Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zephrol Adult Cough Suppressant

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:

Promethazine Hydrochloride	3.6	mg
Pholcodine	5.0	mg
Pseudoephedrine Hydrochloride	20.0	mg

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution
A dark brown oral solution with an odour of aniseed.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the symptomatic relief of the common cold, when accompanied by a dry cough.

4.2 Posology and method of administration

Route of Administration:
Oral.

Dosage:
Adults only: One to two 5 ml spoonfuls 3 or 4 times daily.

4.3 Contraindications

Use in patients with hypersensitivity or idiosyncratic response to the active ingredients.

This product should not be administered to patients who are receiving monoamine oxidase inhibitors or who have received these within the previous 14 days.

Use in severe hypertension or severe coronary artery disease.

Use in patients who are in a coma or CNS depression.

Use in children.

4.4 Special warnings and precautions for use

This product may cause drowsiness, particularly in combination with alcohol. Patients receiving the product should not

drive or operate machinery unless it has been shown not to affect their mental or physical ability. Pseudoephedrine may occasionally cause insomnia and erythematous patches. Hallucinations have been reported rarely. Side effects due to promethazine include headache, dizziness, restlessness, disorientation, blurred vision, dry mouth and urinary retention occur occasionally. Paradoxical stimulation may occur rarely. Other side effects may include gastrointestinal disturbances, palpitations and arrhythmias. Photosensitivity reactions have occurred.

The product should only be administered with great caution to patients suffering from cardiovascular disease, including hypertension, angina pectoris, or uncontrolled hyperthyroidism.

Asthmatics should consult their doctors before using this product.

This product should be used with caution in patients with epilepsy.

Care should be taken when using this product in patients with hepatic and or renal impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Pseudoephedrine: The effects of anti-hypertensive agents which modify sympathetic activity may be reversed by pseudoephedrine, concomitant use with other sympathomimetic agents such as decongestants, tricyclic antidepressants, appetite suppressants and amphetamine like psychostimulants or monoamine oxidase inhibitors which interfere with the catabolism of sympathomimetic amines may occasionally cause a rise in blood pressure.

The antibacterial agent furazolidone is known to cause a dose related inhibition of monoamine oxidase. Although no reports of hypertensive crisis have occurred the product should not be administered concurrently.

Promethazine: Promethazine may enhance the action of any anticholinergic agent, tricyclic anti-depressant, sedative or hypnotic.

Alcohol should be avoided. Promethazine may interfere with immunologic urine pregnancy tests to produce false-positive or false-negative results. Promethazine has been reported to be incompatible with solutions of a number of compounds including aminophylline, barbiturates, benzylpenicillin salts, carbenicillin, heparin, hydrocortisone sodium succinate, morphine sulphate and some contrast media.

4.6 Pregnancy and lactation

The product should not be used in pregnancy without consulting a doctor. It is recommended that the product should not be administered in the two weeks prior to delivery in view of the risk of irritability and excitement in the neonate. It has been estimated that approximately 0.5-0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in breast milk over 24 hours.

4.7 Effects on ability to drive and use machines

The product may cause drowsiness, if affected patients should not drive or operate machinery.

4.8 Undesirable effects

In some patients, pseudoephedrines may occasionally cause insomnia. Sleep disturbances and hallucinations have been reported rarely. Fixed drug eruption due to pseudoephedrine in the form of erythematous nummular patches may occur.

Side effects due to promethazine include headache, dizziness, restlessness, and disorientation. Anticholinergic side effects such as blurred vision, dry mouth and urinary retention occur occasionally. Paradoxical stimulation may occur rarely, especially in high dosage or in children. Other side effects due to promethazine include psychomotor impairment, gastrointestinal disturbances, anorexia, palpitations and arrhythmias. Photosensitive reactions have been recorded. Urinary retention may occur in patients with prostatic enlargement.

4.9 Overdose

Signs and Symptoms

Symptoms of overdose may include drowsiness, lethargy, dizziness, ataxia, inco-ordination, athetosis, irritability, convulsions, hypertension, palpitations and difficulty in micturition.

Treatment

Gastric lavage and supportive measures to counter respiratory and cardiovascular depression should be performed if indicated.

Convulsions should be controlled with an anticonvulsant. 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

Promethazine is an antihistamine with antimuscarinic, marked central sedative, and some serotonin-antagonist properties. It is used for the symptomatic relief of hypersensitivity reactions, for the control of nausea, vomiting and rhinitis. Pholcodine is a centrally acting cough suppressant which is administered orally in doses of 5 to 10 mg three or four times daily.

Pseudoephedrine is a direct and indirect acting sympathomimetic agent which has less pressor activity and central nervous system effects as compared to ephedrine. It is normally given by mouth for the symptomatic relief of nasal congestion.

5.2 Pharmacokinetic properties

Promethazine is well absorbed after oral administration and the peak plasma concentration are observed after 2-3 hours. Although its systemic bioavailability after oral administration is low due to high first-pass metabolism in the liver, it is widely distributed. Its elimination half-lives have been reported to be 5 to 14 hours and it is excreted slowly via the urine and bile.

There is little or no metabolism of pholcodine to morphine which may contribute to its lack of analgesic activity, morphine-like side effects and addictive potential. Pholcodine has a much longer elimination half-life than codine and its dosing frequency could possibly be reduced to once or twice daily.

Pseudoephedrine is absorbed from the gastro-intestinal tract. It is resistant to metabolism by monoamine oxidase and is largely excreted unchanged in the urine together with small amounts of its hepatic metabolite. It has a half-life of several hours; elimination is enhanced and half-life accordingly shorter in acid urine. Small amounts are excreted in breast milk.

5.3 Preclinical safety data

There are no preclinical safety data of relevance to the prescriber which are additional to that included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Liquid sugar gran liquors
Polysorbate 20

Caramel HT (E150)
Citric acid granules
Sodium citrate
Sodium benzoate (E211)
Cough drop flavour abrac C5562
Ethanol
Ascorbic acid
Sodium sulphite anhydrous (E221)
Sodium metabisulphite (E223)
Purified water

6.2 Incompatibilities

Promethazine has been reported to be incompatible with solutions of a number of compounds including aminophylline, barbiturates, benzylpenicillin salts, carbenicillin, heparin, hydrocortisone sodium succinate, morphine sulphate and some contrast media.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25ºC.

Store in the original container.

6.5 Nature and contents of container

Amber glass bottle, with an aluminium screw cap with a polyethylene seal. Each bottle contains 100 ml and is packed in a unit boxboard carton.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited
Trading as:
Pinewood Healthcare
Ballymacarbry
Clonmel
Co Tipperary

8 MARKETING AUTHORISATION NUMBER

PA 281/105/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 August 1985

Date of last renewal: 30 November 2002

10 DATE OF REVISION OF THE TEXT

November 2002