SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Multi-Action ACTIFED Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Triprolidine hydrochloride	2.5mg
Pseudoephedrine hydrochloride	60.0mg

3 PHARMACEUTICAL FORM

Tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of upper respiratory tract disorders which are benefited by a combination of a nasal decongestant and histamine H1-receptor antagonist, for example:

Allergic Rhinitis

Vasomotor Rhinitis

The Common Cold and Influenza

4.2 Posology and method of administration

Posology

Adults and children over 12 years

One tablet every 4-6 hours up to 4 times a day. Not more than 4 doses

should be given in any 24 hours.

Use in the Elderly

No specific studies have been carried out in the elderly, but triprolidine and pseudoephedrine have been widely used in older people.

Hepatic Dysfunction

Caution should be exercised when administering Multi-Action ACTIFED Tablets to patients with hepatic impairment.

Renal Dysfunction

Caution should be exercised when administering Multi-Action ACTIFED Tablets to patients with moderate renal impairment.

Method of Administration

For oral use.

4.3 Contraindications

Multi-Action ACTIFED is contraindicated in individuals with known hypersensitivity to pseudoephedrine or triprolidine or to any of the excipients listed in section 6.1.

Multi-Action ACTIFED is contraindicated in patients who are taking or have taken monoamine oxidase inhibitors within the preceding 14 days. The concomitant use of pseudoephedrine and this type of product may cause a rise in blood pressure and/or hypertensive crisis (see section 4.5).

Concomitant use of other sympathomimetic decongestants or beta-blockers (see section 4.5).

Cardiovascular disease
Severe hypertension or uncontrolled hypertension
Diabetes mellitus
Phaeochromocytoma
Hyperthyroidism
Closed angle glaucoma
Severe acute or chronic kidney disease/renal failure

4.4 Special warnings and precautions for use

Multi-Action ACTIFED Tablets may cause drowsiness. This product should not be used to sedate a child.

Triprolidine may enhance the sedative effects of central nervous system depressants including alcohol, sedatives and tranquilisers. While taking Multi-Action ACTIFED

Tablets, patients should be advised to avoid alcoholic beverages and consult a healthcare professional prior to taking with central nervous system depressants.

Use with caution in prostatic hypertrophy, urinary retention or susceptibility to angle closure.

Patients with thyroid disease who are receiving thyroid hormones are advised to consult a physician before using this product.

Use with caution in occlusive vascular disease.

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.

Patients with the following conditions should not use Multi-Action Actifed Tablets unless directed by a physician: acute or chronic asthma, chronic bronchitis or emphysema.

There have been no specific studies of Multi-Action ACTIFED Tablets in patients with hepatic and/or renal dysfunction. Caution should be exercised in the presence of hepatic or moderate to severe renal impairment.

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 monoamine oxidase inhibitors (MAOIs) impede the metabolism of sympathomimetic amines and increase the store of releasable noradrenaline in adrenergic nerve endings, MAOIs may potentiate the pressor effect of pseudoephedrine. This product should not be given to patients taking monoamine inhibitors or within 14 days of stopping treatment as there is an increased risk of hypertensive crisis (pseudoephedrine) or serotonin syndrome (triprolidine).

Moclobemide: Risk of hypertensive crisis

Appetite suppressants and amphetamine-like psychostimulants: Concomitant use of this product with sympathomimetic agents, such as decongestants, tricyclic antidepressants, appetite suppressants and amphetamine-like psychostimulants, may cause a rise in blood pressure.

Antihypertensives: Because of its pseudoephedrine content, this product may partially reverse the hypotensive action of antihypertensive drugs which interfere with sympathetic activity including bretylium, betanidine, guanethidine, debrisoquine, methyldopa, adrenergic neurone blockers and beta blockers.

Cardiac glycosides: Increased risk of dysrhythmias

Ergot alkaloids (ergotamine & methysergide): Increased risk of ergotism

Oxytocin: Risk of hypertension

Anticholinergic drugs: Enhances effects of anticholinergic drugs (such as tricyclic antidepressants).

Antimuscarinic drugs: May have an additive muscarinic action with other drugs such as atropine and some antidepressants.

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 CNS depressants including barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, antipsychotics and alcohol.

4.6 Fertility, pregnancy and lactation

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

Pregnancy
There are no adequate and well-controlled studies for pseudoephedrine or triprolidine, or for the combination of pseudoephedrine and triprolidine, in pregnant women.

