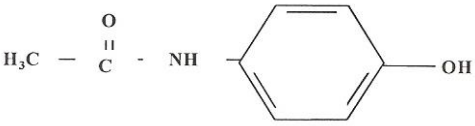
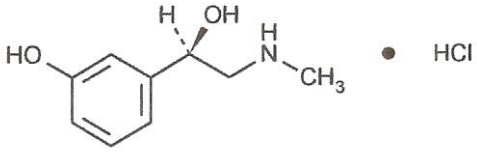
PRODUCT INFORMATION

PANADOL® SINUS PAIN & CONGESTION RELIEF CAPLETS

PANADOL® COLD & FLU PLUS DECONGESTANT CAPLETS

NAME OF THE MEDICINE

Active ingredients	Chemical structure	CAS Registry Number
Paracetamol		103-90-2
Phenylephrine Hydrochloride		61-76-7

DESCRIPTION

White capsule-shaped tablets (caplets) with flat edges, 17.7 mm x 7.1 mm, one face is embossed with sun graphic within an oval.

Formulation

Active Ingredients:

Paracetamol 500 mg/caplet, Phenylephrine HCl 5 mg/caplet

Excipients:

Cellulose – microcrystalline, Potassium sorbate, Povidone, Sodium lauryl sulphate, Starch – maize, Starch – pregelatinised maize, Stearic acid, Talc – purified.

PHARMACOLOGY

Pharmacodynamics

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.

Phenylephrine acts predominantly by a direct effect on alpha adrenergic receptors. Phenylephrine also has an indirect effect by releasing noradrenaline from its storage sites. Phenylephrine is used as a nasal decongestant to provide symptomatic relief by causing vasoconstriction resulting in redistribution of local blood flow to reduce oedema of the nasal mucosa, thus improving ventilation, drainage and nasal stuffiness.

Pharmacokinetics

Absorption

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Food intake delays paracetamol absorption.

Phenylephrine is irregularly absorbed from the gastrointestinal tract. Phenylephrine undergoes first-pass metabolism by monoamine oxidases in the gut and liver; orally administered phenylephrine thus has reduced bioavailability.

Distribution

Paracetamol is distributed into most body tissues. Binding to the plasma proteins is minimal at therapeutic concentrations but increases with increasing doses.

Phenylephrine undergoes rapid distribution into peripheral tissues. The volume of distribution of phenylephrine is between 200 and 500L, there appears to be minimal brain penetration, and does not seem to cross the placenta and does not appear to be distributed to any great extent in breast milk.

Metabolism

Paracetamol is metabolised extensively in the liver and excreted in the urine mainly as inactive glucuronide and sulphate conjugates.

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 150 mg/kg or 10 g 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.

Phenylephrine undergoes extensive metabolism in the intestinal wall (first pass) and in the liver. The principal routes of metabolism involve sulfate conjugation (primarily in the intestinal wall) and oxidative deamination (by monoamine oxidase); glucuronidation also occurs to a lesser extent.

Excretion

Paracetamol is excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted unchanged. Approximately 85% of a dose of paracetamol is excreted in urine as free and conjugated paracetamol within 24 hours of ingestion. Administration of paracetamol to patients with moderate to severe renal impairment may result in accumulation of paracetamol conjugates. The elimination half-life varies from one to three hours.

Phenylephrine and its metabolites are excreted mainly in urine. Following oral administration approximately 80% of the dose is excreted in urine within 48 hours principally as metabolites. Approximately 2.5% of an oral dose is excreted in the urine as unchanged drug. The elimination half life averages 2-3 hours following oral administration.

INDICATIONS

PANADOL Sinus Pain & Congestion Relief Caplets:
For the temporary relief of the pain and congestion of sinusitis.

PANADOL Cold & Flu + Decongestant Caplets:
For the temporary relief of cold & flu symptoms including headache, body aches and pain, blocked or runny nose, sore throat. Reduces fever.

CONTRAINDICATIONS

This product is contraindicated in patients with a previous history of hypersensitivity to paracetamol, phenylephrine hydrochloride or any of the excipients.

