# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Benadryl Allergy Relief Plus Decongestant Capsules

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

This product contains 8 mg acrivastine and 60 mg pseudoephedrine hydrochloride.

Excipient with known effect: Lactose monohydrate 146.8 mg per capsule
For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Capsules

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

This product is indicated for the symptomatic relief of allergic rhinitis.

### 4.2 Posology and method of administration

Posology
**Adults and children 12 years and over:**
One capsule as necessary, up to three times a day.

**Children under 12 years:**
This product is not currently recommended for use in children under 12 years of age.

**Elderly:**
This product is not currently recommended for use in the elderly.

**Hepatic dysfunction:**
Caution should be exercised when administering Benadryl Allergy Relief Plus Decongestant Capsules to patients with severe hepatic impairment.

**Renal dysfunction:**
Caution should be exercised when administering Benadryl Allergy Relief Plus Decongestant Capsules to patients with moderate to severe renal impairment.

Method of administration
For oral use.

## 4.3 Contraindications

- Hypersensitivity to the active substances, triprolidine or to any of the excipients listed in section 6.1.
- Cardiovascular disease including hypertension
- Concomitant use of beta blockers (see section 4.5)
- Concomitant use of other sympathomimetic decongestants.
- Diabetes mellitus
- Phaeochromocytoma
- Closed angle glaucoma
- Hyperthyroidism
- Severe renal impairment.

The concomitant use of a pseudoephedrine-containing product and monoamine oxidase inhibitors may cause a rise in blood pressure or hypertensive crisis. This product is therefore contraindicated in patients who are taking, or have taken, monoamine oxidase inhibitors within the preceding 14 days.

Renal excretion is the principal route of elimination of acrivastine. Until specific studies have been carried out, this product should not be given to patients with significant renal impairment.

## 4.4 Special warnings and precautions for use

It is usual to advise patients not to undertake tasks requiring mental alertness whilst under the influence of alcohol or other CNS depressants including sedatives and tranquilizers. Concomitant administration of this product may, in some individuals, produce additional impairment.

Although pseudoephedrine has virtually no pressor effects in patients with norma blood pressure, this product should be used with caution in patients taking antihypertensive agents, tricyclic antidepressants or other sympathomimetic agents such as decongestants, appetite suppressants or 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.

Patients experiencing difficulty in urination due to enlargement of the prostate, or patients with thyroid disease who are receiving thyroid hormones should not take pseudoephedrine unless directed by a physician.

Patients with the following conditions should be advised to consult a physician before using acrivastine: a respiratory condition such as emphysema, chronic bronchitis, or acute or chronic bronchial asthma, prostate hyperplasia with urinary retention.

Caution should be exercised when using the product in the presence of severe hepatic impairment or moderate to severe renal impairment, or occlusive vascular disease.

This product may cause drowsiness (see section 4.8).

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.

There have been rare cases of posterior reversible encephalopathy syndrome (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. Most cases improved or resolved within a few days following appropriate treatment. Pseudoephedrine should be discontinued, and medical advice sought immediately if signs or symptoms of PRES/RCVS develop.

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

Pseudoephedrine
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 sympathomimetics 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 used in patients taking monoamine inhibitors or within 14 days of stopping treatment as there is a risk of hypertensive crisis.

Concomitant use of pseudoephedrine with tricyclic antidepressants, sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants), may cause a rise in blood pressure (see section 4.3).

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 (see section 4.4).

Anticholinergic drugs: enhances effect of anticholinergic drugs (such as tricyclic antidepressants).

Oxytocin: risk of hypertension.

Cardiac glycosides: increased risk of dysrhythmias.

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

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

Acrivastine
There are no data to demonstrate an interaction between acrivastine and ketoconazole, erythromycin or grapefruit juice. However, due to known interactions between these compounds and other non-sedating antihistamines, caution is advised.

Acrivastine may enhance the sedative effects of central nervous system depressants, including alcohol, sedatives and tranquilizers.

## 4.6 Fertility, pregnancy and lactation

**Pregnancy**
There are no adequate and well-controlled studies in pregnant women.

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

**Breast-feeding**
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.

No information is available on levels of acrivastine which may appear in human breast milk following administration of this product.

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 60mg 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.

## 4.7 Effects on ability to drive and use machines

There have been the following side effects with acrivastine: dizziness and somnolence. Caution should be exercised when driving a motor vehicle or operating machinery.

It is recommended that patients are advised not to undertake tasks requiring mental alertness whilst under the influence of alcohol or other C.N.S. depressants. Concomitant administration of this product 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 acrivastine and pseudoephedrine.

No adverse drug reactions have been identified during post-marketing experience with the combination product acrivastine/pseudoephedrine.