Breastfeeding
Pseudoephedrine is excreted in breast milk in small amounts, but the effect of this on breast-fed infants is not known. It has been estimated that approximately 0.4 to 0.7% of a single 60 mg dose of pseudoephedrine ingested by a nursing mother will be excreted in the breast milk over 24 hours. Data from a study of lactating mothers taking 60 mg pseudoephedrine every 6 hours suggests that from 2.2 to 6.7% of the maximum daily dose (240 mg) may be available to the infant from a breastfeeding mother.

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.

4.7. Effects on Ability to Drive and Use Machines

Multi-action ACTIFED may cause drowsiness and impair performance in tests of auditory vigilance. Patients should not drive or operate machinery until they have determined their own response.

4.8 Undesirable effects

Placebo-controlled studies with sufficient adverse event data are 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 according to the following convention:

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 Confusional state Depression Sleep disorder Anxiety Euphoric mood Excitability Hallucinations Irritability Paranoid delusions Restlessness	Common Common Rare Rare Rare Not Known Not Known Not Known Not Known Not Known Not Known Not Known
Nervous System Disorders	Headache Dizziness Paradoxical stimulation Psychomotor impairment Somnolence Extrapyramidal disorder Seizure Tremor Cerebrovascular accident Paraesthesia Posterior reversible encephalopathy syndrome (PRES) (see section 4.4) /reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4) Psychomotor hyperactivity	Very common Common Common Common Common Rare Rare Rare Not Known Not Known Not Known Not Known

Eye Disorders	Vision blurred	Common
	Ischaemic optic neuropathy	Not Known
Cardiac Disorders	Palpitations Dysrhythmias Myocardial infarction / myocardial ischaemia Tachycardia	Rare Not Known Not Known Not Known
Vascular Disorders	Hypotension Hypertension	Rare Not Known
Respiratory, Thoracic and Mediastinal Disorders	Increased viscosity of bronchial secretion Dry throat Epistaxis Nasal dryness	Common Not known Not known Not known
Gastrointestinal Disorders	Dry mouth Gastrointestinal disorder Nausea Abdominal discomfort Ischaemic colitis Vomiting	Common Common Common Not Known Not Known 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 Not known Not known Not known Not known
Renal and Urinary Disorders	Urinary Retention (in men whom prostatic enlargement could have been an important predisposing factor) Dysuria	Common Not known
General Disorders and Administration Site Conditions	Fatigue	Not known

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
The effects of acute toxicity from Multi-Action ACTIFED may include drowsiness, lethargy, dizziness, ataxia, weakness, hypotonicity, respiratory depression, dryness of the skin and mucous membranes, tachycardia, hypertension, hyperpyrexia, hyperactivity, irritability, seizures, and difficulty with micturition.

Pseudoephedrine
Overdose may result in hyperglycaemia, hypokalaemia, CNS stimulation, insomnia; irritability, restlessness, anxiety, agitation; confusion, delirium, hallucinations, psychoses, seizures, tremor, intracranial haemorrhage including intracerebral haemorrhage, drowsiness in children, mydriasis, palpitations, tachycardia, reflex bradycardia, supraventricular and ventricular arrhythmias, dysrhythmias, myocardial infarction, hypertension, vomiting, ischaemic bowel infarction, acute renal failure and difficulty in micturition.

Triprolidine
Overdose 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
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. It is a potent competitive histamine 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 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 the dose.

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 also less potent in causing stimulation of the central nervous system. Pseudoephedrine produces its decongestant effect within 30 minutes, persisting for at least 4 hours.

5.2. Pharmacokinetic Properties

After the administration of one Multi-Action ACTIFED Tablet (containing 2.5 mg triprolidine hydrochloride and 60 mg pseudoephedrine hydrochloride) in healthy adult volunteers, the peak plasma concentration (C_{max}) of triprolidine is approximately 5.5 ng/ml - 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 C_{max} of pseudoephedrine is approximately 180 ng/ml with T_{max} approximately 2.0 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 is insufficient information available to determine whether triprolidine or pseudoephedrine have mutagenic or carcinogenic potential.

Systematic administration of pseudoephedrine in rats, up to 7 times the human daily dosage in females and 35 times the human daily dosage in males, did not impair fertility nor alter foetal morphological development and survival.

No studies have been conducted in animal to determine if triprolidine has the potential to impair fertility.

Systemic administration of triprolidine in rats and rabbits up to 75 times the human dose 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose

Maize Starch

Povidone

Magnesium Stearate

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C
Store in original package to protect from light and moisture

6.5 Nature and contents of container

12 tablets in pvc/pvdc/aluminium foil blister packs.

6.6 Special precautions for disposal

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
50 – 100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

8. MARKETING AUTHORISATION NUMBER(S)

PL 15513/0014

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

3 July 2001 2 Feb 1997

10 DATE OF REVISION OF THE TEXT

18/05/2025