Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Boots Day Cold & Flu Relief Oral Solution Paracetamol 1000mg/30mg Pholcodine 10mg/30ml Pseudoephedrine Hydrochloride 60mg/30ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients	mg/30ml
Paracetamol	1000
Pseudoephedrine hydrochloride	60
Pholcodine	10

Excipients: Ethanol 1.153g/30ml; Glucose 1.7g/30ml; Glycerol 13g/30ml; sucrose 5.4g/30ml and sodium 35mg/30ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution
Clear orange liquid

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of the symptoms of colds and influenza.

4.2 Posology and method of administration

Take during the day.

Adults and children over 16 years: 30ml every four hours, up to a maximum of 4 doses in 24 hours if needed.

Children under 16 years: Not to be given to children under 16 years of age.

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

For oral administration.

4.3 Contraindications

Hypersensitivity to any of the ingredients. Avoid in patients with angina, cardiovascular disease, hypertension, hyperexcitability, diabetes, hyperthyroidism, phaeochromocytoma, closed angle glaucoma, prostatic enlargement, severe kidney disease or liver failure and in patients with chronic bronchitis and bronchiectasis. Use in patients who are 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.

The physician or pharmacist should check that sympathomimetic containing preparations are not simultaneously administered by several routes i.e. orally and topically (nasal, aural and eye preparations).
Sympathomimetic-containing products should be given with great care in patients receiving phenothiazines or tricyclic antidepressants.

Sympathomimetic-containing products may act as cerebral stimulants giving rise to insomnia, nervousness, hyperpyrexia, tremor and epileptiform convulsions.

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.

Severe cutaneous adverse reactions (SCARs) including acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in patients treated with pholcodine-containing products, most likely in the first week. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, Boots Day Cold & Flu Relief Oral Solution should be withdrawn immediately.

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.

Contains paracetamol.

Warning: Do not exceed the stated dose.

Asthmatics should consult their doctor before using this product.
Do not use this product for longer than 7 days unless your doctor agrees.

If symptoms persist, consult your doctor.

Children under 16 years should not be given this medicine.

Do not take any other paracetamol containing products.

Keep all medicines out of the reach of children.
Label:
Immediate medical advice should be sought in the event of overdosage even if you feel well.

Leaflet or combined Label/Leaflet:
Immediate medical advice should be sought in the event of overdosage, even if you feel well, because of the risk of irreversible liver damage.
Information related specifically to the excipients in this formulation (see section 2)
Sodium: Each 30ml dose contains 35 mg sodium. To be taken into consideration by patients on a controlled sodium diet.

Ethanol (alcohol): Each 30ml dose contains 1153 mg alcohol (ethanol), equivalent to 29ml of beer or 12ml of wine. Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast feeding women, children at high risk groups such as patients with liver disease or epilepsy.

Sucrose: Each 30ml dose contains 5.4g sucrose. This should be taken into account by patients with diabetes mellitus. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Glucose: Each 30ml dose contains 1.79g glucose. This should be taken into account by patients with diabetes mellitus. Patients with rare glucose-galactose malabsorptin should not take this medicine.

Glycerol: Each 30ml dose contains 13g glycerol. Glycerol may cause headache, upset stomach and diarrhoea.

4.5 Interaction with other medicinal products and other forms of interactions

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

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged used of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data on the use of pseudoephedrine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3)
Boots Day Cold and Flu Relief Oral Solution is not recommended during pregnancy.
The use of pseudoephedrine during the first trimester of pregnancy has been associated with an increased frequency of gastroschisis (a developmental defect in the abdominal wall with intestinal herniation) and of small intestinal atresia (congenital obstruction of small intestine).
Due to the vasoconstrictive properties of pseudoephedrine, it should not be used during the third trimester as it can induce a reduction in uteroplacental circulation.

Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results.

Breast-feeding
Pseudoephedrine has been detected in human milk with a small percentage of the maternal dose potentially administered to the breastfed infant. The use of pseudoephedrine should be avoided during breastfeeding as lactation may be suppressed, and irritability and disturbed sleep have been reported in breastfed infants.

Boots Day Cold & Flu Relief Oral Solution should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

No adverse effects known.