This medicine is also contraindicated in patients who are taking, or have taken within the last two weeks, monoamine oxidase inhibitors. (See INTERACTIONS.)

This medicine is contraindicated in patients with severe hypertension or coronary artery disease.

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants). (See INTERACTIONS.)

PRECAUTIONS

Contains paracetamol. Do not use with any other paracetamol-containing products, decongestants, or cold and flu medicines. The concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which can lead to liver transplant or death.

Caution should be exercised in patients with kidney impairment and in those with hepatic impairment due to the paracetamol content of the product.

Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index or are chronic heavy users of alcohol.

Underlying liver disease increases the risk of paracetamol-related liver damage.

Caution should be exercised in patients with glutathione depleted states such as sepsis, the use of paracetamol may increase the risk of metabolic acidosis.

Caution should be exercised in patients with cardiovascular disease, hypertension, diabetes, hyperthyroidism, prostatic enlargement, raised intra ocular pressure (i.e. glaucoma), phaeochromocytoma and occlusive vascular disease (e.g. Raynaud's Phenomenon)

Due to the phenylephrine content of this product, PANADOL Sinus Pain & Congestion Relief & PANADOL Cold & Flu + Decongestant should be used with caution in patients taking beta-blockers or other anti-hypertensives

Due to the phenylephrine content of this product, PANADOL Sinus Pain & Congestion Relief & PANADOL Cold & Flu + Decongestant should be used with caution in patients taking tricyclic antidepressants.

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants.

If symptoms persist, medical advice must be sought.

Keep out of sight and reach of children.

Use in pregnancy

Category B2

Drugs which have 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 show no evidence of an increased occurrence of foetal damage.

This product should not be used during pregnancy without medical advice.

Use in lactation

This product should not be used whilst breast feeding without medical advice.

Paracetamol is excreted in breast milk. Maternal ingestion of paracetamol in usual analgesic doses does not appear to present a risk to the breastfed infants.

Phenylephrine may be excreted in breast milk.

Use in children

Do not give to children under 12 years of age.

Effects on ability to drive and use machinery

Patients should be advised not to drive or operate machinery if affected by dizziness.

INTERACTIONS WITH OTHER MEDICINES

The following interactions with **paracetamol** have been noted:

Coumarins (including warfarin)	Anticoagulant effect may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding. Anticoagulant dosage may require reduction if treatment with paracetamol containing medication is prolonged.
Substances that increase gastric emptying (eg metoclopramide)	These substances increase paracetamol absorption.
Substances that decrease gastric emptying (eg propantheline, antidepressants with anticholinergic properties, narcotic analgesics)	These substances decrease paracetamol absorption.
Chloramphenicol	Concentrations may be increased by paracetamol
Potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes (eg alcohol, anticonvulsants)	Risk of paracetamol toxicity may be increased.
Probenecid	May affect paracetamol excretion and alter paracetamol plasma concentrations.
Colestyramine	Reduces the absorption of paracetamol if given within one hour of paracetamol.

Phenylephrine should be used with caution in combination with the following drugs as interactions have been reported.

Monoamine oxidase inhibitors	Hypertensive crisis or a serious increase in blood pressure may occur between phenylephrine and monoamine oxidase inhibitors (See CONTRAINDICATIONS.)
Sympathomimetic amines such as other decongestants, appetite suppressants and amphetamine-like psychostimulants	Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects and other additive effects (See PRECAUTIONS.)
Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa)	Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased. (See PRECAUTIONS.)
Tricyclic antidepressants (e.g. amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine (See PRECAUTIONS.) Hypertensive crisis may also occur.
Digoxin and cardiac glycosides	Increase the risk of irregular heartbeat or heart attack.

ADVERSE EFFECTS

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled doses and considered attributable are tabulated below by System Organ Class and frequency.

The following convention has been utilised for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from available data).

Adverse event frequencies have been estimated from spontaneous reports received through post-marketing data.

