Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Panadol Sinus Relief Film Coated TabletsParacetamol 500mgCaffeine 25mgPhenylephrine Hydrochloride 5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains paracetamol 500 mg, caffeine 25 mg and phenylephrine hydrochloride 5 mg.

Excipients: also includes sunset yellow (E110), 0.62 mg per tablet. For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet
Orange film-coated tablet embossed with 'B' on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The product is recommended for the relief of the symptoms of nasal and sinus congestion, colds and flus.

4.2 Posology and method of administration

Oral administration only.

Do not exceed the stated dose.

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

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

Adults (including the elderly) and children aged 16 years and over:

One to two tablets every 4-6 hours as required.
Maximum daily dose: Eight tablets in 24 hours.

Children aged 12 – 15 years:

One tablet every 4-6 hours as required.
Maximum daily dose: four tablets in 24 hours.
Not recommended for children under 12 years of age

Minimum dosing interval: 4 hours

Maximum duration of continued use without medical advice: 3 days

4.3 Contraindications

Known hypersensitivity to paracetamol, phenylephrine, caffeine or any of the other ingredients listed in section 6.1.

Use in children under 12 years of age.

Severe hepatic or severe renal impairment, hypertension, hyperthyroidism, diabetes, closed angle glaucoma, phaeochomocytoma, prostate hypertrophy and heart disease. Patients taking tricyclic antidepressants, or beta-blocking drugs and those who are taking or who have taken within the last two weeks monoamine oxidase inhibitors.

4.4 Special warnings and precautions for use

Contains paracetamol. Do not use with any other paracetamol-containing products. The concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which may require liver transplant or lead to death.

Care is advised in the administration of paracetamol to patients with renal or hepatic impairment.

Use with caution in patients with glutathione depletion due to metabolic deficiencies.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Underlying liver disease increases the risk of paracetamol-related liver damage. The hazard of overdose is greater in those with non- cirrhotic alcoholic liver disease.

Do not exceed the stated dose.

Medical advice should be sought before using this product in patients with occlusive vascular disease (e.g. Raynaud's phenomenon).

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

Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.

Contains colour sunset yellow (E110) which may cause allergic-type reactions.

If symptoms persist consult your doctor. Keep out of the sight and reach of children.
Consult your doctor if you are taking warfarin or have been diagnosed with liver or kidney disease.

4.5 Interaction with other medicinal products and other forms of interaction

Medical advice should be sought before taking paracetamol-caffeine-phenylephrine in combination with the following drugs:

Monoamine oxidase inhibitors	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors.
Sympathomimetic amines	Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects.
Beta-blockers, and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa)	Phenylephrine may reduce the efficacy of beta- blocking drugs and hypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased.
Tricyclic antidepressants (e.g, amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine.
Digoxin and cardiac glycosides	Concomitant use of phenylephrine with digoxin or cardiac glycosides may increase the risk of irregular heartbeat or heart attack.
Warfarin and other coumarins	The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional

	doses have no significant effect.
Ergot alkaloids (e.g. ergotamine and methysergide)	Concomitant use of phenylephrine hydrochloride may cause increased risk of ergotism.
Lithium	Caffeine can increase the elimination of lithium from the body. Concomitant use is therefore not recommended.

The speed of absorption of paracetamol may be increased by metoclopramide and domperidone and reduced by cholestyramine, however, these interactions are not considered to be clinically significant in over-the- counter paracetamol-containing products which are intended for short term usage.
Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4)

Enzyme-inducing drugs may increase hepatic damage, as does excessive intake of alcohol.

4.6 Fertility, pregnancy and lactation

Pregnancy

This product is not recommended for use during pregnancy.

Paracetamol
A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however, it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.
Caffeine
This product is not recommended for use during pregnancy due to the possible increased risk of spontaneous abortion associated with caffeine consumption.

Phenylephrine
No relevant data available.

Lactation

This product should not be used while breast-feeding without medical advice. If used, the lowest effective dose and shortest duration of treatment should be considered.

Paracetamol
Human studies with paracetamol at the recommended doses have not identified any risk to lactation or the breast-fed offspring.

Caffeine
Caffeine in the breast milk may potentially have a stimulating effect on breast-fed infants but significant toxicity has not been observed.

