NOCIN TABLETS (Triprolidine and Pseudoephedrine Hydrochlorides Tablets USP)

Module 1- Administrative information and prescribing information

Summary Product Characteristics (SPC)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

NOCIN TABLETS (Triprolidine and Pseudoephedrine Tablets USP)

1.1 Strength

Each uncoated tablets contains:

Triprolidine Hydrochloride USP..... .....2.5 mg

Pseudoephedrine Hydrochloride USP....60 mg

Excipients..... .....Q.S.

1.2 Pharmaceutical form

Uncoated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sr. No.	Name of raw material	Specification	Qty. per Tab (mg)	Purpose of use
1.	Triprolidine Hydrochloride	USP	2.5	Active
2.	Pseudoephedrine Hydrochloride	USP	60.0	Active
3.	Maize Starch	BP	30.0	Diluent
4.	Lactose	BP	37.5	Diluent
5.	Povidone	BP	5.0	Binder
6.	Isopropyl alcohol*	BP	Q.S	Solvent
7.	Magnesium Stearate	BP	5.0	Lubricant
8.	Colloidal Anhydrous Silica	BP	2.0	Disintegrant
9.	Sodium Starch Glycolate	BP	8.0	Disintegrant

USP : United State Pharmacopoeia

BP : British Pharmacopoeia

*Removed after drying and does not present in the finished product

3. PHARMACEUTICAL FORM

Uncoated tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets are indicated for the symptomatic relief of upper respiratory tract disorders which are benefited by a combination of a nasal decongestant and H1-receptor antagonist, for example allergic rhinitis, vasomoter rhinitis and the common cold.

4.2 Posology and method of administration

Posology

Adults and children 12 years and over:

One tablet to be taken every 4-6 hours, up to four times a day.

Children under 12 years:

This medicine is contraindicated in children under the age of 12 years.

The Elderly:

There have been no specific studies of TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets in the elderly. Experience has indicated that normal adult dosage is appropriate.

Hepatic Dysfunction:

Caution should be exercised when administering Triprolidine and Pseudoephedrine Tablets to patients with severe hepatic impairment.

Renal Dysfunction:

Caution should be exercised when administering Triprolidine and Pseudoephedrine Tablets to patients with mild to moderate renal impairment.

Method of Administration

For oral use

4.3 Contraindications

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets are contra-indicated in individuals with known hypersensitivity to pseudoephedrine, triprolidine or to any of the excipients.

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets are contra-indicated in patients with cardiovascular disease including hypertension, and in those who are taking beta-blockers

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets are contra-indicated in individuals who have diabetes mellitus, phaeochromocytoma, hyperthyroidism, closed angle glaucoma, or severe renal impairment.

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets are contra-indicated in patients who are taking, or have taken, monoamine oxidase inhibitors within the preceding two weeks. The concomitant use of pseudoephedrine and this type of product may cause a rise in blood pressure or hypertensive crisis.

This medicine is contra-indicated in individuals at risk of developing respiratory failure.

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets are contra-indicated in patients who are currently taking other sympathomimetic decongestants.

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets are contra-indicated for use in children under 12 years of age

4.4 Special warnings and precautions for use

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets may cause drowsiness. This product should not be used to sedate a child.

If any of the following occur, this product should be stopped:

- Hallucinations
- Restlessness
- Sleep disturbances

Caution should be exercised when administering to patients with severe hepatic impairment or mild to moderate renal impairment.

Although pseudoephedrine has virtually no pressor effects in patients with normal blood pressure, TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets should be used with

caution in patients taking antihypertensive agents and tricyclic antidepressants or other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants. The effects of a single dose on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

The physician or pharmacist should check that sympathomimetic containing preparations are not simultaneously administered by several routes i.e. orally and topically (nasal, aural and eye preparations).

Patients with the following conditions should be advised to consult a physician before using TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets: difficulty in urination due to enlargement of the prostate; or susceptibility to angle-closure.

Patients with the following conditions should not use TRIPROLIDINE AND PSEUDOEPHEDRINE Syrup unless directed by a physician: acute or chronic bronchial asthma chronic bronchitis or emphysema.

Patients with thyroid disease who are receiving thyroid hormones should not take pseudoephedrine unless directed by a physician.

