

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Benylin Day & Night Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each white (day) tablet contains:	Paracetamol 500mg Pseudoephedrine hydrochloride 60mg
Each blue (night) tablet contains:	Paracetamol 500mg Diphenhydramine hydrochloride 25mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Day Tablet

Tablet
White biconvex tablet in oblong form with dissecting score on one side; ‘A7C’ engraved on both sides of the score.
The score is to allow breaking for ease of swallowing.

Night Tablet

Film coated tablet (tablet)
Blue, odourless, round and biconvex tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of the symptoms associated with colds and influenza.

4.2 Posology and method of administration

For oral use.

Adults and children over 12 years:

Four tablets should be taken daily.
One white tablet to be taken every 4 to 6 hours (one tablet in the morning, at midday and in the afternoon). Do not take more than 3 white day-time tablets in 24 hours.
One blue tablet to be taken at night.
Do not take the night-time tablets during the day.

Elderly

As for adults.

Children

Not recommended for children under 12 years.

4.3 Contraindications

Use in patients hypersensitive to the active ingredients.

Use in patients who are currently receiving or have within two weeks received, monoamine oxidase inhibitors (MAOIs).

The concomitant use of pseudoephedrine and this type of product may occasionally cause a rise in blood pressure.

Use in patients with severe hypertension or coronary heart disease.

4.4 Special warnings and precautions for use

Although pseudoephedrine has virtually no pressor effects in normotensive patients, Benylin Day and Night should be used with caution in patients suffering mild to moderate hypertension. The product should also be used with caution in patients with heart disease, diabetes mellitus, hyperthyroidism, elevated intraocular pressure and 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). The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Concomitant use of other products containing paracetamol or decongestants with Benylin Day and Night could lead to overdosage and should, therefore, be avoided.

Night time tablets only: May cause drowsiness. If affected do not drive or operate machinery. Avoid alcoholic drink.

If you are taking medication, or are under medical care, consult your doctor before using.

Prolonged use without medical supervision may be harmful.

If symptoms persist please consult your doctor or pharmacist.

Keep medicines out of the reach of children.

Do not exceed the stated dose.

Immediate medical advice should be sought in the event of an overdose, even if you feel well. Please read the enclosed leaflet carefully (label).

Immediate medical advice should be sought in the event of an overdose, because of the risk of irreversible liver damage (leaflet).

Do not take with any other paracetamol containing products.

Use only when clearly necessary.

4.5 Interaction with other medicinal products and other forms of interaction

Diphenhydramine may potentiate the effects of alcohol and other CNS depressants. The effects of anticholinergics (such as atropine and some psychotropic drugs) may be potentiated by this product.

Concomitant use of Benylin Day and Night with tricyclic antidepressants, sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like stimulants) or with monoamine oxidase inhibitors, which interfere with the catabolism of sympathomimetic amines, may occasionally cause a rise in blood pressure.

Because of the pseudoephedrine contents, Benylin Day and Night may partially reverse the hypotensive action of drugs which interfere with sympathetic activity including bretylium bethanide, guanethidine, debrisoquine, methyldopa, alpha- and beta-adrenergic blocking agents.

The use of drugs that induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptives, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of paracetamol and a faster elimination rate.

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 regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Fertility, pregnancy and lactation

Not recommended for use during pregnancy or lactation in nursing mothers.

4.7 Effects on ability to drive and use machines

May cause drowsiness. If affected, do not drive or operate machinery.

4.8 Undesirable effects

Serious side-effects associated with the use of pseudoephedrine are extremely rare. Symptoms of central nervous system excitation may occur, including sleep disturbances and rarely hallucinations have been reported. Urinary retention has been reported occasionally in men receiving pseudoephedrine, prostatic enlargement could have been a predisposing factor. Skin rashes, with or without irritation, have occasionally been reported with pseudoephedrine.

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis following paracetamol use, but these were not necessarily causally related to the drug.

Side effects of diphenhydramine include drowsiness, dizziness, blurred vision, gastrointestinal disturbances, dry mouth, nose and throat, or urinary retention. Hypersensitivity reactions have been reported, in particular, skin rashes but also bronchospasm, angioedema and anaphylaxis.

4.9 Overdose

Paracetamol: Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention, and any patient who has ingested around 10g or more of paracetamol in the preceding 4 hours should undergo gastric lavage. Administration of oral methionine or intravenous N-acetylcysteine, which may have a beneficial effect up to at least 48 hours after the overdose, may be required. General supportive measures must be available.

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Liver damage is possible in adults who have taken 10 g or more of paracetamol.

Pseudoephedrine: As with other sympathomimetic agents, symptoms of overdose include irritability, restlessness, tremor, convulsions, palpitations, hypertension and difficulty in micturition.

Necessary measure should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed if indicated. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

Diphenhydramine: Symptoms of overdose may include drowsiness, hyperpyrexia and anticholinergic effects. With higher doses, and particularly in children, symptoms of CNS excitation including insomnia, nervousness, tremors and epileptiform convulsions may appear. With massive overdose, coma or cardiovascular collapse may follow.