Paracetamol

The frequency of these reactions is unknown but considered likely to be very rare.

Body System	**Undesirable Effect**
Blood and lymphatic system disorders	Thrombocytopenia
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angioedema and Stevens Johnson syndrome
Respiratory, thoracic and mediastinal disorders	Bronchospasm, especially in patients sensitive to aspirin and other NSAIDs.
Hepatobiliary disorders	Hepatic dysfunction

Phenylephrine

The following adverse events have been observed in clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events.

Body System	**Undesirable Effect**
Psychiatric disorders	Nervousness
Nervous system disorders	Headache, dizziness, insomnia
Cardiac disorders	Increased blood pressure, tachycardia or arrhythmias
Gastrointestinal disorders	Nausea, vomiting
Central nervous stimulation	Anxiety

Adverse reactions identified during post-marketing use are listed below.

Body System	Undesirable Effect	Frequency
Eye disorders	Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma (See PRECAUTIONS.)	Rare
Cardiac disorders	Tachycardia, palpitations	Rare
Skin and subcutaneous disorders	Allergic reactions (e.g. rash, urticaria, allergic dermatitis)	Rare
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction such as prostatic hypertrophy.	Rare

DOSAGE AND ADMINISTRATION

Adults and children aged 12 years and over: 2 caplets every 4 – 6 hours as necessary. Maximum 8 caplets in 24 hours.

Do not use for more than a few days at a time in adults except on medical advice.

Should not be used for more than 48 hours for children aged 12 – 17 except on medical advice.

Do not give to children under 12 years of age.

Do not exceed the stated dose or frequency of dosing.

The lowest dose necessary to achieve efficacy should be used.

Should not be used with other paracetamol-containing products, decongestants or cough and cold medicines.

Do not use within several hours of going to bed as it may cause sleeplessness.

Minimum dosing interval: 4 hours

Renal and Hepatic impairment

Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication. The restrictions related to the use of such combinations in these patients is primarily a consequence of the paracetamol content of the product. (See PRECAUTIONS.)

OVERDOSAGE

Immediate medical management is required in the event of an overdose even if the symptoms of overdose are not present.

If an overdose is taken or suspected, contact the Poisons Information Centre immediately for advice (13 11 26) or the patient should go to the nearest hospital straight away. This should be done even if they feel well because of the risk of delayed, serious liver damage.

Paracetamol

Symptoms and signs

Paracetamol overdose may cause liver failure which can lead to liver transplant or death.

Treatment

Immediate medical management is required in the event of overdose, even if symptoms of overdose are not present. Administration of N-acetylcysteine may be required.

Phenylephrine

Symptoms and Signs

Overdose is likely to result in effects similar to those listed under Adverse Reactions. Additional symptoms may include irritability, restlessness, hypertension, and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur.

Treatment

Treatment should be as clinically appropriate. Severe hypertension may need to be treated with an alpha blocking drug such as phentolamine.

PRESENTATION AND STORAGE CONDITIONS

PANADOL Sinus Pain & Congestion Relief Caplets

White capsule-shaped tablets with flat edges, 17.7 mm x 7.1 mm, one face is embossed with sun graphic within an oval.

Blister packs of 10 & 24 caplets

Store below 30ºC

PANADOL Cold & Flu Plus Decongestant Caplets

White capsule-shaped tablets with flat edges, 17.7 mm x 7.1 mm, one face is embossed with sun graphic within an oval.

Blister packs of 20 caplets

Store below 30ºC

NAME AND ADDRESS OF THE SPONSOR

GlaxoSmithKline Consumer Healthcare

82 Hughes Avenue, Ermington, NSW 2115

POISON SCHEDULE OF THE MEDICINE

Packs of 24 caplets or less: Unscheduled

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

PANADOL Sinus Pain & Congestion Relief Caplets	AUST R 147590	22 November 2007
PANADOL Cold & Flu Plus Decongestant Caplets	AUST R 156874	17 November 2008

DATE OF THE MOST RECENT AMENDMENT

30 SEP 2015

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