NEW ZEALAND DATASHEET

COLDREX PE PHENYLEPHRINE SINUS TABLETS
PANADOL SINUS RELIEF PE TABLETS
PANADOL COLD & FLU MAX + DECONGESTANT TABLETS
Paracetamol (BP) 500mg and Phenylephrine Hydrochloride (BP) 5mg

Presentation

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

Indications

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

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.

Dosage and 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.
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 WARNINGS AND PRECAUTIONS.)

Contraindications

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.)

Warnings and precautions

Medical advice should be sought before taking this product in patients with these conditions:

- Hypertension
- Cardiovascular disease
- Diabetes
- Hyperthyroidism
- Angle closure glaucoma
- Phaeochromocytoma
- An enlargement of the prostate gland
- Occlusive vascular disease (eg Raynaud’s Phenomenon)
- Liver and kidney impairment. Underlying liver disease increases the risk of paracetamol-related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.

Use with caution in patients taking:

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

If symptoms persist, medical advice must be sought.

Keep out of sight and reach of children.

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

*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.

Use in Lactation
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.

Use in children
Do not use in children under 12 years of age.
**Effects on ability to drive and use machines**

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

**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 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.

<table>
<thead>
<tr>
<th>Body System</th>
<th>Undesirable Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td></td>
<td>Cutaneous hypersensitivity reactions including skin rashes, angioedema and Stevens Johnson syndrome</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Bronchospasm</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>Hepatic dysfunction</td>
</tr>
</tbody>
</table>
**Phenylephrine**

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

<table>
<thead>
<tr>
<th>Body System</th>
<th>Undesirable Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric disorders</td>
<td>Nervousness</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache, dizziness, insomnia</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Increased blood pressure</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea, vomiting</td>
</tr>
</tbody>
</table>

**Post Marketing Experience**

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

<table>
<thead>
<tr>
<th>Body System</th>
<th>Undesirable Effect</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye disorders</td>
<td>Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma (See WARNINGS AND PRECAUTIONS.)</td>
<td>Rare</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Tachycardia, palpitations</td>
<td>Rare</td>
</tr>
<tr>
<td>Skin and subcutaneous disorders</td>
<td>Allergic reactions (eg rash, urticaria, allergic dermatitis)</td>
<td>Rare</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction such as prostatic hypertrophy.</td>
<td>Rare</td>
</tr>
</tbody>
</table>
### Interactions

#### Paracetamol

The following interactions with paracetamol have been noted:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coumarins (including warfarin)</td>
<td>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.</td>
</tr>
<tr>
<td>Substances that increase gastric emptying (e.g., metoclopramide)</td>
<td>These substances increase paracetamol absorption.</td>
</tr>
<tr>
<td>Substances that decrease gastric emptying (e.g., propantheline, antidepressants with anticholinergic properties, narcotic analgesics)</td>
<td>These substances decrease paracetamol absorption.</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Concentrations may be increased by paracetamol</td>
</tr>
<tr>
<td>Potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes (e.g., alcohol, anticonvulsants)</td>
<td>Risk of paracetamol toxicity may be increased.</td>
</tr>
<tr>
<td>Probenecid</td>
<td>May affect paracetamol excretion and alter paracetamol plasma concentrations.</td>
</tr>
<tr>
<td>Colestyramine</td>
<td>Reduces the absorption of paracetamol if given within one hour of paracetamol.</td>
</tr>
</tbody>
</table>
**Phenylephrine**

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

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Interaction Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoamine oxidase inhibitors</td>
<td>Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors (See CONTRAINDICATIONS.)</td>
</tr>
<tr>
<td>Sympathomimetic amines</td>
<td>Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects (See WARNINGS AND PRECAUTIONS.)</td>
</tr>
<tr>
<td>Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa)</td>
<td>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 WARNINGS AND PRECAUTIONS.)</td>
</tr>
<tr>
<td>Tricyclic antidepressants (eg amitriptyline)</td>
<td>May increase the risk of cardiovascular side effects with phenylephrine (See WARNINGS AND PRECAUTIONS.)</td>
</tr>
<tr>
<td>Digoxin and cardiac glycosides</td>
<td>Increase the risk of irregular heartbeat or heart attack.</td>
</tr>
</tbody>
</table>

**Overdosage**

**Symptoms and signs**

Paracetamol overdose may cause liver failure.

Phenylephrine overdosage is likely to result in effects similar to those listed under ADVERSE EFFECTS. Additional symptoms may include irritability, restlessness, hypertension and possibly reflux brachycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur. However the amount required to produce serious phenylephrine toxicity would be greater than required to cause paracetamol-related liver toxicity.
Treatment
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. (See ADVERSE EFFECTS.)

Administration of N-acetylcysteine may be required.

In cooperative adults, activated charcoal may reduce absorption of the medicine if given within one hour after ingestion.

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

Further Information

Actions

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

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).

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.

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.

Other

Chemical Structure

Paracetamol \((C_8H_9NO_2)\)

Phenylephrine Hydrochloride \((C_{9H_{13}}NO_2 \cdot HCl)\)

List of Excipients

Maize starch
Microcrystalline cellulose
Potassium sorbate
Povidone
Pregelatinised Maize starch
Purified talc
Sodium laurilsulfate
Stearic acid
Pharmaceutical Precautions

Shelf life
36 months from date of manufacture.

Special storage precautions
Store below 30ºC.

Incompatibilities
Not applicable

Use and handling
No special requirements

Package Quantities
Blister pack of 20 capsule-shaped tablets (caplets). Each caplet contains 500mg Paracetamol and 5mg Phenylephrine Hydrochloride.

Medicine Schedule
General Sale

Sponsor Details
GlaxoSmithKline (NZ) Ltd
Trading as GlaxoSmithKline Consumer Healthcare
Auckland, New Zealand
Telephone: (09) 367 2970

Date of Preparation
13 April 2012