Treatment of overdosage should be symptomatic and supportive. Measures to promote rapid gastric emptying (such as induced emesis or gastric lavage), and in cases of acute poisoning activated charcoal, may be useful. The intravenous use of physostigmine may be efficacious in antagonising severe life-threatening anticholinergic symptoms, but its use is controversial.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol: Paracetamol is an analgesic and antipyretic. The therapeutic effects of paracetamol are thought to be related to inhibition of prostaglandin synthesis, as a result of the inhibition of cyclo-oxygenase. There is some evidence that it is a more effective inhibitor of central as opposed to peripheral cyclo-oxygenase. Paracetamol has only weak anti-inflammatory properties. The antipyretic action of paracetamol appears to stem from a direct action on the hypothalamic heat-regulating centres, producing peripheral vasodilation, and consequent loss of heat.

Pseudoephedrine: Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.

Diphenhydramine hydrochloride: This is an antihistamine which competes with histamine cell receptor sites on effector cells. The compound also possesses antispasmodic, antitussive, antiemetic, sedative and secretolytic effects.

5.2 Pharmacokinetic properties

Paracetamol: Paracetamol is rapidly absorbed from the gastrointestinal tract; with peak plasma concentrations occurring approximately 30 to 90 minutes following oral administration. Paracetamol is incompletely available to the systemic circulation after oral administration since a variable proportion is lost through first pass metabolism. Oral bioavailability in adults appears to depend on the amount of paracetamol administered, increasing from 63 % following a 500mg dose, to nearly 90% after 1 or 2 g. Effects are apparent within 30 minutes and last for between 4 and 8 hours. Less than 50% is protein bound. The compound is extensively metabolised in the liver to inactive conjugates of glucuronic and sulphonic acids (saturable) and to a hepatotoxic intermediate metabolite (first order) by P450 mixed function oxidase. The intermediate is detoxified by glutathione (saturable). Less than 4% is excreted unchanged in the urine.

Half-life for the drug usually lies in the range 2.75 - 3.25 hours although this may be mildly increased in chronic liver disease, or extended to 12 hours in acute paracetamol poisoning.

There is some evidence to suggest that serum half-life is increased and clearance of paracetamol is decreased in frail, immobile, elderly subjects when compared to mobile, elderly subjects. However the clinical significance of these differences is unclear. Differences in pharmacokinetic parameters observed between fit young and fit elderly subjects are not thought to be of clinical significance.

Pseudoephedrine: Pseudoephedrine is rapidly and completely absorbed after oral administration. After the administration of an oral dose of 60mg to healthy adults, a peak plasma concentration of 180 ng/ml was obtained approximately 2 hours post dose. The plasma half-life is approximately 5.5 hours. Urinary elimination is accelerated, and half-life consequently decreased, when the urine is acidified. Conversely, as the urine pH increases, the urinary elimination is reduced and half-life is increased. Pseudoephedrine is partly metabolised in the liver by N-demethylation to an active metabolite. Excretion of pseudoephedrine and its metabolite is mainly in the urine.

Diphenhydramine Hydrochloride: Diphenhydramine is well absorbed from the gastrointestinal tract. Peak serum levels are reached at between 2 - 2.5 hours after an oral dose. Duration of activity is between 4 - 8 hours. The drug is widely distributed throughout the body, including the CNS and some 78% is bound to plasma proteins. Estimates of the volume of distribution lie in the range 3.3 - 6.8 L/kg.

Diphenhydramine undergoes extensive first-pass metabolism, two successive N-demethylations, and the resultant amine is then oxidised to a carboxylic acid. Values for plasma clearance lie in the range 600-1300 ml/min and the terminal elimination half-life lies in the range 3.4 - 9.3 hours. Little unchanged drug is excreted in the urine.

Pharmacokinetic studies in elderly subjects indicate no major differences in drug distribution or elimination compared with younger adults.

5.3 Preclinical safety data

The active ingredients of Benylin Day & Night tablets are well-known constituents of medicinal products and their safety is well-documented. The results of pre-clinical studies do not add anything of relevance for therapeutic purposes.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each white (day) tablet contains:

Pregelatinised maize starch
Povidone K30
Crospovidone
Stearic acid
Microcrystalline cellulose
Croscarmellose sodium
Magnesium stearate

Each blue (night) tablet contains:

Microcrystalline cellulose
Maize starch
Sodium starch glycollate
Hydroxypropylcellulose
Pregelatinised maize starch
Croscarmellose sodium
Stearic acid
Magnesium stearate

Film coating (blue tablet only):

Methylcellulose (Methocel E5)
Propylene glycol
Opaspray M-IF-4315B:
 Titanium dioxide (E171)
 Indigo carmine (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original container.

6.5 Nature and contents of container

16 tablet carton containing 12 opaque PVC/PVDC blister packed 'Day' tablets and 4 opaque PVC/PVDC blister packed 'Night' tablets.

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

McNeil Healthcare (Ireland) Ltd.
Airton Road
Tallaght
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0823/019/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 November 1988

Date of last renewal: 10 November 2008

10 DATE OF REVISION OF THE TEXT

September 2010