There have been reports of ischemic colitis with pseudoephedrine. Pseudoephedrine should be discontinued immediately and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischemic colitis develop

There have been rare cases of posterior reversible encephalopathy (PRES) / reversible cerebral vasoconstriction syndrome (RCVS) reported with sympathomimetic drugs, including pseudoephedrine. Symptoms reported include sudden onset of severe headache, nausea, vomiting, and visual disturbances. Pseudoephedrine should be discontinued, and medical advice sought immediately if signs or symptoms of PRES/RCVS develop.

Triprolidine may enhance the sedative effects of central nervous system depressants including alcohol, sedatives and tranquilizers. While taking TRIPROLIDINE AND PSEUDOEPHEDRINE tablets, patients should be advised to avoid alcoholic beverages and consult a healthcare professional prior to taking with central nervous system depressants.

This product may act as a cerebral stimulant giving rise to insomnia, nervousness, hyperpyrexia, tremors and epileptiform convulsions. Care should be taken when used in epileptic patients

Use with caution in occlusive vascular disease.

Pseudoephedrine may induce positive results in certain anti-doping tests

This medicinal product contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine..

4.5 Paediatric population

Not Applicable

4.6 Interaction with other medicinal products and other forms of interaction

MAOIs and/or RIMAs: Pseudoephedrine exerts its vasoconstricting properties by stimulating α-adrenergic receptors and displacing noradrenaline from neuronal storage sites. Since MAOIs impede the metabolism of sympathomimetic amines and increase the store of releasable norepinephrine in adrenergic nerve endings, MAOIs may potentiate the pressor effect of pseudoephedrine. This medicine should not be used in patients treated with MAOIs or within 14 days of stopping treatment as there is an increased risk of hypertensive crisis.

Moclobemide: risk of hypertensive crisis.

Oxytocin: risk of hypertension.

Cardiac glycosides: increased risk of dysrhythmias.

Ergot alkaloids (ergotamine & methysergide): increased risk of ergotism.

Anticholinergic drugs: The effects of anti-cholinergics e.g., some psychotropic drugs (such as tricyclic antidepressants) and atropine, may be potentiated by this product, giving rise to tachycardia, mouth dryness, gastrointestinal disturbances, e.g., colic, urinary retention and headache.

Sympathomimetic agents: Concomitant use of TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets with tricyclic antidepressants, other sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) may cause a rise in blood pressure.

Antihypertensives: The effect of antihypertensive agents which interfere with sympathetic activity may be partially reversed by the pseudoephedrine in TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets, e.g. bretylium, betanidine, guanethidine, reserpine, debrisoquine, methyldopa, adrenergic neurone blockers and beta-blockers.

Anaesthetic agents: Concurrent use with halogenated anaesthetic agents such as chloroform, cyclopropane, halothane, enflurane or isoflurane may provoke or worsen ventricular arrhythmias.

CNS depressants: Triprolidine may enhance the sedative effects of alcohol and other central nervous system depressants including barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and antipsychotics.

4.7 Additional information on special populations

Not known

4.8 Fertility, pregnancy and lactation

There are no adequate and well-controlled studies for pseudoephedrine, triprolidine in pregnant or breast-feeding women.

Fertility

There is no information on the effects of TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets on human fertility.

Pregnancy

This product should not be used during pregnancy unless the potential benefit of treatment to the mother outweighs the possible risks to the developing foetus.

Breast-feeding

Pseudoephedrine distributes into and is concentrated in breast milk.

Triprolidine is excreted in breast milk, it has been estimated that approximately 0.06 to 0.2% of a single 2.5 mg dose of triprolidine ingested by a nursing mother will be excreted in the breast-milk over 24 hours.

This product should not be used during lactation unless the potential benefit of treatment to the mother outweighs the possible risks to the nursing infant.

4.9 Effects on ability to drive and use machines

TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets may have a moderate influence on the ability to drive and use machines. TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets may cause dizziness or drowsiness and impair performance in tests of auditory

vigilance. Patients should be cautioned about engaging in activities requiring mental alertness, such as driving a car or operating machinery, until they have established their own response to the drug.

It is recommended that patients are advised not to undertake tasks requiring mental alertness whilst under the influence of alcohol or other CNS depressants. Concomitant administration of TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets may, in some patients, produce additional impairment.

4.10 Undesirable effects

Placebo-controlled studies with sufficient adverse event data were not available for the combination of pseudoephedrine and triprolidine.

