New Zealand Data Sheet

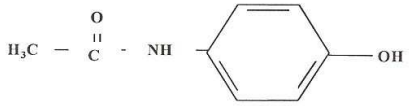
1 PRODUCT NAMES

COLDREX® PE PHENYLEPHRINE SINUS
COLDREX® PE PHENYLEPHRINE CONGESTION CLEAR
PANADOL® COLD & FLU MAX + DECONGESTANT
PANADOL® SINUS PAIN & CONGESTION RELIEF

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

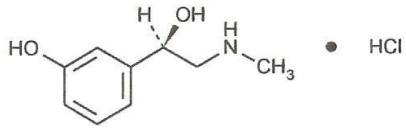
Active ingredient: Paracetamol (BP) 500 mg and Phenylephrine Hydrochloride (BP) 5 mg

CAS: 103-90-2



Paracetamol $C_8 H_9 NO_2$

CAS: 61-76-7



Phenylephrine Hydrochloride $C_9H_{13} NO_2$. HCl

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

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

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

COLDREX PE Phenylephrine Sinus
PANADOL Sinus Pain & Congestion Relief PE
Fast, effective, temporary relief of sinusitis symptoms including sinus headache, sinus pain, nasal congestion.

COLDREX PE Phenylephrine Congestion Clear
Fast, effective temporary relief of cold and flu symptoms including headache, body aches and pain, blocked or runny nose, sore throat. Reduces fever

PANADOL Cold & Flu Max + Decongestant Tablet
Fast, effective temporary relief of cold and flu symptoms including headache, body aches and pain, blocked or runny nose, sore throat. Reduces fever.

4.2 Dose and method of administration

Adults and children aged 12 years and over
Two caplets every four to six hours as necessary, taken with water. Maximum of 8 caplets within 24 hours.

Do not use for more than a few days at a time in adults without medical advice. Should not be used for more than 48 hours in children aged 12 to 17 except on medical advice.

Do not use in children under 12 years of age.

Do not exceed the stated dose or frequency of dose.

The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

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.

Use in children

Do not use in children under 12 years of age.

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 **4.4 Special warnings and precautions for use**).

4.3 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 **4.5 Interaction with other medicines and other forms of interaction**).

4.4 Special warnings and precautions for use

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 or have sepsis. 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 these products, they should be used with caution in patients taking beta-blockers or other anti-hypertensives

Due to the phenylephrine content of these products, they should be used with caution in patients taking tricyclic antidepressants.

Due to the phenylephrine content of these products, they should be used with caution in patients taking ergot alkaloids (e.g. ergotamine and methysergide).

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

Medical advice should be sought if symptoms worsen, persist for more than 7 days, or are accompanied by high fever, skin rash or persistent headache.
Keep out of sight and reach of children.

4.5 Interaction with other medicines and other forms of interaction

Paracetamol: 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. Occasional doses have no significant effect. 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 interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors (See **4.3 Contraindications**).

Sympathomimetic amines	Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects (See **4.4 Special warnings and precautions for use**).
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 **4.4 Special warnings and precautions for use**).
Tricyclic antidepressants (eg amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine (See **4.4 Special warnings and precautions for use**).
Digoxin and cardiac glycosides	Increase the risk of irregular heartbeat or heart attack.
Ergot alkaloids (e.g. ergotamine and methysergide)	Concomitant use of phenylephrine may cause increased risk of ergotism (See **4.4 Special warnings and precautions for use**).

4.6 Pregnancy and lactation

This product should not be used during pregnancy without medical advice. The lowest effective dose and shortest duration of treatment should be considered.

Pregnancy

Phenylephrine - 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.

Paracetamol – Category A

Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed. Paracetamol crosses the placental barrier. Animal studies with paracetamol have not identified any risk to pregnancy or embryo-foetal development.

Breast-feeding
This product should not be used while breastfeeding without medical advice.

Paracetamol is excreted in breast milk. Human studies with paracetamol have not identified any risk to lactation or the breast-fed offspring.

