Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Panadol Night

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains paracetamol 500.0mg and diphenyhydramine hydrochloride 25.0mg.

Excipients: contains lactose.

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Film coated Tablet
Blue film coated capsule shaped tablets with flat edges and “PM” debossed on one side, blank on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the short term treatment of bedtime symptoms of colds and flu pain, for example rheumatic and muscle pain, backache, toothache, headache and period pain.

4.2 Posology and method of administration

Oral administration only.

Adults (including the elderly) and children 16 years and over: 2 tablets to be taken 20 minutes before bedtime.

Other products containing paracetamol may be taken during the day but the total daily dose of paracetamol must not exceed 4000mg (including this product) in any 24 hour period.

Children aged 12 – 15 years:
1 tablet to be taken 20 minutes before bedtime.

Other products containing paracetamol may be taken during the day but the total daily dose of paracetamol must not exceed 2000mg (including this product) in any 24 hour period.

Children under 12 years:
Not recommended for children under 12 years of age except on medical advice.

Allow at least four hours between taking any paracetamol-containing product and this product.

Do not take for more than 7 consecutive nights without consulting your doctor.

Do not exceed the stated dose.

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

Should not be used with other antihistamine-containing preparations, including those used on the skin (see Warnings and Precautions).

Should not be taken by elderly with confusion. Sedating antihistamines may cause confusion and paradoxical excitation in the elderly.

Caution should be exercised in those with moderate to severe hepatic or renal impairment.

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

Hypersensitivity to paracetamol or diphenhydramine, or excipients (closed angle glaucoma, porphyria).

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 a liver transplant or lead to death.

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

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.

Do not take for more than 7 days without consulting a doctor. If symptoms persist, medical advice must be sought.

Diphenhydramine may increase the sedative effects of alcohol therefore, concurrent use with alcohol should be avoided (see *Interactions*).

Medical advice should be sought before taking in patients with:

- Hepatic or renal impairment. Underlying liver disease increases the risk of paracetamol-related liver damage
- Glutathione depleted states as the use of paracetamol may increase the risk of metabolic acidosis. Concurrent use of drugs which cause sedation such as tranquillizers, hypnotics and anxiolytics may cause an increase in sedative effects therefore medical advice should be sought before taking diphenhydramine with such medicines (see *Interactions*).

Use with caution in:

- Patients with epilepsy or seizure disorders, myasthenia gravis, narrow-angle glaucoma, prostatic hypertrophy, urinary retention, asthma, bronchitis and chronic obstructive pulmonary disease (COPD), moderate to severe hepatic impairment and moderate to severe renal impairment.
- Patients taking monoamine oxidase inhibitors (MAOIs) or within 2 weeks of stopping an MAOI (see *Interactions)*.
- Patients taking other drugs with antimuscarinic properties (e.g. atropine, tricyclic antidepressants) (see *Interactions).*

Avoid use with other antihistamine-containing preparations, including topical antihistamines and cough and cold medicines.

Use with caution in the elderly, who are more likely to experience adverse effects. Avoid use in elderly patients with confusion.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Keep out of sight and reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of paracetamol may be increased by metoclopramide and domperidone and reduced by cholestyramine. However, the interactions are not considered to be clinically significant for over-the-counter products intended for short term use.

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.

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)

Diphenhydramine may potentiate the sedative effects of alcohol and other CNS depressants (e.g. codeine, tranquillizers, hypnotics, opioid analgesics, and anxiolytics) and other antihistamines (see Warnings and Precautions).

Monoamine oxidase inhibitors may prolong and intensify the anticholinergic effects of diphenhydramine.

As diphenhydramine has some anticholinergic activity, the effects of some anticholinergic drugs (e.g. atropine, tricyclic antidepressants) may be potentiated. This may result in tachycardia, dry mouth, blurred vision, gastrointestinal disturbances (e.g. colic), urinary retention and headache.

Diphenhydramine is an inhibitor of the cytochrome p450 isoenzyme CYP2D6. Therefore, there may be a potential for interaction with drugs which are primarily metabolised by CYP2D6, such as metoprolol and venlafaxine.

4.6 Fertility, pregnancy and lactation

Pregnancy

This product should not be used during pregnancy without medical advice, unless the expected benefit justifies the potential risk to the foetus.

As with the use of any medicines during pregnancy, pregnant women should seek medical advice before taking paracetamol. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, the lowest effective dose and shortest duration of treatment should be considered.

There are no adequate data from the use of diphenhydramine in pregnant women.

Animal studies are insufficient with respect to effects on pregnancy. The potential risk for humans is unknown. Use of sedating antihistamines during the third trimester may result in reactions in the newborn or premature neonates.

Lactation

This product should not be used whilst breast feeding unless the expected benefit justifies the potential risk to the new-born.

Human studies with paracetamol have not identified any risk to lactation or the breastfed offspring. Paracetamol crosses the placental barrier and is excreted in breast milk, but not in clinically significant amounts.

Diphenhydramine has been detected in breast milk, but the effects of this on breastfed infants are unknown.

