SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dolvan Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Diphenhydramine Hydrochloride BP 7.50mg Ephedrine Hydrochloride BP 7.50mg
Paracetamol BP 300.00mg
Caffeine BP 30.00mg

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Sugar coated tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oral symptomatic relief in the common cold and influenza and in nasal congestion associated with allergic stimuli.

4.2 Posology

To be taken by mouth
Adults and children over 12 years: One or two tablets three times a day
Elderly: One tablet three times a day
Children under 12 years: Not recommended

4.3 Contraindications

Hypersensitivity to paracetamol and/or any of the active ingredients and porphyria. Contraindicated in persons under treatment with monoamine oxidase inhibitors and within two weeks of stopping such treatment. Known hepatic or renal impairment.

4.4 Special warnings and precautions for use

Dolvan may potentiate the effects of alcohol or other sedatives, use with caution in patients with cardiovascular disorders, prostatic enlargement or bladder dysfunction. Care is advised in the administration of Paracetamol to patients with severe renal or severe hepatic impairment. Patients are advised not to take any other

paracetamol containing products concurrently. If symptoms persist the patient should consult their doctor. Keep out of the reach of children.

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 or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or 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 case of HAGMA in patients with multiple risk factors.

4.5 Interaction with other medicinal products and other forms of interaction

Ephedrine and MAO Inhibitors causes Hypertensive crisis.
Ephedrine and Beta blockers causes Hypertensive crisis (rarely reported).
Ephedrine antagonises Bethanidine and Debrisoquine.
Paracetamol absorption is reduced by Cholestyramine. Paracetamol is potentiated by Metoclopramide and Domperidone.
The anticoagulant effect of Warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding.
Diphenhydramine may potentiate hypnotics and anxiolytics.
Diphenhydramine and betahistine are antagonistic.

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 risk factors (see section 4.4).

4.6 Pregnancy and lactation

Safety in pregnancy has not been established. Epidemiological studies in human pregnancy have shown no effects due to paracetamol in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

Paracetamol is excreted in breast milk but not in a clinically significant amount.

4.7 Effects on ability to drive and use machines

Diphenhydramine may cause drowsiness, if affected do not drive or operate machinery.

4.8 Undesirable effects

Frequency unknown:
Drowsiness may occasionally occur but is less likely with this combination.

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur.
There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causality related to paracetamol.

Metabolism and nutrition disorders:
High anion gap metabolic acidosis: Cases of high anion gap 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 patients.

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

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

Ephedrine Hydrochloride
Symptoms Convulsions, palpitations, hypertension and circulation problems.
Treatment Supportive measures for respiration and circulation and anti-convulsant measures should be given as required. Catheterization of the bladder

as required. Alpha-adrenergic blockade for hypertensive crisis. Beta- adrenergic blockade to control supraventricular dysrhythmias. Elimination of ephedrine may be accelerated by acid diuresis or dialysis.

Diphenhydramine
Symptoms Dizziness, hypotension, incoordination, nausea, diarrhoea, vomiting, dryness of mouth. Difficulty in micturation and convulsions may occur.
Treatment Gastric lavage in the conscious patient (emetics should not be given) and intensive symptomatic supportive therapy where necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N02BE

Diphenhydramine Hydrochloride
Antihistamine. May suppress cough centre (mechanism uncertain). Gives subjective relief of effects of allergic stimuli

Ephedrine Hydrochloride
Has direct and indirect sympathomimetic activity and is an effective upper respiratory tract decongestant.

Paracetamol
Analgesic, Antipyretic

Caffeine
Methylxanthine alkaloid, mild stimulant. Counteracts drowsiness produced by diphenhydramine.

5.2 Pharmacokinetic properties

Diphenhydramine
Histamine H1 receptor antagonist, main site of metabolic transformation is the liver. Oral availability - 50%, plasma bound 80%, half life 4 hours.

Ephedrine
Completely absorbed from the GI tract and peak plasma concentrations reached in about 1 hour. Largely excreted unchanged in the urine. Plasma half life 3 to 6 hours.

Paracetamol
Is readily absorbed from the gastro intestinal tract. Peak plasma levels ½ to 2 hours. Metabolised in the liver and excreted in the urine as glucuronide and sulphate conjugates. Half life 1 to 4 hours. Peak plasma concentration in about 1 hour.

Caffeine
Readily absorbed from the GI tract but absorption may be erratic in individuals. Passes into CNS. Metabolised almost completely and excreted in urine as 1-methyluric acid, 1-methylxanthine and other metabolites with only 1% unchanged.

5.3 Preclinical safety data

None

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextrin, Corn Starch, Polyvinylpyrolidone, Stearic Acid, Magnesium Stearate, Sucrose, Kaolin, Talc, Calcium Carbonate, Sodium Benzoate, Opaseal, Gelatine, Acacia, Beeswax, and colourings E171 and E127.

6.2 Incompatibilities

Diphenhydramine is incompatible with barbiturates and iodo compounds in solution.

6.3 Shelf life

36 months in sealed blisters. Should only be removed from blister immediately prior to use.

6.4 Special precautions for storage

Store below 25°C

6.5 Nature and contents of container

Cartons containing blisters of 20 tablets

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Norma Chemicals Ltd
51-53 Stert Street Abingdon Oxfordshire OX14 3JF United Kingdom, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00386/5006R

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25/07/1990 / 24/01/2005

10 DATE OF REVISION OF THE TEXT

03/03/2025