Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Panadol Max Strength Fever and Congestion Hot Lemon Powder for Oral SolutionParacetamol 1000mgPhenylephrine hydrochloride 10mgAscorbic Acid 40mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains paracetamol 1000.0 mg, ascorbic acid 40.0 mg and phenylephrine hydrochloride 10 mg.

Excipients: Contains Sucrose 3.7g and sodium 0.12g per sachet

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution

Off white free flowing powder with an odour of lemon.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Short term symptomatic relief of influenza, fever, chills and colds including headache, sore throat pain, aches and pains, nasal congestion, sinusitis and its associated pain and acute nasal catarrh.

4.2 Posology and method of administration

Directions for Use

Empty contents of sachet into a beaker. Half fill with very hot water. Stir well. Add cold water as necessary and sugar if desired.

Recommended dose

Adults (including the elderly) and children 16 years and over:
One sachet to be taken every four to six hours as necessary. Do not exceed four doses per 24 hours. Not to be given to children under 16 years except on medical advice.
Use the lowest amount needed for the shortest duration of treatment to relieve symptoms. If symptoms persist or get worse, consult your doctor.
The product should not be used continuously for more than seven days without medical advice.

Renal impairment:
It is recommended, when giving paracetamol to patients with renal impairment, to reduce the dose and to increase the minimum interval between each administration to at least 6 hours unless directed otherwise by a physician. See Table below:

Adults:

Glomerular filtration rate	Dose
10-50 ml/min	500mg every 6 hours
<10ml/min	500mg every 8 hours

Hepatic impairment:
In patients with hepatic impairment or Gilbert's Syndrome, the dose should be reduced or the dosing interval prolonged.

The daily dose should not exceed 2g/day unless directed by a physician.

The elderly:
Experience has indicated that normal adult dosage is usually appropriate. However in frail, immobile,elderly subjects or in elderly patients with renal or hepatic impairment, a reduction in the amount or frequency of dosing may be appropriate.
The maximum daily dose should not exceed 60mg/kg/day (up to a maximum of 2g per day) in the following situations, unless directed by a physician:

- Weight less than 50kg
- Chronic alcoholism
- Dehydration
- Chronic malnutrition

4.3 Contraindications

The product is contraindicated in patients with any of the following conditions

- Known hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Hepatic impairment
- Severe renal impairment
- Hypertension
- Hyperthyroidism
- Diabetes
- Heart disease
- Glaucoma
- Urinary retention

The product must not be taken by patients using:

- Tricyclic antidepressants
- Beta-blocking drugs
- Other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants)
- Monoamine oxidase inhibitors (taken within the last 2 weeks)

4.4 Special warnings and precautions for use

Contains paracetamol. Concomitant use of other flu, cold or decongestant medicines, or other paracetamol-containing medicines should be avoided. Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. The hazard of overdose is greater in those with liver disease.

Consult your doctor if you are taking warfarin.

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

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- Phaeochromocytoma
- Occlusive vascular disease (e.g. Raynaud's Phenomenon)
- Mild to moderate kidney impairment
- Glutathione depletion due to metabolic deficiencies
- Chronic alcoholism
- Renal impairment (GFR ≤ 50ml/min)
- Gilbert's syndrome (familial non-haemolytic jaundice)
- Concomitant treatment with medicinal products affecting hepatic function
- Glucose-6-phosphate dehydrogenase deficiency
- Haemolytic anaemia
- Dehydration
- Chronic malnutrition
- Weight less than 50kg
- Elderly

The physician or pharmacist should check that sympathomimetic containing preparations are not simultaneously administered by several routes i.e. orally and topically (nasal, aural and eye preparations).

Patients with prostatic hypertrophy may have increased difficulty with micturition and should use this product with caution.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Contains 3.7 g sucrose per dose. To be taken into account in patients with diabetes.

Contains 116 mg sodium per dose. To be taken into consideration by patients on a sodium controlled diet.

If symptoms persist for more than 7 days, or are accompanied by high fever, skin rash or persistent headache, consult your doctor.

Do not exceed the stated dose.

Minimum dosing interval: 4 hours.

Keep out of reach and sight of children.

4.5 Interaction with other medicinal products and other forms of interaction

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 effects. Enzyme-inducing drugs may increase hepatic damage, as does excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. These interactions are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed. Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4)

Interactions have been reported between phenylephrine and the following drugs:

Monoamine 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 anti-hypertensives (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.
Tricyclic antidepressants (e.g. amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine
Digoxin and cardiac glycosides	Increase the risk or irregular heartbeat or heart attack.
Ergot alkaloids (e.g. ergotamine and methysergide)	Concomitant use of phenylephrine may cause increased risk of ergotism

4.6 Fertility, pregnancy and lactation

Pregnancy

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

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.

Phenylephrine
No relevant data are available for products containing phenylephrine.

Lactation

This product should not be used whilst breast feeding without medical advice. The product should only be used if the expected benefit to the mother justifies the potential risk to the newborn.
Paracetamol is excreted in breast milk but not in clinically significant amounts.
Phenylephrine hydrochloride 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.
Adverse 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 have been 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).