Phenylephrine
Phenylephrine may be excreted in breast milk. The drug should not be used while breast-feeding without medical advice.

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 MedDRA System Organ Class. As these reactions are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown but considered likely to be very rare (<1/10,000) or not known (cannot be estimated from available data).

Body System	Undesirable effect	Frequency
Blood and lymphatic system disorders	Thrombocytopaenia	Very rare
Immune System disorders	Anaphylaxis, Cutaneous hypersensitivity reactions, Angiodema, Stevens Johnson syndrome, Toxic Epidermal Necrolysis Very rare cases of serious skin reactions have been reported.	Very rare
Metabolism and nutrition disorders	High anion gap metabolic acidosis*	Not known
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin and other non-steroidal anti-inflammatory drugs	Very rare
Hepatobiliary	Hepatic dysfunction	Very rare

*** cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.**

Caffeine

Adverse reactions identified through post-marketing use with caffeine are listed below. The frequency of these reactions is unknown.

Body System	**Undesirable effect**
Central Nervous System Disorders	Dizziness, headache
Psychiatric disorders	Nervousness, insomnia, restlessness, anxiety and irritability
Cardiac disorders	Palpitations
Gastrointestinal disorders	Gastrointestinal disturbances

When the recommended paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects.

Phenylephrine

The following adverse events have been observed in clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events. Adverse events are listed below by MedDRA System Organ Class:

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. The frequency of these reactions is unknown but likely to be rare (<1/1000).

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance website: www.hpra.ie.

4.9 Overdose

Paracetamol

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity. Some patients may be at increased risk of liver damage from paracetamol toxicity.

Risk factors include:

If the patient a, Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes. Or b, Regularly consumes ethanol in excess of recommended amounts. Or c, Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms and signs
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 and peaks after 4 to 6
days. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Treatment
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. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous Nacetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.
If overdose is confirmed or suspected, seek immediate advice from your Poison Centre and refer patient to nearest Emergency Medical Centre for management and expert treatment. This should happen even in patients without symptoms or signs of overdose due to the risk of delayed liver damage.

Phenylephrine

Symptoms and signs
Phenylephrine overdosage 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. However the amount required to produce serious phenylephrine toxicity would be greater than required to cause paracetamol-related liver toxicity.

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

Caffeine

Symptoms and signs
Overdose of caffeine may result in epigastric pain, vomiting, diuresis, tachycardia or cardiac arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related liver toxicity.

Treatment
No specific antidote is available, but supportive measures may be used such as beta adrenoceptor antagonists to reverse the cardiotoxic effects.

Summary

Treatment of overdose requires assessment of plasma paracetamol levels for antidote treatment, with signs and symptoms of caffeine toxicity being managed symptomatically.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02BE51

Paracetamol is a well established analgesic and antipyretic. 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.

Caffeine is the most active xanthine derivative in respect of stimulation of the central nervous system, producing a condition of wakefulness and increased mental activity.

5.2 Pharmacokinetic properties

Paracetamol is metabolised by the hepatic microsomal enzymes. It is rapidly and completely absorbed from the gastro-intestinal tract. Plasma concentration reaches a peak in half to one hour, the plasma half-life is one to three hours and it is uniformly distributed throughout the body.

Phenylephrine hydrochloride is irregular absorbed from the gastro-intestinal tract. When injected intramuscularly it takes 10-15 minutes to act and subcutaneous and intramuscular injections are effective for about one hour. Intravenous injections are effective for about 20 minutes.

Caffeine is readily absorbed from the gastro-intestinal tract.

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Pregelatinised Starch
Povidone
Potassium sorbate
Sodium laurilsulfate
Eurocol sunset yellow (E110)
Stearic acid
Talc
Microcrystalline cellulose

Film coating

Hypromellose 6cps
Macrogol 400
Titanium dioxide (E171)
Sunset yellow aluminium lake (E110)
Quinoline yellow lake (E104)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container in order to protect from moisture.

6.5 Nature and contents of container

White, opaque PVC aluminium foil blisters in boxes. Pack sizes are 10, 12, 16, 20, 24, 40 and 48 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Haleon Ireland Limited
Clocherane
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8 MARKETING AUTHORISATION NUMBER

PA0678/044/001

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