Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Actifed 60mg/2.5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 60 mg Pseudoephedrine hydrochloride and 2.5 mg Triprolidine hydrochloride.
Excipients: contains 127.5 mg lactose monohydrate per tablet.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet.
White, round biconvex tablet with bisecting score and M2A engraved on one side.
The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ACTIFED Tablets are indicated for the symptomatic relief of upper respiratory tract disorders which are benefited by a combination of a nasal decongestant and H_1-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 (see section 4.3).

The Elderly:
There have been no specific studies of ACTIFED Tablets in the elderly. Experience has indicated that normal adult dosage is appropriate.

Hepatic Dysfunction:
Caution should be exercised when administering Actifed Tablets to patients with severe hepatic impairment.

Renal Dysfunction:
Caution should be exercised when administering Actifed Tablets to patients with mild to moderate renal impairment.

Method of Administration
For oral use.

4.3 Contraindications

ACTIFED Tablets are contra-indicated in individuals with known hypersensitivity to pseudoephedrine, triprolidine or to any of the excipients listed in section 6.1.

ACTIFED Tablets are contra-indicated in patients with cardiovascular disease, severe hypertension or uncontrolled hypertension, and in those who are taking beta-blockers

ACTIFED Tablets are contra-indicated in individuals who have diabetes mellitus, phaeochromocytoma, hyperthyroidism, closed angle glaucoma, severe acute or chronic kidney disease / renal failure.

ACTIFED 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 and/or hypertensive crisis.

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

ACTIFED Tablets are contra-indicated in patients who are currently taking other sympathomimetic decongestants.

ACTIFED Tablets are contra-indicated for use in children under 12 years of age

4.4 Special warnings and precautions for use

ACTIFED 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

Severe Skin reactions
Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of this medicine should be discontinued and appropriate measures taken if needed.

Ischaemic colitis
Some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Ischaemic optic neuropathy
Cases of ischaemic optic neuropathy have been reported with pseudoephedrine. Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)
Cases of PRES and RCVS have been reported with the use of pseudoephedrine-containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure (see section 4.3).
Pseudoephedrine should be discontinued and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances. Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

There have been no specific studies of ACTIFED Tablets in patients with hepatic and/or renal dysfunction. 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, ACTIFED 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 ACTIFED Tablets: difficulty in urination and/or enlargement of the prostate; or susceptibility to angle-closure.

Patients with the following conditions should not use ACTIFED 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.
Triprolidine may enhance the sedative effects of central nervous system depressants including alcohol, sedatives and tranquilizers. While taking ACTIFED 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, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 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 ACTIFED 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 ACTIFED 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.

4.6 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 ACTIFED 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.

4.7 Effects on ability to drive and use machines

ACTIFED Tablets may have a moderate influence on the ability to drive and use machines. ACTIFED 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 ACTIFED Tablets may, in some patients, produce additional impairment.

4.8 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'.

System Organ Class (SOC)	Adverse Drug Reaction (Preferred Term)	Frequency
Blood and Lymphatic System Disorders	Blood disorder	Rare
Immune System Disorders	Hypersensitivity – cross sensitivity may occur with other sympathomimetics	Rare
Psychiatric Disorders	Insomnia[†] Nervousness[†]	Common
	Hallucination Confusional state Depression Sleep disorder	Rare
	Agitation	Not known

	Anxiety Delusion Euphoric mood Hallucination, visual Irritability Restlessness	
Nervous System Disorders	Headache	Very common
	Extrapyramidal disorder Seizure Tremor	Rare
	Dizziness[†] Paradoxical dug reaction Psychomotor hyperactivity Somnolence	Common
	Cerebrovascular accident Epilepsy Paraesthesia Posterior reversible encephalopathy syndrome (PRES) (see section 4.4) / Reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4)	Not Known
Eye Disorders	Vision blurred Ischaemic optic neuropathy	Common Not known
Cardiac Disorders	Arrhythmia Palpitations	Rare
	Myocardial infarction / Myocardial ischaemia Tachycardia	Not Known
Vascular Disorders	Hypotension	Rare
	Hypertension	Not known
Respiratory, Thoracic and Mediastinal Disorders	Increased viscosity of bronchial secretion	Common
	Dry throat Epistaxis Nasal dryness	Not Known
Gastrointestinal Disorders	Dry mouth[†] Gastrointestinal disorder Nausea[†]	Common
	Abdominal discomfort Ischaemic colitis Vomiting	Not Known
Hepatobiliary Disorders	Liver disorder	Rare
Skin and Subcutaneous Tissue Disorders	Angioedema Pruritus Rash Severe skin reactions, including acute generalised exanthematous pustulosis (AGEP) Urticaria	Not Known
Renal and Urinary Disorders	Urinary Retention	Common
	Dysuria	Not Known

General Disorders and Administration Site Conditions	Fatigue Hyperpyrexia	Not Known

†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.

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. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

Symptoms

The effects of acute toxicity from ACTIFED 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.

Management
The treatment of overdosage is likely to be symptomatic and supportive. Necessary measures should be taken to maintain and support respiration and control convulsions. 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 H_1-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 ACTIFED Tablet in healthy adult volunteers, the peak plasma concentration (C_{max}) of triprolidine is approximately 5.5 - 6.0 ng/ml, occurring at about 2.0 hours (T_{max}) after drug administration. The plasma half-life of triprolidine is approximately 3.2 hours. The peak plasma concentration (C_{max}) of pseudoephedrine is approximately 180 ng/ml, with T_{max} 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 rabbitssystemic 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 ACTIFED Tablets on human fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Povidone (E1201)
Magnesium stearate (E572)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C. Store in original container to protect from moisture and light.

6.5 Nature and contents of container

12 tablets in PVC/PVDC Aluminium foil blister packs.
500 tablets in polypropylene containers with polyethylene snap-fitting lids.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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