4.8 Undesirable effects

Paracetamol
Immune system disorders: adverse events of paracetamol are rare but hypersensitivity including skin rash may occur.
Blood and lymphatic system disorders: very rarely there have been reports of blood dyscrasias including thrombocytopaenia and agranulocytosis, but these were not necessarily related to paracetamol.
Skin and subcutaneous tissue disorders: very rare cases of serious skin reactions have been reported.

Pholcodine
Gastrointestinal disorders: nausea, vomiting, diarrhoea, epigastric pain, upset stomach.
Immune system disorders: hypersensitivity reactions and anaphylaxis.
Respiratory, thoracic and mediastinal disorders: sputum retention.
Skin and subcutaneous tissue disorders: skin rashes. . Acute generalized exanthematous pustulosis(AGEP) (see section 4.4) (frequency unknown).

Pseudoephedrine
Cardiovascular disorders: tachycardia.
Very rarely, coronary vasospasm leading to myocardial ischaemia has been reported.
Ear and labyrinth disorders: tinnitus.
Eye disorders: Blurred vision. Ischaemicoptic neuropathy (frequency unknown).
Gastrointestinal disorders: nausea, vomiting.
Frequency unknown: Ischaemic colitis

General disorders and administration site conditions: irritability.
Metabolism and nutrition disorders: anorexia.
Nervous system disorders: headache, tremor, anxiety, restlessness, insomnia, hallucinations (particularly in children).
Psychiatric disorders: nightmares.
Renal and urinary disorders: difficulty in micturition including urinary retention.
Skin and subcutaneous disorders: skin rash, sweating. Severe skin reactions, including acute generalised exanthematous pustulosis (AGEP) – frequency unknown.
Vascular disorders: very rarely, vasospasm associated with ischaemic colitis has been reported.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Paracetamol overdose can result in liver damage which may be fatal.

Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain or patients may be asymptomatic.

Overdose if paracetamol can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

Liver damage is likely in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity:
Risk factors include:

- Patients with liver disease
- Elderly patients
- Young children
- Patients receiving long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes
- Patients who regularly consume ethanol in excess of recommended amounts
- Patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Acute renal failure with acute tubular necrosis may also develop.

Cardiac arrhythmias and pancreatitis have also been reported.

Emergency Procedure
Immediate transfer to hospital.
Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured 4 hours post ingestions. Administration of charcoal should be considered if the overdose of paracetamol has been ingested within the previous hour. The antidote N-acetylcysteine, should be administered as soon as possible in accordance with national treatment guidelines.

Symptomatic treatment should be implemented.

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 little analgesic activity.

ATC Classification: RO5X (Other cold combination products).

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours 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, with about 10% as glutathione conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half life varies from about 1 to 4 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 at about 4-8 hours. The elimination half life ranges from 32 to 43 hours. The drug has a large column of distribution and is only 23.5% protein bound. Pholcodine is metabolised in the liver but undergoes little conjugation with glucuronide and sulphate.

5.3 Preclinical safety data

Paracetamol
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

Pseudoephedrine
In a study of a pseudoephedrine/cetirizine combination product, at doses of 160 mg/kg/day in pregnant rats (~7.5 x therapeutic exposure in humans for pseudoephedrine, and around therapeutic exposure for cetirizine) observations included decreased pup survival, a small increase in bone deformations, and delay of some development parameters.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acesulfame Potassium
Citric acid monohydrate
Sodium benzoate
Sodium citrate
Levomenthol
Propylene glycol
Glycerol
Ethanol 96%
Liquid sugar (containing sucrose)
Liquid glucose
Peach flavour
Pear drops flavour
Lime flavour
Riboflavine sodium phosphate (E101)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25C.

6.5 Nature and contents of container

Bottle of clear polyethylene terephthalate fitted with a child resistant closure of polypropylene with polyethylene liner.
Pack sizes: 210ml, 240ml.

Bottle of amber polyethylene terephthalate fitted with a child resistant closure of polypropylene with polyethylene liner.
Pack sizes: 210ml, 240ml.

Not all pack sizes will be marketed.

A 30ml polypropylene measuring cup is provided.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA0004/061/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th December 2003

Date of last renewal: 18th December 2008

10 DATE OF REVISION OF THE TEXT

December 2020