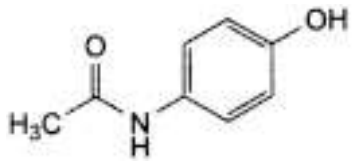
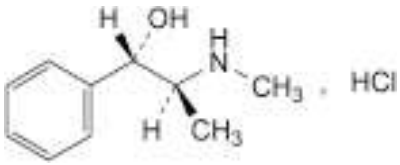
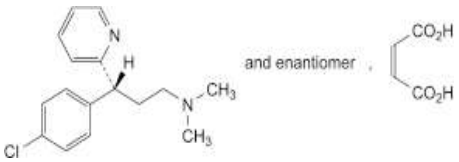
PRODUCT INFORMATION

Name of the Medicine

Trust Fludol Day & Night

Paracetamol (Day & Night Tablets)	Pseudoephedrine hydrochloride (Day & Night Tablets)	Chlorphenamine maleate (Night Tablets Only)
		
Molecular Formula: $C_8H_9NO_2$	Molecular Formula: $C_{10}H_{16}ClNO$	Molecular Formula: $C_{20}H_{23}ClN_2O_4$
Molecular Weight: 151.2	Molecular Weight: 201.7	Molecular Weight: 390.9
CAS No.: 103-90-2	CAS No.: 345-78-8	CAS No.: 113-92-8

Description

Each Day tablet contains the active ingredients:
- Paracetamol 500mg
- Pseudoephedrine hydrochloride 30mg

Each Night tablet contains the active ingredients:
- Paracetamol 500mg
- Pseudoephedrine hydrochloride 30mg
- Chlorphenamine maleate 2mg

The tablets also contain:
- Crospovidone
- Erythrosine aluminium lake (Night tablets only)
- Magnesium stearate
- Microcrystalline cellulose
- Povidone
- Pregelatinised maize starch
- Stearic acid
- Purified water

Paracetamol is a white or almost white crystalline powder. It is sparingly soluble in water, freely soluble in alcohol and very slightly soluble in methylene chloride.

Pseudoephedrine hydrochloride is a white or almost white crystalline powder or colourless crystals. It is freely soluble in water and in ethanol (96 per cent), sparingly soluble in methylene chloride. Its melting point is at about 184ºC.

Chlorphenamine maleate is a white or almost white, crystalline powder. It is freely soluble in water and soluble in ethanol (96 per cent).

Pharmacology

Paracetamol is a p-aminophenol derivative that exhibits analgesic and antipyretic activity. It does not possess anti-inflammatory activity. Paracetamol is thought to produce analgesia through a central inhibition of prostaglandin synthesis.

Pseudoephedrine has direct- and indirect- sympathomimetic activity and is an effective decongestant in the upper respiratory tract. It is a stereoisomer of ephedrine and has a similar action, but has been found to have less pressor activity and fewer central nervous system (CNS) effects. Sympathomimetic agents are used as nasal decongestants to provide symptomatic relief. They act by causing vasoconstriction resulting in redistribution of local blood flow to reduce oedema of the nasal mucosa, thus improving ventilation, drainage and nasal stuffiness.

Chlorphenamine competes with histamine at central and peripheral histamine$_1$-receptor sites, preventing the histamine-receptor interaction and subsequent mediator release. It is a highly lipophilic molecule that readily crosses the blood-brain barrier. It is highly selective for histamine$_1$-receptors but has little effect on histamine$_2$ or histamine$_3$ receptors. Chlorphenamine also activates 5-hydroxytryptamine (serotonin) and α-adrenergic receptors and blocks cholinergic receptors.

Pharmacokinetics

Absorption

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 10 to 60 minutes after oral administration.

Pseudoephedrine is readily absorbed from the gastrointestinal tract.

Chlorphenamine maleate is absorbed relatively slowly from the gastrointestinal tract, with peak plasma concentrations occurring about 2.5 to 6 hours after oral administration. Bioavailability is low, values of 25 to 50% having been reported. A duration of action of 4 to 6 hours has been reported; this is shorter than may be predicted from pharmacokinetic parameters. More rapid and extensive absorption has been reported in children compared to adults.

Distribution

Paracetamol is distributed into most body tissues. Plasma protein binding is negligible at usual therapeutic doses but increases with increasing doses.

Small amounts of pseudoephedrine are distributed into breast milk.

