1. **NAME OF THE MEDICINAL PRODUCT**
   Non-Drowsy SUDAFED 12 Hour Relief

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**
   Non-Drowsy SUDAFED 12 Hour Relief tablets each contain 120 mg pseudoephedrine hydrochloride in a modified-release formulation.

3. **PHARMACEUTICAL FORM**
   Modified-release tablet.

4. **CLINICAL PARTICULARS**

4.1 **Therapeutic indications**
   Non-Drowsy SUDAFED 12 Hour Relief tablets are indicated for the symptomatic relief of conditions such as allergic rhinitis, vasomotor rhinitis, the common cold and influenza.

4.2 **Posology and method of administration**

   **Posology**

   **Adults and children 12 years and over:**
   Oral: One tablet (120 mg pseudoephedrine hydrochloride) every 12 hours.
   Maximum daily dose: 2 tablets (240 mg pseudoephedrine hydrochloride).
   Non-Drowsy SUDAFED 12 Hour Relief tablets should be swallowed whole without chewing.

   **Children under 12 years:**
   Non-Drowsy SUDAFED 12 Hour Relief tablets are not suitable for administration to children under 12 years of age.

   **The Elderly:**
   Normal adult dosage is appropriate (See Pharmacokinetics in Elderly).

   **Hepatic Dysfunction:**
   Experience with the use of the product suggests that normal adult dosage is appropriate, although it may be prudent to exercise caution in the
presence of severe hepatic impairment (See Pharmacokinetics).

**Renal Dysfunction:**

Caution should be exercised when administering Non-Drowsy SUDAFED 12 Hour Relief tablets to patients with moderate to severe renal impairment, particularly if accompanied by cardiovascular disease (See Pharmacokinetics in Renal Impairment).

### 4.3 Contraindications

Non-Drowsy SUDAFED 12 Hour Relief tablets are contraindicated in individuals with known hypersensitivity to the product or any of its components.

Non-Drowsy SUDAFED 12 Hour Relief tablets are contraindicated in patients with severe hypertension or severe coronary artery disease.

Non-Drowsy SUDAFED 12 Hour Relief tablets are contraindicated in patients who are taking, or have taken, monoamine oxidase inhibitors and the antibacterial agent furazolidone within the preceding two weeks.

### 4.4 Special warnings and precautions for use

Although pseudoephedrine has virtually no pressor effects in normotensive patients Non-Drowsy SUDAFED 12 Hour Relief tablets should be used with caution in patients suffering from mild to moderate hypertension.

As with other sympathomimetic agents, Non-Drowsy SUDAFED 12 Hour Relief tablets should be used with caution in patients with heart disease, diabetes, hyperthyroidism, elevated intra-ocular pressure or prostatic enlargement.

Caution should be exercised when using the product in the presence of severe hepatic impairment or moderate to severe renal impairment (particularly if accompanied by cardiovascular disease (See Pharmacokinetics).

### 4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of Non-Drowsy SUDAFED 12 Hour Relief tablets with other pseudoephedrine-containing products, tricyclic antidepressants, monoamine oxidase inhibitors and furazolidone, which interfere with the catabolism of sympathomimetics amines, may occasionally cause a rise in blood pressure.

A rise in blood pressure may also occur with the concomitant use of other sympathomimetic agents such as decongestants, appetite suppressants
and amphetamine-like psychostimulants.

Because of their pseudoephedrine content, Non-Drowsy SUDAFED 12 Hour Relief tablets 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 (See Special Warnings and Precautions for Use).

4.6 Pregnancy and lactation

Insufficient information is available on the effects of administration of Non-Drowsy SUDAFED 12 Hour Relief tablets during human pregnancy.

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 (non-controlled release) dose of pseudoephedrine ingested by a nursing mother will be excreted in the breast milk over 24 hours.

Non-Drowsy SUDAFED 12 Hour Relief tablets, like most medicines, should not be used during pregnancy and lactation unless the potential benefit of treatment to the mother outweighs any possible risk.

4.7 Effects on ability to drive and use machines

No special comment.

4.8 Undesirable effects

Serious adverse effects associated with the use of pseudoephedrine are extremely rare. Symptoms of central nervous system excitation may occur including sleep disturbance and, rarely, hallucinations.

Skin rashes, with or without irritation, have occasionally been reported with pseudoephedrine.

Urinary retention has been reported occasionally in men receiving pseudoephedrine; prostatic enlargement could have been an important predisposing factor.