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

Very rare cases of serious skin reactions have been reported.
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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

Phenylephrine hydrochloride

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	Headache, dizziness, insomnia
Cardiac disorders	Increased blood pressure
Gastrointestinal disorders	Nausea, vomiting

Adverse reactions identified during post-marketing use are listed below. As these reactions are reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown but considered likely to be rare (;:1/10,000, <1/1000).

Body System	Undesirable effect
Eye disorders	Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma
Cardiac disorders	Tachycardia, palpitations
Immune system disorder	Hypersensitivity, urticaria, allergic dermatitis
Skin and subcutaneous disorders	Rash
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction such as prostatic hypertrophy.

4.9 Overdose

ParacetamolSymptoms and Signs

Some patients may be at increased risk of liver damage from paracetamol toxicity:
Risk factors include;

- Patients with liver disease
- Elderly patients
- Young children
- Patients receiving long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Patients who regularly consume ethanol in excess of recommended amounts
- Patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Ingestion of more than 12 g paracetamol (24 standard 500 mg tablets) or more than 150 mg paracetamol per kg bodyweight (9 g paracetamol in a 60 kg individual), whichever is the smaller, can cause severe liver damage. Liver damage (as demonstrated by a rise in plasma transaminase levels) may be apparent between 8 and 36 hours following overdose. Biochemical evidence of maximal damage, however, may not be attained until 72-96 hours after ingestion of the overdose. Overdose of paracetamol can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.
Symptoms of paracetamol overdose in the first 24 hours may include pallor, nausea, vomiting, anorexia, and abdominal pain. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity. Liver damage results when excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Treatment

Immediate medical attention (in-hospital, if possible) is required in the event of overdose, even if there are no significant early symptoms. There may be no early symptoms following a life-threatening overdose.
Intravenous N-acetylcysteine (NAC) is effective when initiated within 8 hours of the overdose. Efficacy declines progressively after this time, but NAC may provide some benefit up to and possibly beyond 24 hours. Oral methionine is also effective provided that it is given within 10 to 12 hours of the overdose. Activated charcoal should be considered if the dose of paracetamol ingested exceeds 12 g or 150 mg/kg, whichever is the smaller, and the procedure can be undertaken within 1 hour of the overdose. There is little evidence that undertaking gastric lavage will be of benefit to a patient in whom paracetamol is known to have been the only substance ingested.
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 reflux 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 as clinically appropriate. Severe hypertension may need to be treated with an alpha blocking drug such as phentolamine.

Ascorbic Acid

Symptom and Signs

High doses of ascorbic acid (>3000mg) may cause transient osmotic diarrhoea and gastrointestinal effects such as nausea and abdominal discomfort.
Effects of overdose of ascorbic acid would be subsumed by serious liver toxicity caused by paracetamol overdose.
General considerations
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.
Where a Poison Information Centre is not available, refer patient to the nearest Emergency Medical Centre for management and expert treatment.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02BE51.
Paracetamol – an analgesic and antipyretic.
Ascorbic acid – a common ingredient of cold and influenza combination products included to compensate for Vitamin C losses which may occur in the initial stages of acute viral infections.

Phenylephrine hydrochloride – a sympathomimetic decongestant.
The active ingredients are not known to cause sedation.

5.2 Pharmacokinetic properties

Paracetamol – is readily absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted in the urine, mainly as glucuronide and sulphate conjugates.

Ascorbic Acid – is readily absorbed from the gastrointestinal tract and is widely distributed in the body tissues, 25% bound to plasma proteins. Ascorbic Acid in excess of the body's needs is eliminated in the urine as metabolites.
Phenylephrine hydrochloride – is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate.

5.3 Preclinical safety data

Pre-clinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not already been mentioned elsewhere in this Summary.
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.
The toxicity of paracetamol has been extensively studied in numerous animal species. Preclinical studies in rats and mice have indicated singledose oral LD50 values of 3.7g/kg and 338 mg/kg, respectively. Chronic toxicity in these species at large multiples of the human therapeutic dose, occurs as degeneration and necrosis of hepatic, renal and lymphoid tissue, and blood count changes. The metabolites believed to be responsible for these effects have also been demonstrated in man.
Paracetamol should not, therefore, be taken for long periods of time and in excessive doses. At normal therapeutic doses, paracetamol is not associated with genotoxic or carcinogenic risk.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Citric acid
Sodium citrate
Maize starch
Sodium cyclamate
Saccharin sodium
Colloidal anhydrous silica
Lemon flavour
Natural curcumin (E 100)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

The product is packed in laminate sachets comprising paper/polythene/aluminum foil/polythene.

Five or ten sachets may be contained in a boxboard carton.

Not all pack sizes may be marketed

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Haleon Ireland Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/035/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19th February 1999
Date of last renewal: 19th February 2009

10 DATE OF REVISION OF THE TEXT

May 2023