Chlorphenamine is widely distributed in the body and enters the CNS. About 70% of chlorphenamine in the circulation is bound to plasma proteins.

Metabolism

Paracetamol is metabolised extensively in the liver. The metabolites of paracetamol include a minor hydroxylated intermediate which has hepatotoxic activity. This intermediate metabolite is detoxified by conjugation with glutathione, however, it can accumulate following paracetamol

overdosage (more than 150mg/kg or 10g total paracetamol ingested) and if left untreated can cause irreversible liver damage.

Paracetamol is metabolised differently by premature infants, newborns, infants and young children compared to adults, the sulfate conjugate being predominant.

Pseudoephedrine is incompletely metabolised (less than 1%) in the liver to an inactive metabolite by N-demethylation.

Chlorphenamine maleate is metabolised extensively. Metabolites include desmethyl- and didesmethylchlorphenamine.

Excretion

Paracetamol is excreted in the urine mainly as inactive glucuronide and sulfate conjugates. Less than 5% is excreted unchanged. The elimination half-life varies from about 1 to 3 hours.

Pseudoephedrine is largely excreted unchanged in the urine, together with small amounts of its hepatic metabolite. It has a half-life of about 5-8 hours; elimination is enhanced and half-life reduced accordingly in acid urine.

Unchanged chlorphenamine and metabolites are excreted primarily in the urine; excretion is dependent on urinary pH and flow rate. Only trace amounts have been found in the faeces. There is wide inter-individual variation in the pharmacokinetics of chlorphenamine; half-life values ranging from 2 to 43 hours have been reported. Faster clearance and a shorter half-life have been reported in children compared to adults.

Indications

Trust Fludol Day & Night is indicated for temporary relief from the following cold & flu symptoms: nasal congestion, sinus pain, runny nose, headache, body aches & pains. Reduces fever. The night tablets also provide relief from sneezing and itchy or watery eyes, and assist rest by providing relief from these symptoms.

Contraindications

Trust Fludol Day & Night is contraindicated for use in patients with the following conditions:

- Known hypersensitivity or idiosyncratic reaction to paracetamol, pseudoephedrine, chlorphenamine (or substances of a similar chemical structure) or any of the other ingredients in this medicine.
- Severe hypertension or coronary artery disease.
- Taking monoamine oxidase inhibitors (MAOIs) or who have taken MAOIs within the previous 14 days.
- Narrow-angle glaucoma
- Stenosing peptic ulcer
- Symptomatic prostatic hypertrophy
- Bladder neck obstruction
- Pyloroduodenal obstruction

- Lactating women

Refer also to 'Interactions with other medicines' for additional information.

Precautions

Trust Fludol Day & Night should be used with caution in patients with the following conditions:

- Impaired hepatic function
- Impaired renal function
- Hypertension
- Hyperthyroidism
- Diabetes mellitus
- Coronary heart disease
- Ischaemic heart disease
- Glaucoma
- Prostatic hypertrophy
- Epilepsy

Chlorphenamine may cause drowsiness and may increase the effects of alcohol. Drowsiness may continue the following day. Those affected should not drive or operate machinery; alcohol should be avoided.

This medicine contains pseudoephedrine which may cause sleeplessness if taken up to several hours before going to bed.

Refer to 'Interactions with other medicines' for additional information.

Use in pregnancy

Category B2: Pseudoephedrine has been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals are inadequate or may be lacking, but available data shows no evidence of an increased occurrence of foetal damage.

Trust Fludol Day & Night should not be used in pregnancy unless the potential benefits to the patient are weighed against the possible risk to the foetus.

Use in lactation

Paracetamol is excreted in small amounts (< 0.2%) in breast milk. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infants.

It has been estimated that 0.5% to 0.7% of a single dose of pseudoephedrine ingested by the mother will be excreted in the breast milk over 24 hours.

Chlorphenamine is excreted in breast milk.

Therefore, Trust Fludol Day & Night is not recommended for breastfeeding mothers (see also Contraindications).

Use in the elderly

The elderly may experience paradoxical excitation with chlorphenamine. The elderly are more likely to have central nervous system (CNS) depressive side effects, including confusion.

Use in children

Children may experience paradoxical excitation with chlorphenamine.

