:

Primary packing: 10 capsules are packed in ALU-PVC blister.
Secondary packing: Such 10 blisters are packed in a carton along with leaflet.
Tertiary packing: Such 10 cartons are packed in a shrink. Such 20 shrinks are packed in 5 Ply corrugated box sealed with BOPP tape & strap with strapping roll.

1.3.1.6.5 Special precautions for disposal and other handling

None.

1.3.1.7 Applicant / Manufacturer

Applicant

Applicant name and address	**M/s. ANISUN PHARMACEUTICALS CO. NIG.LTD.** No. 29, Heritage Avenue Omgba phase II, Onitsha, Anambra State.
Contact person's phone number	
Contact person's email	

Manufacturer

Manufacturer name and address	**M/s. IMPULSE PHARMA PVT. LTD.** J-201, J-202/1 MIDC Tarapur, Boisar, Dist. Palghar - 401506, Maharashtra State, India.
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