Adverse drug reactions identified during clinical trials and post-marketing experience with pseudoephedrine, triprolidine or the combination are listed below by System Organ Class (SOC). The frequencies are defined in accordance with current guidance, as:

Very common ≥1/10

Common ≥1/100 and < 1/10

Uncommon ≥1/1,000 and <1/100

Rare ≥1/10,000 and <1/1,000

Very rare <1/10,000

Not known (cannot be estimated from the available data)

ADRs are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available, or 2) when incidence cannot be estimated, frequency category is listed as 'Not known'.

ADRs Identified During Post-Marketing Experience with Pseudoephedrine or the Combination of Pseudoephedrine and Triprolidine by Frequency Category Estimated from Clinical Trials or Epidemiology Studies

System Organ Class (SOC)	**Adverse Drug Reaction (Preferred Term)**	**Frequency**
Blood and Lymphatic System	Blood disorder	Rare

Disorders		
Immune System Disorders	Hypersensitivity – cross sensitivity may occur with other sympathomimetics	Rare
Psychiatric Disorders	Insomnia[f]	Common
	Nervousness[f]	Common
	Hallucination	Rare
	Confusional state	Rare
	Depression	Rare
	Sleep disorder	Rare
	Agitation	Not known
	Anxiety	Not known
	Delusion	Not known
	Euphoric mood	Not Known
	Hallucination, visual	Not known
	Irritability	Not known
	Restlessness	Not known
Nervous System Disorders	Headache	Very common
	Dizziness[f]	Common
	Paradoxical drug reaction	Common
	Psychomotor hyperactivity	Common

	Somnolence	Common
	Extrapyramidal disorder	Rare
	Seizure	Rare
	Tremor	Not Known
	Epilepsy	Not Known
	Paraesthesia	Not Known
Eye Disorders	Vision blurred	Common
Cardiac Disorders	Arrhythmia	Rare
	Palpitations	Rare
	Tachycardia	Not Known
	Myocardial infarction / Myocardial ischemia	Not Known
	Posterior reversible encephalopathy (PRES) / Reversible cerebral vasoconstriction syndrome (RCVS)	Not Known Not known
	Cerebrovascular accident	
Vascular Disorders	Hypotension	Rare
	Hypertension	Not known
Respiratory, Thoracic and Mediastinal Disorders	Dry throat	Not Known
	Epistaxis	Not Known
	Nasal dryness	Not Known
Gastrointestinal	Increased viscosity of bronchial	Common

Disorders	secretions	Common
	Dry mouth[f]	Common
	Gastrointestinal disorder	Common
	Nausea [f]	Not Known
	Abdominal discomfort	Not Known
	Vomiting	
Hepatobiliary Disorders	Liver disorder	Rare
Skin and Subcutaneous Tissue Disorders	Acute generalised exanthematous pustulosis	Not Known
	Angioedema	Not Known
	Pruritus	Not Known
	Rash	Not Known
	Urticaria	Not Known
Renal and Urinary Disorders	Urinary Retention	Common
	Dysuria	Not Known
General Disorders and Administration Site Conditions	Fatigue	Not Known
	Hyperpyrexia	Not known

[f] Adverse events reported by ≥ 1% of subjects in randomised, placebo-controlled trials with single-ingredients pseudoephedrine

No differences between adult and paediatric safety profiles have been identified.

4.11 Overdose

Symptoms

The effects of acute toxicity from TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets may include drowsiness, lethargy, dizziness, ataxia, weakness, hypotonicity, respiratory depression, dryness of skin and mucous membranes, tachycardia, hypertension, hyperpyrexia, hyperactivity, irritability, palpitations, convulsions and difficulty with micturition.

Pseudoephedrine

Overdose may result in:

Metabolism and nutrition disorders: hyperglycaemia, hypokalaemia

Psychiatric disorders: CNS stimulation, insomnia; irritability, restlessness, anxiety, agitation; confusion, delirium, hallucinations, psychoses

Nervous system disorders: seizures, tremor, intracranial haemorrhage including intracerebral haemorrhage, drowsiness in children

Eye disorders: mydriasis

Cardiac disorders: palpitations, tachycardia, reflex bradycardia, supraventricular and ventricular arrhythmias, dysrhythmias, myocardial infarction

Vascular disorders: hypertension, hypertensive crisis

Gastrointestinal disorders: nausea, vomiting, ischaemic bowel infarction

Musculoskeletal and connective tissue disorders: rhabdomyolysis

Renal and urinary disorders: acute renal failure, difficulty in micturition

Triprolidine

Overdosage of an H1 receptor antagonist may result in CNS depression, hyperthermia, anticholinergic syndrome (mydriasis, flushing, fever, dry mouth, urinary retention, decreased bowel sounds), tachycardia, hypotension, hypertension, nausea, vomiting, agitation, confusion, hallucinations, psychosis, seizures, or dysrhythmias. Rhabdomyolysis and renal failure may rarely develop in patients with prolonged agitation, coma or seizures.