Interactions with other medicines

The following interactions with paracetamol have been noted:

- Anticoagulant drugs (warfarin) - dosage may require reduction if paracetamol and anticoagulants are taken for a prolonged period of time
- Paracetamol absorption is increased by substances that increase gastric emptying, e.g. metoclopramide
- Paracetamol absorption is decreased by substances that decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties, and narcotic analgesics
- Paracetamol may increase chloramphenicol concentrations
- The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes such as alcohol and anticonvulsant agents
- Paracetamol excretion may be affected and plasma concentrations altered when given with probenecid
- Colestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol.

The following interactions with pseudoephedrine have been noted:

- Antidepressant medication e.g. tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) – may cause a serious increase in blood pressure or hypertensive crisis
- other sympathomimetic agents, such as decongestants, appetite suppressants and amphetamine-like psychostimulants – may cause an increase in blood pressure and additive effects
- methyldopa and β-blockers – may cause an increase in blood pressure
- urinary acidifiers enhance elimination of pseudoephedrine
- urinary alkalinisers decrease elimination of pseudoephedrine

The following interactions with chlorphenamine have been noted:

- Central nervous system (CNS) depressants (alcohol, sedatives, opioid analgesics, hypnotics) – may cause an increase in sedation effects
- Monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) – may prolong and intensify the anticholinergic and CNS depressive effects
- When taken concomitantly with phenytoin may cause a decrease in phenytoin elimination

Adverse effects

Side effects of paracetamol are rare and usually mild, although haematological reactions have been reported. Skin rashes and hypersensitivity reactions occur occasionally. Overdosage with paracetamol if left untreated can result in severe, sometimes fatal liver damage and rarely, acute renal tubular necrosis.

Adverse effects of pseudoephedrine include:

- cardiovascular stimulation – elevated blood pressure, tachycardia or arrhythmias
- central nervous system (CNS) stimulation – restlessness, insomnia, anxiety, tremors and (rarely) hallucinations
- skin rashes and urinary retention

Children and the elderly are more likely to experience adverse effects than other age groups.

CNS depressive effects of Chlorphenamine include sedation and impaired performance (impaired driving performance, poor work performance, incoordination, reduced motor skills, and impaired information processing). Performance may be impaired in the absence of sedation and may persist the morning after a night-time dose.

CNS stimulatory effects of Chlorphenamine may include anxiety, hallucinations, appetite stimulation, muscle dyskinesias and activation of epileptogenic foci.

High doses of chlorphenamine may cause nervousness, tremor, insomnia, agitation, and irritability.

Side effects of chlorphenamine associated with cholinergic blockage include dryness of the eyes, mouth and nose, blurred vision, urinary hesitancy and retention, constipation and tachycardia.

Dosage and Administration

Adults & Children 12 years & over:
Take 2 white Day tablets every 4 to 6 hours if required.
Take 2 pink Night tablets at bed-time if required.
Repeat dosage after 4 to 6 hours if required.
Do not take the Night tablet within 4 hours of taking a Day tablet.
Do not take more than a total of 4 doses (8 Day and Night tablets) in a 24-hour period.

This medicine should not be taken with other medicines containing paracetamol unless advised to do so by a doctor or pharmacist.

Use in adults
This medicine should not be taken for more than a few days at a time except on medical advice.

Use in children
Do not give to children under 12 years of age.
This medicine should not be taken for more than 48 hours except on medical advice.

Overdosage

If an overdose is taken or suspected, immediately contact the Poisons Information Centre (in Australia, call 131 126; in New Zealand call 0800 764 766) for advice, or go to a hospital straight away even if you feel well because of the risk of delayed, serious liver damage.

Presentation and Storage Conditions

Day tablets are white, round tablets with a break-line on one side.
Night tablets are pink, round tablets with a break-line on one side.

The tablets are presented in PVC/PVDC/Aluminium blister packs which are enclosed in a carton. Each blister pack contains 12 tablets: 8 white day tablets and 4 pink night tablets.

The pack sizes are

- 24 tablets (2 x 12 tablet blister packs in a carton)
- 12 tablets (1 x 12 tablet blister packs in a carton)

Trust Fludol Day & Night should be stored below 30°C.

Name and Address of the Sponsor

Pharmacor Pty Ltd.
Suite 501, 7 Oaks Avenue,
Dee Why, NSW, 2099
Australia

Poison Schedule of the Medicine

Pharmacist Only Medicine (S3)

Date of First Inclusion in the Australian Register of Therapeutic Goods (the ARTG)

24th July 2000

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Date of Most Recent Amendment

17th October 2017