1. Name of the medicinal product
Avrofed Syrup

2. Qualitative and quantitative composition
Each 5ml syrup contains:-
Triprolidine hydrochloride 1.25mg
Pseudoephedrine hydrochloride 30.0 mg

3. Pharmaceutical form
Syrup for oral administration.

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 H_1-receptor antagonist, for example:
Allergic Rhinitis
Vasomotor Rhinitis
The Common Cold and Influenza

4.2 Posology and method of administration
Adults and children over 12 years
10ml 3 times a day

Children
2 – 5 years: 2.5ml 3 times a day
6 – 12 years: 5ml 3 times a day

If there is need for dilution, Avrofed Syrup may be diluted with Syrup B.P.

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 Avrofed Syrup to patients with severe hepatic impairment.

Renal Dysfunction
Caution should be exercised when administering Avrofed Syrup to patients with moderate to severe renal impairment.

4.3 Contraindications
Avrofed is contraindicated in individuals who have previously exhibited intolerance to it or to pseudoephedrine or triprolidine.
Avrofed is contraindicated 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 occasionally cause a rise in blood pressure.
Avrofed is contraindicated in patients with severe hypertension or severe coronary artery disease.
The antibacterial agent furazolidone, is known to cause a dose-related inhibition of monoamine oxidase. Although there are no reports of hypertensive crises caused by the concurrent administration of Avrofed Syrup and furazolidone they should not be taken together.

4.4 Special warnings and precautions for use
Avrofed Syrup 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.
Although there are no objective data, users of Avrofed Syrup should avoid the concomitant use of alcohol or other centrally acting sedatives.
Although pseudoephedrine has virtually no pressor effect in normotensive patients, Avrofed Syrup should be used with caution in patients taking anti-hypertensive agents, tricyclic antidepressants or other

sympathomimetic agents, such as decongestants, appetite suppressants and amfetamine-like psychostimulants. The effects of a single dose of Avrofed Syrup on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.
As with other sympathomimetic agents Avrofed Syrup should be used with caution in patients with hypertension, heart disease, diabetes, hyperthyroidism, elevated intraocular pressure and prostatic enlargement.
There have been no specific studies of Avrofed Syrup in patients with hepatic and/or renal dysfunction. Caution should be exercised in the presence of severe renal or hepatic impairment.
There is insufficient information available to determine whether triprolidine or pseudoephedrine have mutagenic or carcinogenic potential.
Systemic 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 animals to determine if triprolidine has the potential to impair fertility.
There is no information on the effects of Avrofed on human fertility.
The packs carry the following statements:-
Store below 30°C
Protect from light.
Keep out of the reach of children
Warnings, may cause drowsiness. If affected do not drive or operate machinery. Avoid alcoholic drink and central sedatives.
Additional statements:-
If symptoms persist consult your doctor.
Do not exceed the stated dose.
As with all medicines if you are pregnant, or currently taking any other medicine, consult your doctor or pharmacist before taking this product.

4.5 Interaction with other medicinal products and other forms of interaction
Concomitant use of Avrofed Syrup with sympathomimetic agents, such as decongestants, tricyclic antidepressants, appetite suppressants and amfetamine-like psychostimulants, or with monoamine oxidase inhibitors which interfere with the catabolism of sympathomimetic amines, may occasionally cause a rise in blood pressure.
Because of its pseudoephedrine content, Avrofed may partially reverse the hypotensive action of drugs which interfere with sympathetic activity including bretylium, betanidine, guanethidine, debrisoquine, methyldopa, alpha-and beta-adrenergic blocking agents.

4.6 Pregnancy and lactation
Pregnancy
Although pseudoephedrine, and triprolidine have been in widespread use for many years without apparent ill consequence, there are no specific data on their use during pregnancy. Caution should therefore be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus.
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.
Lactation
Pseudoephedrine and triprolidine are 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 0.5 to 0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in the breast-milk over 24 hours.

4.7 Effects on ability to drive and use machines
Avrofed 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
Central nervous system depression or excitation may occur, drowsiness being reported most frequently. Sleep disturbance and, rarely, hallucinations have been reported.

Skin rashes, with or without irritation, tachycardia, dryness of mouth, nose and throat, have occasionally been reported.
Urinary retention has been reported occasionally in men receiving pseudoephedrine; prostatic enlargement could have been an important predisposing factor.

4.9 Overdose
The effects of acute toxicity from Avrofed may include drowsiness, lethargy, dizziness, ataxia, weakness, hypotonicity, respiratory depression, dryness of the skin and mucous membranes, tachycardia, hypertension, hyperpyrexia, hyperactivity, irritability, convulsions, and difficulty with micturition. 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
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 or 10ml syrup, 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 produces its decongestant effect within 30 minutes, persisting for at least 4 hours.

5.2 Pharmacokinetic properties
After the administration of 10ml Avrofed Syrup or 1 tablet Avrofed 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/nl, 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 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
Glycerol
Sucrose
Methyl Hydroxybenzoate
Sodium Benzoate
FD & C No. 6 Soluble Uscert

N/1 Sodium Hydroxide Solution
Deionised Water

6.2 Incompatibilities
None known

6.3 Shelf life
3 Years

6.4 Special precautions for storage
Store below 30°C
Store in original package to protect from light and moisture

6.5 Nature and contents of container
50 ml amber bottles with Aluminium screw cap.
A calibrated measuring cup with a 10ml, 5ml and 2.5ml measure is supplied with this product.

6.6 Special precautions for disposal and other handling
None

7. Marketing authorisation holder
Avro Pharma Limited
Daid House Plot 2, Block J, Limca Way,
Isolo Industrial Estate, Oshodi-Apapa Expressway,
Isolo, Lagos State, Nigeria.
Tel: +234(1)2913955
Email: avro@rumon-org.com