Adverse drug reactions identified during clinical trials and post-marketing experience with acrivastine or pseudoephedrine as single ingredient products 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) | Frequency | Adverse Drug Reaction (Preferred Term) |
|---|---|---|
| **Immune System Disorders** | Not Known | Hypersensitivity* (including dyspnoea and face swelling)#<br>Cross-sensitivity may occur with other sympathomimetics |
| **Psychiatric Disorders** | Common | Insomnia*<br>Nervousness* |
| | Not known | Anxiety*<br>Euphoric mood*<br>Excitability*<br>Hallucinations*<br>Irritability*<br>Paranoid delusions*<br>Restlessness*<br>Sleep disorder* |
| **Nervous System Disorders** | Very common | Headache*<br>Somnolence#* |
| | Common | Dizziness#* |
| | Not Known | Cerebrovascular accident*<br>Posterior reversible encephalopathy syndrome (PRES)/reversible cerebral vasoconstriction syndrome (RCVS)*<br>Psychomotor hyperactivity* |
| **Eye Disorders** | Not known | Ischaemic optic neuropathy |
| **Cardiac Disorders** | Not Known | Dysrhythmias*<br>Myocardial infarction/myocardial ischaemia*<br>Palpitations#*<br>Tachycardia* |
| **Vascular Disorders** | Not known | Hypertension* |
| **Gastrointestinal Disorders** | Common | Dry mouth*<br>Nausea* |
| | Not Known<br>Not Known | Ischaemic colitis*<br>Vomiting* |
| **Skin and Subcutaneous Tissue Disorders** | Not Known | Angioedema*<br>Pruritus*<br>Rash#*<br>Severe skin reactions, including acute generalised exanthematous pustulosis (AGEP)* |
| **Renal and Urinary Disorders** | Not Known | Dysuria*<br>Urinary retention in men* in whom prostatic enlargement could have |

| | | |
|---|---|---|
| | | been an important predisposing factor |

*# Associated with Acrivastine*
** Associated with Pseudoephedrine*

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 Yellow Card Scheme: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

**Acrivastine**
When the recommended therapeutic dose has been exceeded, acrivastine has been found to impair the ability to drive. This effect is related to the amount of acrivastine taken beyond the recommended maximum daily dosage.

**Pseudoephedrine**
Symptoms
Overdose may result in:
Hyperglycaemia, hypokalaemia, CNS stimulation, insomnia, irritability, restlessness, anxiety, agitation, confusion, delirium, hallucinations, psychoses, tremor, seizures, 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, difficulty in micturition.

Management
Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed 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: Nasal decongestants for systemic use ATC code: R01BA52

Acrivastine is a potent, competitive $H_1$-receptor antagonist that lacks significant anticholinergic effects and has a low potential to penetrate the central nervous system. Acrivastine is chemically related to triprolidine. Acrivastine provides symptomatic relief in conditions believed to depend wholly, or partly, upon the triggered release of histamine.

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. Pseudoephedrine produces its decongestant effect within 30 minutes, persisting for at least 4 hours.

After oral administration of a single dose of 8 mg acrivastine to adult volunteers, the onset of action, as determined by the ability to antagonise histamine induced wheals and flares in the skin, is 15 minutes. Peak effects occur at 2 hours, and although activity declines slowly thereafter, significant inhibition of histamine induced wheals and flares still occur 8 hours after dose.

Relief from the histamine-mediated symptoms of allergic rhinitis is apparent within 1 hour of systemic administration of the drug and lasts for up to 8 hours.

## 5.2 Pharmacokinetic properties

After the administration of one this product to healthy adult volunteers, the peak plasma concentration ($C_{max}$) for acrivastine is approximately 140 ng/ml, occurring at about 1.3 hours ($T_{max}$) after drug administration. The plasma half-life is approximately 1.6 hours. Acrivastine is approximately 50% protein bound, principally to albumin. The peak plasma concentration for pseudoephedrine is approximately 210 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. Renal excretion is the principal route of elimination of both acrivastine and pseudoephedrine.

## 5.3 Preclinical safety data

Pre-clinical safety data do not add anything of further significance to the prescriber.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Lactose monohydrate
Sodium starch glycollate

Magnesium stearate
Gelatin
Titanium dioxide (E171)
Patent Blue V (E131)

### 6.2 Incompatibilities

None known

### 6.3 Shelf life

3 years.

### 6.4 Special precautions for storage

Do not store above 25°C.

Store in the original package to protect from moisture.

### 6.5 Nature and contents of container

6 or 12 capsules in PVC/PVDC Aluminium foil blister packs.
6 capsules in polypropylene containers with polyethylene snap-fitting lids.
Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

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

## 7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
Foundation Park
Roxborough Way
Maidenhead
Berkshire SL6 3UG
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER

PL 15513 / 0017

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/02/1997 / 13/12/2004

## 10 DATE OF REVISION OF THE TEXT

15/06/2020