4.7 Effects on ability to drive and use machines

May cause drowsiness, dizziness, blurred vision, cognitive and psychomotor impairment, which can seriously affect the patient's ability to drive or operate machinery. If affected, do not drive or operate machinery.

4.8 Undesirable effects

Undesirable effects are listed below by System Organ Class and frequency. Frequencies are defined as: very common (<1/10), common (<1/100 to <1/10), uncommon (<1/1,000 to <1/100), rare (<1/10,000 to <1/1,000) and very rare (<1/10,000), not known (cannot be estimated from the available data).

Paracetamol

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. As the adverse reactions identified from postmarketing use are reported voluntarily from a population of uncertain size, the frequency is not known but 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, among others, skin rashes, angioedema, and Stevens Johnson syndrome and Toxic Epidermal Necrolysis. Very rare cases of serious skin reactions have been reported.
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin and other NSAIDs.
Hepatobiliary disorders	Hepatic dysfunction.

Diphenhydramine

Adverse reactions which have been observed in clinical trials and which are considered to be common or very common are listed below by MedDRA System Organ Class. The frequency of other adverse reactions identified during postmarketing use is not known, but these reactions are likely to be uncommon or rare.

Body System	**Undesirable effect**
General disorders and administration site conditions	Common: Fatigue
Immune system disorders	Not known: Hypersensitivity reactions including rash, urticaria, dyspnoea and angioedema
Psychiatric disorders	Not known: Confusion*, paradoxical excitation* (e.g. increased energy, restlessness, nervousness) * The elderly are more prone to confusion and paradoxical excitation
Nervous system disorders	Common: Sedation, drowsiness, disturbance in attention, unsteadiness, dizziness Not known: Convulsions, headache, paraesthesia, dyskinesias
Eye disorders	Not known: Blurred vision
Cardiac disorders	Not known: Tachycardia, palpitations
Respiratory, thoracic & mediastinal disorders	Not known: Thickening of bronchial secretions
Gastrointestinal disorders	Common: Dry mouth. Not known: Gastrointestinal disturbance including nausea, vomiting.

Musculoskeletal and connective tissue disorders	Not known: Muscle twitching
Renal and urinary disorders	Not known: Urinary difficulty, urinary retention

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.

4.9 Overdose

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

Symptoms and signs
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 4-6 days after ingestion of the overdose.

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. 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 acute 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.

Diphenhydramine Hydrochloride

Symptoms and signs

Diphenhydramine overdose is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include mydriasis, fever, flushing, agitation tremor, dystonic reactions, hallucinations and ECG changes including QT prolongation. Large overdose may cause rhabdomyolysis, convulsions, delirium, toxic psychosis, arrhythmias, coma and cardiovascular collapse.

Treatment

Treatment should be supportive and directed towards specific symptoms. The stomach should be emptied by aspiration and gastric lavage. Convulsions and marked CNS stimulation should be treated with parenteral diazepam. Further management should be as clinically indicated or as recommended by the national poisons centres where applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol has analgesic and antipyretic effects. It is only a weak inhibitor of prostaglandin biosynthesis, although there is some evidence to suggest that it may be more effective against enzymes in the CNS than those in the periphery. This fact may

partly account for its ability to reduce fever (a central action) and to induce analgesia. Diphenhydramine is an ethanolamine class antihistamine that acts predominantly as a competitive but reversible inhibitor of antihistamine at the H_1 receptor sites. However, like most H_1 antihistamines it has additional sedative anticholinergic (muscarinic) and local anaesthetic properties.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. Concentration in plasma generally reaches a peak in 30-120 minutes; plasma half-life is 1-4 hours.Paracetamol is relatively uniformly distributed throughout most body fluids.Plasma binding is variable. Excretion is almost exclusively renal in the form of conjugates. Diphenhydramine is well absorbed from the gastrointestinal tract following oral administration. Peak, plasma concentrations are achieved in 2 to 3 hours and the effects usually last 4 to 6 hours. Diphenhydramine is extensively metabolised mainly in the liver, and excreted usually as metabolites in the urine.

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

Table core
Maize starch
Pregelatinised starch
Potassium sorbate
Povidone K25
Talc
Stearic acid

Film coat
Opadry II Blue 33G20500
Containing: Hypromellose (E464), Titanium dioxide (E171), Lactose monohydrate, Macrogol 400, Triacetin, Brilliant Blue FCF, Aluminium Lake (E133), Indigo
Carmine Aluminium Lake (E132).
Polishing agent
Carnauba wax

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25^{o}C. Store in the original package to protect from light.

6.5 Nature and contents of container

Panadol Night tablets are packaged in either:

- Opaque PVC/PVDC (250/40µm)/ aluminium foil (30µm) blister strips

- Child resistant opaque PVC/PVDC (250/40µm) / aluminium foil (20µm) /PET 8µm blister strips

Then packed into outer cardboard cartons. Pack sizes: 4, 10 or 20 tablets.

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

PA0678/039/008

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 September 1998

Date of last renewal: 18 September 2008

10 DATE OF REVISION OF THE TEXT

December 2023