SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Panadol Night

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol 500 mg and Diphenhydramine hydrochloride 25 mg ,also

contains lactose monohydrate.

3. PHARMACEUTICAL FORM

Film-coated tablets

Panadol Night tablets are blue film coated capsule-shaped tablets with slightly curved edges. Each tablet is debossed with 'PM' on one side, blank on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the short term treatment of bedtime pain, for example rheumatic and muscle pain, backache, toothache, migraine, headache and period pain which is causing difficulty in getting to sleep.

4.2. Posology and Method of Administration

Oral administration only.

Do not exceed the stated dose or frequency of dosing

Adults (including the elderly) and children aged 16 years and over:
Two tablets to be taken 20 minutes before bedtime. Maximum daily dose: Two tablets (1000 mg paracetamol, 50 mg diphenhydramine hydrochloride) in 24 hours. Other products containing paracetamol may be taken for daytime pain relief but at a reduced maximum dose of 6 tablets in 24 hours. The dose should not be repeated more frequently than every four hours.
Should not be used with other antihistamine-containing preparations, including those used on the skin (see Warnings and Precautions)

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

Not recommended for children under 16 years of age except on medical advice.

Patients should not take the tablets for more than 7 consecutive nights without consulting their doctor.

Elderly: Should not be taken by elderly patients with confusion. Sedating antihistamines may cause confusion and paradoxical excitation in the elderly (see section 4.4).

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

4.3 Contraindications

Hypersensitivity to paracetamol, diphenhydramine hydrochloride or other constituents. 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 liver transplant or lead to death.

The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Use with caution in patients with glutathione depletion due to metabolic deficiencies.
Avoid use of other antihistamine-containing preparations, including topical antihistamine and cough and cold medicines.

Avoid concurrent use with alcohol, as diphenhydramine may increase the sedative effects of alcohol. Therefore, alcohol should be avoided (see Interactions).

Patients should be advised to consult their doctor if their headaches become persistent.

Patients should be advised not to take other paracetamol containing products, other drugs with sedating properties, or alcohol concurrently.

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 as diphenhydramine may cause an increase in sedative effects (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), hepatic impairment and mild to moderate 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).

Do not take for more than 7 days unless it is supported by a favourable benefit/risk ratio. If symptoms persist, medical advice must be sought.

May cause drowsiness.

Keep out of the sight and reach of children.

Use with caution in the elderly as they may be more susceptible to adverse effects. Avoid use in elderly with confusion.

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

4.5 Interaction with Other Medicaments and Other Forms of Interaction

Paracetamol

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. 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.

Diphenhydramine

Diphenhydramine hydrochloride may potentiate the sedative action of alcohol and other central nervous system depressants (e.g. codeine, tranquilizers, hypnotics and anxiolytics) and other antihistamines.

Monoamine Oxidase inhibitors (MAOIs) may prolong and intensify the antimuscarinic effects of diphenhydramine. The product should be used with caution with MAOIs or within 2 weeks of stopping an MAOI.

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

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

4.6 Pregnancy and Lactation

Pregnancy

This product should not be used during pregnancy unless the expected benefit justifies the potential risk to the foetus. The lowest effective dose and shortest duration of treatment should be considered.

Paracetamol
As with the use of any medicine 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.

Diphenhydramine
There are no adequate data from the use of diphenhydramine in pregnant women. Animal studies are insufficient with respects to 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 without medical advice.

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

Diphenhydramine has been detected in breast milk, but the effects of this on breast-fed 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 patients' ability to drive and use machinery. If affected they should not drive or operate machinery.

4.8 Undesirable Effects

Adverse events from historical clinical trials data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labeled dose and considered attributable are tabulated below by System Organ Class and frequency. The following convention has been utilized for the classification of

undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10.000, <1/1000), very rare (<1/10,000), not known (cannot be estimated from available data).

Paracetamol

As the adverse reactions identified from post-marketing use are reported voluntarily from a population of uncertain size, the frequency is not known.

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema.Very rare cases of serious skin reactions have been reported.
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction

*There have been case of bronchospasm with paracetamol, but there are more likely in asthmatics sensitive to aspirin or other NSAIDs.

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 post-marketing use is unknown, 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* (eg 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 and 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 the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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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.

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk Factors:

If the patient

- Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

Or

- Regularly consumes ethanol in excess of recommended amounts.

Or

- Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdose 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 liver injuries peak after 4-6 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.

Management

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, see BNF overdose section.

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 N-acetylcysteine, 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. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

Diphenhydramine

Diphenhydramine overdose is likely to result in effects 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 should be supportive and directed towards specific symptoms. 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 histamine at the H_1 receptor sites. However, like most H_1 antihistamines it has additional sedative anticholinergic (antimuscarinic) 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

Tablet cores:
Maize starch
starch pregelatinised
potassium sorbate
povidone K-25

purified talc
stearic acid

Film coating:
Hypromellose 2910 (E 464)
titanium dioxide (E 171)
lactose monohydrate
Polyethylene Glycol 3350
triacetin
brilliant blue FCF Aluminium Lake (E133
indigo carmine (E 132)
carnauba wax.

6.2 Incompatibilities (Major) None.

6.3 Shelf-life

24 months.

6.4 Special Precautions for Storage

Store below 30 °C in a dry place.

6.5 Nature and Contents of Container

Panadol Night tablets are packaged in either:

- Opaque 250/40µm PVC/PVDC and aluminium foil (30µm) child-resistant blisters
- or Child resistant 250/40µm PVC/PVDC blisters heat sealed to a bilayer of 20µm Aluminium foil/8µm PET

Then packed into outer cardboard cartons, containing 10 or 20 tablets.

Not all pack sizes may be marketed.

6.6 Instructions for Use/Handling

Not applicable

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (UK) Trading Limited
980 Great West Road
Brentford
Middlesex
TW8 9GS
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 44673/0076

9. DATE OF FIRST AUTHORISATION

19 January 1996

10. DATE OF (PARTIAL) REVISION OF THE TEXT

4th June 2020