

# New Zealand Datasheet

## Name of Medicine

### CALM-U Tablets

Salicylamide, diphenhydramine hydrochloride.

## Presentation

Calm-U Tablets are white, round bevel-edged tablets, flat in shape and with a break-line on one side. Each tablet contains diphenhydramine hydrochloride 32mg and salicylamide 250mg.

## Uses

### Actions

Diphenhydramine is an H<sub>1</sub>-receptor antagonist. Histamine H<sub>1</sub>-receptors are responsible for vasodilation, increased capillary permeability, flare and itch reactions in the skin and to some extent for contraction of smooth muscle in the bronchii and gastro-intestinal area. Diphenhydramine hydrochloride diminishes or abolishes the main actions of histamine in the body by competitive, reversible blockade of histamine receptor sites on tissues – it does not inactivate histamine or prevent its synthesis or release.

Salicylamide has some analgesic and antipyretic properties. It acts as an inhibitor of the enzyme cyclo-oxygenase which results in the inhibition of the biosynthesis of prostglandins.

### Pharmacokinetics

Diphenhydramine hydrochloride is well absorbed from the gastro-intestinal tract, though high first pass metabolism appears to affect systemic availability. Peak plasma concentrations are achieved about 1-4 hours after administration by mouth. A mean peak plasma diphenhydramine concentration of 110ng/mL has been reported after administration of 50mg four times daily by mouth. Diphenhydramine is widely distributed throughout the body including the CNS. Diphenhydramine is highly bound to plasma proteins. Metabolism is extensive, and it is excreted mainly in the urine as metabolites – little is excreted as unchanged drug. Excretion is almost complete within 24 hours of administration.

Salicylamide is readily absorbed from the gastro-intestinal tract but is almost completely metabolised to inactive metabolites during absorption and on first pass through the liver. Salicylamide is distributed to most body tissues. It is rapidly excreted in the urine, mainly as the glucuronide and sulphate conjugates.

### Indications

Calm-U Tablets are indicated as a mild sedative and hypnotic to ease anxiety due to excitement, restlessness and nervous exhaustion.

Calm-U tablets ease tension and over-excitement. They help to induce restful sleep and secondary analgesic properties are useful for mild pain.

### Dosage and Administration

One or two tablets may be taken two or three times daily or as directed by a physician.

Night-time dose: 2 or 3 tablets taken with a warm drink 20 minutes before retiring (to induce sleep). Should not be given to children under 12 years of age except on medical advice.

The maximum dose should not be exceeded.

Calm-U tablets are intended for short-term use only.

## **Contraindications**

Calm-U tablets are not suitable for children under 12 years old.

Contraindicated in patients with acute porphyria, or a known sensitivity to diphenhydramine, or salicylamide or other aspirin-like compounds.

## **Warnings and Precautions**

This medicine is intended for short-term use only – prolonged or excessive use can be harmful. The maximum dose should not be exceeded.

A doctor should be consulted if sleeplessness or anxiety persists.

Elderly patients may be more susceptible to the sedative effects of Calm-U Tablets.

Because of antimuscarine properties of Calm-U Tablets, they should be used with care in conditions such as closed-angle glaucoma, urinary retention, prostatic hypertrophy or pyloroduodenal obstruction.

Caution is suggested in patients with epilepsy, severe cardiovascular disorders and asthma. Calm-U Tablets should also be used with caution in patients prone to dyspepsia or known to have a lesion of the gastric mucosa.

Salicylates lower blood-glucose concentrations, and salicylate-induced hypoglycaemia has been reported in adults and children.

## **Use in Pregnancy and Lactation**

Calm-U Tablets should not be used in pregnant or nursing mothers – diphenhydramine crosses the placenta and has been detected in breast milk. Additionally, salicylates readily cross the placenta and have been shown to be teratogenic.

## **Effect on Ability to Drive and Use Machines**

Causes drowsiness – patients should not drive a vehicle or operate machinery within 8 hours of taking this medicine.

## **Adverse Effects**

Due to the content of diphenhydramine, Calm-U tablets adverse effects profile is that common for H<sub>1</sub>-receptor antagonists. These are:-

- Paradoxical CNS stimulation may occur especially in children, with insomnia, irritability, tremors and rarely nightmares, hallucinations and convulsions.
- Antimuscarinic adverse effects including dry mouth, thickened respiratory tract secretions and tightness of the chest, blurred vision, urinary difficulty and retention, a reduction in tonicity and motility of the gastro-intestinal tract resulting in constipation and increased gastric reflux. In high doses,

transient bradycardia followed by tachycardia with palpitations and arrhythmias.

- Gastro-intestinal disturbances such as nausea, vomiting, diarrhoea or epigastric pain
- Rarely, hypotension, tinnitus, headache and paraesthesias
- Blood disorders including agranulocytosis, leucopenia, haemolytic anaemia and thrombocytopenia, though rare, have been reported.

Elderly patients are more susceptible to many adverse effects of antihistamines, including antimuscarinic effects and hypotension.

Additionally, Calm-U Tablets may cause gastro-intestinal disturbances such as nausea, dyspepsia and vomiting. Irritation of the gastrointestinal mucosa with erosion, ulceration, haematemesis and melaena may occur.

Salicylamide may cause hepatotoxicity, particularly in patients with juvenile arthritis and other connective tissue disorders.

## **Interactions**

Calm-U Tablets may enhance the sedative effects of central nervous system depressants including alcohol, barbituates, hypnotics, opioid analgesics, anxiolytic sedatives and neuroleptics. MAOI's may enhance the antimuscarinic effects, and the antimuscarinic effects are additive with drugs such as atropine and tricyclic antidepressants.

It has been suggested that antihistamines could mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics.

Antihistamines may suppress positive skin test results and should be stopped several days before the test.

Since diphenhydramine inhibits the cytochrome P-450 enzyme system, Calm-U Tablets may interfere with debrisoquine testing for genetic polymorphism.

## **Overdosage**

Symptoms of Overdosage: In cases of overdosage of diphenhydramine hydrochloride, a correlation between plasma concentration and frequency or extent of symptoms has been demonstrated. The most common symptom is impaired consciousness. Additionally, psychosis, seizures, antimuscarinic symptoms such as mydriasis, tachycardia and tachyarrhythmias, and respiratory failure have been observed. Acute delirium with visual and auditory hallucinations have also been reported.

Mild chronic salicylate intoxication usually occurs only after repeated administration of large doses. Symptoms include dizziness, tinnitus, deafness, sweating, nausea and vomiting, headache and mental confusion. Symptoms of more severe intoxication or of acute poisoning following overdosage include hyperventilation, fever, restlessness, ketosis, and respiratory alkalosis and metabolic acidosis. Depression of the central nervous system may lead to coma. Cardiovascular collapse and respiratory failure may also occur. In children, drowsiness and metabolic acidosis commonly occur, and hypoglycaemia may be severe.

Treatment of Overdosage: In severe overdosage the stomach should be emptied by aspiration and lavage. Symptoms should be treated as for salicylates and antihistamines in general.

## **Pharmaceutical Precautions**

Store below 25°C.

Shelf life of the product is 5 years from the date of manufacture.

## **Medicine Classification**

Restricted Medicine.

## **Package Quantities**

Calm-U tablets are supplied in cartons contained 24 strip-packed tablets.

## **Further Information**

### **Excipients**

Microcrystalline cellulose, talc, silicon dioxide, magnesium stearate and calcium phosphate.

### **Name and Address**

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### **Date of Preparation**

26 May 1999