ManagementThe treatment of overdosage is likely to be symptomatic and supportive. Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed up to 3 hours after ingestion if indicated. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sympathomimetics, pseudoephedrine, combinations

ATC code: R01BA52

Triprolidine provides symptomatic relief in conditions believed to depend wholly, or partly, upon the triggered release of histamine. Triprolidine is a potent, competitive H1-receptor antagonist of the pyrrolidine class with mild central nervous system depressant properties which may cause drowsiness.

Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective upper respiratory decongestant. Pseudoephedrine is less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and is less potent in causing stimulation of the central nervous system.

After oral administration of a single dose of 2.5 mg triprolidine to adults the onset of action, as determined by the ability to antagonise histamine-induced weals and flares in the skin, is within 1 to 2 hours. Peak effects occur at about 3 hours, and although activity declines thereafter, significant inhibition of histamine-induced weals and flares still occurs 8 hours after dose. Pseudoephedrine produces its decongestant effect within 30 minutes persisting for at least 4 hours.

5.2 Pharmacokinetic properties

After the administration of one TRIPROLIDINE AND PSEUDOEPHEDRINE Tablet in healthy adult volunteers, the peak plasma concentration (Cmax) of triprolidine is approximately 5.5 - 6.0 ng/ml, occurring at about 2.0 hours (Tmax) after drug administration. The plasma half-life of triprolidine is approximately 3.2 hours. The peak plasma concentration (Cmax) of pseudoephedrine is approximately 180 ng/ml, with Tmax approximately 2 hours after drug administration. The plasma half-life is approximately 5.5 hours (urine pH maintained between 5.0 - 7.0). The plasma half-life of pseudoephedrine is markedly decreased by acidification of urine and increased by alkalination.

In a limited study, three mothers nursing healthy infants were given an antihistamine-decongestant preparation containing 60 mg of pseudoephedrine and 2.5 mg of triprolidine.

Milk concentrations of pseudoephedrine were higher than plasma levels in all three patients, with peak milk concentrations occurring at 1.0–1.5 hours. The investigators calculated that 1000 ml of milk produced during 24 hours would contain approximately 0.5%–0.7% of the maternal dose. However, following a single-blind, crossover study of a single dose of pseudoephedrine 60 mg vs. placebo conducted in 8 lactating mothers, and assuming maternal intake of 60 mg pseudoephedrine hydrochloride four times daily, the estimated infant dose of pseudoephedrine based on AUC and an estimated milk production rate of 150 ml/kg/day was 4.3% (95% CI, 3.2, 5.4%; range 2.2 to 6.7%) of the weight-adjusted maternal dose.

5.3 Preclinical safety data

Mutagenicity

There is insufficient information available to determine whether triprolidine or pseudoephedrine has mutagenic potential.

Carcinogenicity

There is insufficient information available to determine whether triprolidine or pseudoephedrine has carcinogenic potential.

Teratogenicity

In rats and rabbits systemic administration of triprolidine up to 75 times the human daily dosage did not produce teratogenic effects. Systemic administration of pseudoephedrine up to 50 times the human daily dosage in rats, and up to 35 times the human daily dosage in rabbits, did not produce teratogenic effects.

Fertility

No studies have been conducted in animals to determine whether triprolidine or pseudoephedrine have potential to impair fertility. There is no information on the effect of TRIPROLIDINE AND PSEUDOEPHEDRINE Tablets on human fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch	BP
Lactose	BP

Povidone	BP
Isopropyl alcohol*	BP
Magnesium Stearate	BP
Colloidal Anhydrous Silica	BP
Sodium Starch Glycolate	BP

6.2 Incompatibilities

None

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a dark, dry place , Not exceeding 30^0C temp.

6.5 Nature and contents of container

Pack Style: 10 x 10 Blister pack

Primary Packing: 10 tablets are packed in Alu-PVC Blister.

Secondary Packing: 10 Blister pack is packed in a carton along with package insert.

6.6 Special precautions for disposal and other handling

Not applicable

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

MARKETING AUTHORISATION

Aquatix Pharmaceuticals Limited

No.14, Prince Bode Olowo Street,

Mende, Maryland,

Lagos, Nigeria