4.9 Overdose

Symptoms and Signs

As with other sympathomimetic-containing products, symptoms and signs of overdose may include irritability, restlessness, tremor, convulsions, palpitations, hypertension and difficulty with micturition.
Treatment

Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage may be undertaken if indicated. Catheterisation of the bladder may be necessary. Acid diuresis can accelerate the elimination of pseudoephedrine although the potential therapeutic gain of this procedure is now in dispute. The value of dialysis in overdose is not known, although four hours of haemodialysis removed approximately 20% of the total body load of pseudoephedrine in an instant-release combination product containing 60 mg pseudoephedrine and 8 mg acrivastine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 in a bioequivalent controlled-release formulation has been shown to produce its decongestant effect within 1 hour of dosing, persisting for up to 12 hours.

5.2 Pharmacokinetic properties

Bioequivalence between Non-Drowsy SUDAFED 12 Hour Relief tablets and instant release Sudafed Elixir has been demonstrated.

Absorption

After the administration of one tablet of Non-Drowsy SUDAFED 12 Hour Relief (containing 120 mg pseudoephedrine) to healthy adult volunteers, the $C_{\text{max}}$ for pseudoephedrine was approximately 293 ng/ml irrespective of whether the tablet was taken with or without food. The $t_{\text{max}}$ occurred at about 5.5 hours when the tablet was taken by fasting subjects or at approximately 5.9 hours when taken with food.

At steady state, following multiple dosing for Non-Drowsy SUDAFED 12 Hour Relief tablets, the $C_{\text{max}}$ and $C_{\text{min}}$ for pseudoephedrine have been estimated to be 459 ng/ml and 243 ng/ml respectively.

Distribution
The volume of distribution for Non-Drowsy SUDAFED 12 Hour Relief tablets has not been identified. However, the apparent volume of distribution of immediate-release pseudoephedrine (Vd/F) is approximately 2.8 l/kg.

**Metabolism and Elimination**

Pseudoephedrine is partly metabolised in the liver by N-demethylation to norpseudoephedrine, an active metabolite. Pseudoephedrine and its metabolite are excreted in the urine; 55% to 90% of a dose is excreted unchanged.

Following administration of 1 tablet of Non-Drowsy SUDAFED 12 Hour Relief to fasted healthy volunteers, the elimination t½ was approximately 6.3 hours, or 5.78 hours when taken with food. The rate of urinary excretion is accelerated when the urine is acidified. Conversely, as the urine pH increases, the rate of urinary elimination is slowed.

**Pharmacokinetics in Renal Impairment**

There have been no specific studies of Non-Drowsy SUDAFED 12 Hour Relief in renal impairment.

Following the administration of a single dose on instant-release DUACT capsules (8 mg acrivastine + 60 mg pseudoephedrine) to patients with varying degrees of renal impairment, the C\text{max} for pseudoephedrine increased approximately 1.5 fold in patients with moderate to severe renal impairment when compared to the C\text{max} in healthy volunteers. The t\text{max} was not affected by renal impairment. The t½ increased 3 -12 fold in patients with mild to severe renal impairment respectively, when compared to the t½ in healthy volunteers.

**Pharmacokinetics in Hepatic Impairment**

There have been no specific studies of Non-Drowsy SUDAFED 12 Hour Relief or pseudoephedrine in hepatic impairment.

**Pharmacokinetics in the Elderly**

There have been no specific studies of Non-Drowsy SUDAFED 12 Hour Relief in the elderly. In elderly volunteers, following the administration of instant-release DUACT capsules (8 mg acrivastine + 60 mg pseudoephedrine), the t\text{½} for pseudoephedrine was 1.4 - fold that seen in healthy volunteers. The apparent C1/F was 0.8 - fold that seen in healthy volunteers, and the Vd/F was essentially unchanged.

5.3 Preclinical safety data
Mutagenicity

The results of a wide range of tests indicate that pseudoephedrine does not pose a mutagenic risk to man.

Carcinogenicity

There is insufficient information available to determine whether pseudoephedrine has carcinogenic potential.

Teratogenicity

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

Systemic administration of pseudoephedrine to rats, up to 7 times the human daily dosage in females and 35 times the human daily dosage in males, did not impair fertility or alter foetal morphological development and survival.

There is insufficient information relating to the effect of SUDAFED 12 hour tablets on human fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxypropyl Methylcellulose

Magnesium Stearate

Microcrystalline Cellulose

Povidone

Titanium Dioxide

Polyethylene Glycol

Candelilla Wax

Purified Water
6.2 Incompatibilities
   None known

6.3 Shelf life
   3 years

6.4 Special precautions for storage
   Do not store above 25°C. Keep dry. Protect from light.

6.5 Nature and contents of container
   6 tablets presented in a PVC or PVC/PVdC blister card backed with aluminium foil.

6.6 Special precautions for disposal and other handling
   Not applicable