

Summary of Product Characteristics

1. Trade Name of the Medicinal Product

Actifed Syrup

2. Qualitative and Quantitative Composition

Pseudoephedrine Hydrochloride BP 30mg and Triprolidine Hydrochloride BP 1.25mg in each 5ml

3. Pharmaceutical Form

Oral solution

Clinical Particulars

4.1. Therapeutic Indications

Actifed Syrup is indicated for the symptomatic relief of nasal congestion and rhinitis associated with upper respiratory tract disorders.

4.2. Posology and Method of Administration

Users should be advised to seek medical advice if symptoms persist for more than 7 days.

Do not exceed the stated dose or frequency of dosing.

Avoid use with other anti-histamine-containing products, including cough and cold medicines (see Section 4.4.).

Adults (including the elderly) and children aged 12 years and over

10 ml every 4-6 hours as required.

Maximum daily dose: 40ml syrup in any 24 hours.

Actifed Syrup may be diluted 1:1 (1 in 2) or 1:3 (1 in 4) with Syrup BP. These dilutions have a shelf life of 4 weeks if stored at 25°C.

Older people

There have been no specific studies of pseudoephedrine or triprolidine in the elderly. The elderly are more likely to experience the neurological anticholinergic effects of triprolidine, including confusion, and to develop paradoxical excitation [see Section 4.4.].

Patients with hepatic impairment

Triprolidine is eliminated primarily by hepatic metabolism therefore consideration should be given to reducing the dose in those with severe hepatic impairment [see Section 4.4.]

Patients with renal impairment

Pseudoephedrine is primarily excreted renally. Renal impairment will increase plasma levels of pseudoephedrine. Pseudoephedrine should not be used by those with severe renal impairment (see contraindications) and should be used with caution in those with moderate renal impairment [see Section 4.4.].

For oral administration.

4.3. Contra-indications

Hypersensitivity to pseudoephedrine hydrochloride, triprolidine hydrochloride, or excipients.

Severe hypertension or severe coronary artery disease.

Severe renal impairment.

Patients receiving other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants).

Patients receiving monoamine oxidase inhibitors (MAOI's) or for two weeks after stopping a MAOI drug.

4.4. Special Warnings and Precautions for Use

Caution should be exercised in patients with cardiovascular disease, arrhythmias, hypertension, hyperthyroidism, prostatic enlargement, diabetes, elevated intraocular pressure including glaucoma, epilepsy, asthma, bronchitis and bronchiectasis, moderate renal impairment severe hepatic impairment, or pheochromocytoma.

Use with caution in patients taking beta-blockers or other anti-hypertensives [see Section 4.5.].

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

May cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously affect the patient's ability to drive or operate machinery. If affected, do not drive or operate machinery.

May increase the effects of alcohol therefore concurrent use of alcohol should be avoided [see Section 4.5.].

Avoid use with other antihistamine-containing products, including cough and cold medicines.

Children and the elderly are more likely to experience neurological anticholinergic

effects and paradoxical excitation.

Keep out of sight and reach of children.

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

Actifed Syrup contains 3.93g of sucrose per 5ml. This should be taken into account in patients with diabetes mellitus.

Actifed Syrup contains methyl parahydroxybenzoate, which may cause allergic reactions (possibly delayed) and, exceptionally, bronchospasm.

Actifed Syrup contains colours E104 and E110 which may cause allergic reactions.

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

4.5. Interactions with other Medicaments and other forms of Interaction

Concomitant administration of pseudoephedrine hydrochloride and MAOIs (or within two weeks of stopping an MAOI) may lead to hypertensive crisis. The anticholinergic effects of triprolidine are intensified by MAOIs [see Section 4.3.].

Concomitant use with sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) which interfere with the catabolism of sympathomimetic amines, may occasionally cause a rise in blood pressure [see Section 4.3.].

Concurrent use of triprolidine and hypnotics, sedatives or anxiolytics may potentiate drowsiness. Concurrent use of alcohol may have a similar effect [See Section 4.4.].

Pseudoephedrine may antagonise the effect of certain classes of antihypertensives (e.g. beta-blockers, methyl-dopa, reserpine, debrisoquine, guanethidine) [see Section 4.4.].

4.6. Fertility, Pregnancy and Lactation

Pregnancy

Pseudoephedrine and triprolidine should not be used in pregnancy without medical advice. Although pseudoephedrine and triprolidine have been in widespread use for many years, their safe use in pregnancy has not been established. Caution should therefore be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus.

Lactation

Pseudoephedrine and triprolidine should not be used whilst breastfeeding without medical advice. Pseudoephedrine and triprolidine are excreted in breast milk in small amounts but the effect of this on breastfed infants is unknown.

Fertility

No information is available.

4.7. Effects on Ability to Drive and Use Machines

Actifed Syrup may influence the ability to drive and use machines.

It is recommended that patients are advised not to engage in activities requiring mental alertness, such as driving a car, or operating machinery, until they have established their own response to the drug.