Phenylephrine may be excreted in breast milk.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable 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 dose 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 among others, skin rashes, angioedema, Stevens Johnson syndrome and Toxic Epidermal Necrolysis.
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
Gastrointestinal disorders	Nausea, vomiting

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	Rare
Cardiac disorders	Tachycardia, palpitations	Rare
Skin and subcutaneous disorders	Allergic reactions (eg 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
Immune system disorders	Hypersensitivity	Rare

4.9 Overdose

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 (0800 764 766) 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. Acute pancreatitis has been observed, usually with hepatic dysfuction and liver toxicity.

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics, paracetamol, combinations excluding psycholeptics. ATC code: N02BE51

Mechanism of action
Paracetamol is a para-aminophenol derivative that exhibits analgesic and anti-pyretic activity. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system.

Phenylephrine hydrochloride is a sympathomimetic agent with mainly direct effects on adrenergic receptors (predominantly alpha-adrenergic activity) producing nasal decongestion.

Pharmacodynamic Effects
The lack of peripheral prostaglandin inhibition by paracetamol confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract. Paracetamol is, therefore, particularly suitable for patients with a history of disease or on concomitant medication, where peripheral prostaglandin inhibition would be undesirable (such as, for example, those with a history of gastrointestinal bleeding or the elderly).

5.2 Pharmacokinetic properties

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.

Distribution

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

Metabolism

Paracetamol is metabolised in the liver and excreted in the urine mainly as 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 200 mg/kg or 10 g total paracetamol ingested) and, if left untreated, can cause irreversible liver damage.

Phenylephrine undergoes first-pass metabolism by monoamine oxidases in the gut and liver; orally administered phenylephrine thus has reduced bioavailability.

Elimination

Paracetamol is excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unmodified paracetamol with 85% to 90% of the administered dose eliminated in the urine within 24 hours of ingestion. The elimination half-life varies from one to three hours.

Phenylephrine is irregularly absorbed from the gastrointestinal tract. It undergoes first-pass metabolism by monoamine oxidases in the gut and liver; orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Paracetamol (BP) 500 mg and Phenylephrine Hydrochloride (BP) 5 mg tablets contains the following excipients:

Maize starch
Microcrystalline cellulose
Potassium sorbate
Povidone
Pregelatinised Maize starch
Purified talc
Sodium lauril sulfate
Stearic acid

6.2 Incompatibilities

Not applicable

6.3 Shelf life
36 months from date of manufacture.

6.4 Special precautions for storage
Store below 30°C.

6.5 Nature and contents of container
Blister pack of 20 capsule-shaped tablets (caplets). Each caplet contains 500mg Paracetamol and 5mg Phenylephrine Hydrochloride.

Instructions for Use/Handling:
No special requirements.

6.6 Special precautions for disposal
No special requirements.

7 MEDICINE SCHEDULE
General Sale

8 SPONSOR
GlaxoSmithKline Consumer Healthcare
Level 11 Zurich House
21 Queen Street
Auckland 1010, New Zealand
FREECALL NZ: 0800 540 144

9 DATE OF FIRST APPROVAL
17 January 2008

10 DATE OF REVISION OF THE TEXT
12 April 2019

SUMMARY TABLE OF CHANGES

Section changed		Summary of new information
All		Transferred to new data sheet template
4.2	**Dose and method of administration**	Safety statement shortest duration of treatment.
4.4	**Special warnings and precautions for use**	Additional safety statements, sepsis, ergot alkaloids usage and worsening symptoms after 7 days.
4.5	**Interaction with other medicines and other forms of interaction**	Additional safety statements in relation to ergot alkaloids
4.6	**Pregnancy and lactation**	Safety statement around effective dose and shortest duration of treatment.
4.8	**Undesirable effects**	Additional safety statements in relation to Immune System

	disorders and Ergot alkaloids.
4.9 Overdose	Safety statements around Acute pancreatitis.