IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA0004/027/001
Case No: 2032173

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

The Boots Company Plc

1 Thane Road, **Nottingham NG2 3AA**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Night Cold Comfort

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **07/02/2007** until **18/04/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Night Cold Comfort

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Paracetamol	600 mg/30 ml
Pseudoephedrine hydrochloride	40 mg/30 ml
Pholcodine	10 mg/30 ml
Diphenhydramine hydrochloride	10 mg/30 ml
Ethanol	6 ml /30 ml

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Oral solution
A clear, green slightly viscous solution with a peppermint and aniseed flavour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of the symptoms of colds and influenza.

4.2 Posology and method of administration

For oral administration.

Adults and children over 12 years: 30ml to be given at bedtime only.

Children under 12 years: Not to be given to children under 12 years of age, except on medical advice.

Elderly: There is no specific requirement for dosage reduction in the elderly.

4.3 Contraindications

1. Use in patients who are receiving monoamine oxidase inhibitors, or within fourteen days of stopping such treatment.
2. Not for use in children under 12 years.
3. Use in patients currently receiving other sympathomimetic drugs.

4.4 Special warnings and precautions for use

Should be given with caution to patients with impaired kidney or liver function, and in patients with chronic bronchitis and bronchiectasis.
This product may act as a cerebral stimulant in children and occasionally in adults. The product should be used with care in epileptic patients.
This product should be given with care to patients suffering from cardiovascular disease or prostatic enlargement.

Contains paracetamol.
Do not exceed the stated dose.
Children under 12 years should not be given this medicine.

Warning: May cause drowsiness. If affected do not drive or operate machinery. Avoid alcoholic drink.
Asthmatics should consult their doctor before using this product.
If symptoms persist, consult your doctor.
Should not be used for prolonged periods except under medical supervision.
Talk to your doctor before taking this medicine if you are receiving medical treatment or advice.
Keep all medicines out of the reach of children.
Do not take other medicines containing paracetamol while using Night Cold Comfort, except Day Cold Comfort.
Immediate medical advice should be sought in the event of an overdose, even if you feel well.

4.5 Interaction with other medicinal products and other forms of interaction

Should not be given to patients being treated with mono amine oxidase inhibitors or within 14 days of stopping such treatment. May enhance the sedative effect of central nervous system depressants including alcohol, barbiturates, hypnotics, narcotic analgesics, sedatives and tranquillisers. The effects of anticholinergic drugs such as atropine and tricyclic antidepressants may also be enhanced. May diminish the antihypertensive effects of hypotensive drugs and increase the possibility of arrhythmias in digitalised patients.

4.6 Pregnancy and lactation

In view of the possible association of foetal abnormalities with first trimester exposure to pseudoephedrine and diphenhydramine, use of the product during pregnancy should be avoided. In view of the significant amounts of pseudoephedrine secreted into breast milk, use of the product during lactation should be avoided.

4.7 Effects on ability to drive and use machines

The product may cause drowsiness and patients should be warned not to drive or operate machinery.

4.8 Undesirable effects

May occasionally cause drowsiness, lassitude, dizziness and muscular weakness. The sedative effects when they occur may diminish after a few days. Other side effects include nausea, vomiting, diarrhoea or constipation, epigastric pain, headache, blurred vision, tinnitus, irritability, nightmares, anorexia, difficulty in micturition, dryness of the mouth, tachycardia, tremors and skin rashes.

4.9 Overdose

Symptoms of overdose may include drowsiness, dryness of the mouth, headache, nausea, vomiting, tachycardia, urinary retention, disorientation, staggering gait, hallucinations, stupor, coma, hyperreflexia, tremor, excitement, nystagmus, hyperthermia, convulsions, respiratory depression, hypertension and arrhythmias. Hepatic and renal impairment may occur after 3-5 days, together with hypoprothrombinaemia, metabolic acidosis, hypoglycaemia or hyperglycaemia. Treatment consists of emesis or gastric lavage, if indicated. Plasma paracetamol levels should be checked. If patient presents less than 16 hours after ingestion, 2.5g methionine should be given orally every four hours for four doses. Alternatively, or if the patient is vomiting or unconscious, acetylcysteine should be given intravenously, 150mg/kg over 15 minutes, followed by an infusion of 50mg/kg in 500ml of 5% dextrose over 4 hours and then 100mg/kg in a litre of 5% dextrose over the next 16 hours. In addition, symptomatic and supportive therapy may be necessary including the administration of a beta-blocker if supraventricular tachycardia supervenes and the administration of the specific narcotic antagonist naloxone.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol has analgesic and antipyretic actions. Pseudoephedrine is a sympathomimetic agent with both direct and indirect effects on adrenergic receptors. Pholcodine is a cough suppressant with mild sedative but little analgesic activity. Diphenhydramine is an antihistamine with anticholinergic properties.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10-60 minutes after oral administration. Paracetamol is distributed into most body tissues.
It crosses the placenta and is present in breast milk. Plasma protein binding is negligible at usual therapeutic concentrations. Paracetamol is metabolised predominantly in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half life varies from about 1 to 3 hours.

Pseudoephedrine is absorbed from the gastrointestinal tract. It is resistant to metabolism and is excreted largely unchanged in the urine. It has a half life of several hours but elimination is enhanced and half life shortened in acid urine.

Pholcodine is rapidly absorbed after oral administration and maximum plasma concentrations are attained in about 4-8 hours. The elimination half life ranged from 32 to 43 hours. The drug has a large volume of distribution and is only 23.5% protein bound. Pholcodine is metabolised in the liver but undergoes little conjugation with glucuronide and sulphate.

Diphenhydramine hydrochloride is well absorbed from the gastrointestinal tract, though high first-pass metabolism appears to affect systemic availability. Peak plasma concentrations are achieved about 1 to 4 hours after administration by mouth. Diphenhydramine is widely distributed throughout the body including the CNS. It crosses the placenta and has been detected in breast milk. Diphenhydramine is highly protein bound. Metabolism is extensive and diphenhydramine is excreted mainly in the urine as metabolites, little being excreted as unchanged drug. Excretion is almost complete within 24 hours of administration.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium benzoate (E211)
Hydroxyethylcellulose
Saccharin sodium
Sodium citrate
Citric acid
Sucrose
Glycerol
Peppermint oil
Aniseed flavour
Tingle flavour
Quinoline yellow
Blue 12401 (E131)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Keep the container tightly closed. Store in the original package.

6.5 Nature and contents of container

Either clear glass bottle with pilfer proof aluminium screw cap or a clear PET bottle with child resistant cap. Each contains 210 ml of liquid.

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

The Boots Company Plc.
1 Thane Road West
Nottingham NG2 3AA
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 4/27/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 April 1983

Date of last renewal: 19 April 2003

10 DATE OF REVISION OF THE TEXT

April 2003