4.8. Undesirable Effects

Pseudoephedrine

The following adverse reactions have been reported with pseudoephedrine:

Psychiatric disorders

Common ($\geq 1/100$ to $< 1/10$): nervousness, insomnia

Uncommon ($\geq 1/1,000$ to $< 1/100$): agitation, restlessness

Rare ($\geq 1/10,000$ to $< 1/1000$): hallucinations (particularly in children)

Nervous System Disorders

Common ($\geq 1/100$ to $< 1/10$): dizziness

Cardiac disorders

Rare ($\geq 1/10,000$ to $< 1/1000$): tachycardia, palpitations

Vascular disorders

Rare ($\geq 1/10,000$ to $< 1/1000$): increased blood pressure*

*Increases in systolic blood pressure have been observed. At therapeutic doses, the effects of pseudoephedrine on blood pressure are not clinically significant.

Gastrointestinal disorders

Common ($\geq 1/100$ to $< 1/10$): dry mouth, nausea, vomiting

Skin and subcutaneous tissue disorders

Rare ($\geq 1/10,000$ to $< 1/1000$): rash, allergic dermatitis*

*A variety of allergic skin reactions, with or without systemic features such as bronchospasm, angioedema have been reported following use of pseudoephedrine

Renal and urinary disorders

Uncommon ($\geq 1/1,000$ to $< 1/100$): dysuria, urinary retention*

*Urinary retention is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Tripolidine

The following adverse reactions have been reported with tripolidine hydrochloride:

Psychiatric disorders

Unknown: paradoxical excitation*, confusion**, nightmares***, hallucinations***

* Children and the elderly are more susceptible to paradoxical excitation (e.g. increased energy, restlessness, nervousness).

** The elderly are more prone to confusion.
***Hallucinations and nightmares have been reported mainly in children

Nervous System Disorders

Very common ($\geq 1/10$): sedation, drowsiness

Common ($\geq 1/100$ to $< 1/10$): disturbance in attention, abnormal coordination, dizziness

Eye disorders

Unknown: blurred vision

Respiratory, thoracic and mediastinal disorders

Unknown: thickening of bronchial secretions

Gastrointestinal disorders

Common ($\geq 1/100$ to $< 1/10$): dry mouth, nose and throat

Unknown: gastrointestinal disturbance including nausea, vomiting

Skin and subcutaneous tissue disorders

Unknown: rash, urticaria

Renal and urinary disorders

Unknown: urinary retention

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 the national reporting system:

ADR Reporting

Website: www.medicinesauthority.gov.mt/adrportal

4.9. Overdose

Pseudoephedrine overdose may result in symptoms due to central nervous system and cardiovascular stimulation (e.g. excitement, restlessness, hallucinations, hypertension and arrhythmias). In severe cases, psychosis, convulsions, coma and hypertensive crisis may occur.

Serum potassium levels may be low due to extracellular to intracellular shifts in potassium.

Triprolidine overdose is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include ataxia, weakness, respiratory depression, dryness of the skin and mucous membranes, hyperpyrexia, tremor, psychosis, convulsions, tachycardia and arrhythmias.

5. Pharmacological Properties

5.1. Pharmacodynamic Properties

Triprolidine provides symptomatic relief in conditions believed to depend wholly or partly upon the triggered release of histamine. It is a potent competitive histamine 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 tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and considerably less potent in causing stimulation of the central nervous system

After oral administration of a single dose of 2.5mg 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 10ml Actifed Syrup (containing 2.5mg triprolidine hydrochloride and 60 mg pseudoephedrine hydrochloride) in healthy adult volunteers. The peak plasma concentration (C_{MAX}) of triprolidine is approximately 5.5ng/ml - 6.0 ng/ml occurring at about 1.5 hours (T_{MAX}) after drug administration. The plasma half life of triprolidine is approximately 3.2 hours. The C_{MAX} of pseudoephedrine is approximately 180ng/ml with T_{MAX} approximately 1.5 hours after drug administration. The plasma half life of pseudoephedrine 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 alkalinisation.

5.3. Preclinical Safety Data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. Pharmaceutical Particulars

6.1. List of Excipients

Syrup BP
Glycerol PH.EUR
Methyl Hydroxybenzoate PH.EUR
Sodium Benzoate PH.EUR
Quinoline Yellow, E104 HSE
Sunset Yellow, E110/F.D. & C Yellow No. 6 HSE
Sodium Hydroxide BP
Purified Water PH. EUR

6.2. Incompatibilities

None known.

6.3. Shelf Life

48 months

6.4. Special Precautions for Storage

Store below 25°C, protect from light.

6.5. Nature and Contents of Container

Amber glass bottles (EP Type III) capped with metal roll-on closures or polypropylene caps or child resistant, tamper evident closure fitted with PVDC faced wads. A 5ml polypropylene spoon is included. The bottles are contained within a rectangular, printed cardboard carton.

Pack size: 100ml

6.6. Instruction for Use/Handling

None applicable.

Administrative Data

7. Marketing Authorisation Holder

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8. Marketing Authorisation Number

MA192/02006

9. Date of First Authorisation/Renewal of Authorisation

29th May 2006/03rd October 2011

10. Date of (Partial) Revision of the Text

27th October 2017

11. Legal Status

OTC