New Zealand Datasheet

1 PRODUCT NAME
DOZILE 25 mg capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Doxylamine Succinate 25 mg Capsules

3 PHARMACEUTICAL FORM
Liquid filled soft gel capsules, purple, containing 25 mg doxylamine succinate.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Temporary use in the relief of insomnia.

4.2 Dose and method of administration
Adults: 1 capsule 30 minutes before retiring, or as directed by a pharmacist or physician. Maximum stated dose should not be exceeded.

Dozile is recommended for occasional use only i.e. for periods of no longer than a week at a time. If sleeplessness persists, consult your doctor.

Note: Dozile is not recommended for children under 12 years of age.

4.3 Contraindications
Hypersensitivity to doxylamine, other ethanolamine derivative antihistamines or to any other ingredient in the product.

4.4 Special warnings and precautions for use
Caution should be used if taken with alcohol. Due to the anticholinergic properties of antihistamines, caution should be used when Dozile is taken concurrently with other medications. (See section 4.5)

Caution should be taken by those with narrow angle or open-angle glaucoma, urinary retention, prostate enlargement, pyloroduodenal obstruction, epilepsy or severe cardiovascular disorders.

Doxylamine may suppress positive skin test results.

Use in Children
Dozile is not recommended for children under 12 years of age. The safety and efficacy of doxylamine as a night time sleep aid in children younger than 12 years of age have not been established. In addition, children may be more prone than adults to experience paradoxical CNS stimulation rather than sedation when antihistamines are used as night time sleep aids.

Use in the Elderly
The elderly may be more sensitive to the effects of the usual adult dose.

4.5 Interaction with other medicines and other forms of interaction
Dozile produces an additive effect when administered with other CNS depressants such as opioid analgesics, neuroleptics, alcohol, hypnotics and psychotherapeutic drugs.

MAOIs may enhance the antimuscarinic effects of doxylamine.

Doxylamine has additive antimuscarinic action with other antimuscarinic drugs such as atropine and tricyclic antidepressants.

Dozile may decrease the emetic response to apomorphine.

Concurrent use of oral contraceptives does not appear to affect the pharmacokinetics of doxylamine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category A

Drugs that have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed. Use of Dozile should be avoided during pregnancy.

Breast feeding

Use of Dozile should be avoided during lactation. First generation antihistamines may inhibit lactation because of their anticholinergic actions. Small amounts of antihistamines are distributed in human breast milk. Use is not recommended in nursing mothers because of the risk of adverse effects, such as unusual excitement or irritability in infants.

Because of the potential for serious adverse reactions to antihistamines in nursing infants, a decision should be made as to whether to discontinue nursing or doxylamine taking into account the importance of the drug to the woman.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Doxylamine causes drowsiness. Patients should not drive or operate machinery if affected.

4.8 Undesirable effects

CNS: CNS depression, stimulation (insomnia, nervousness, euphoria, irritability, tremors, nightmares, hallucinations, convulsions), headache, lack of coordination, dizziness, psychomotor impairment.

Gastrointestinal: Constipation, nausea, vomiting, diarrhoea, increased gastric reflux, epigastric pain.

Respiratory: Thickened respiratory tract secretions.

Local: Dry mouth.

Cardiovascular: Palpitations, arrhythmias.

Ophthalmic: Blurred vision.

Renal: Urinary difficulty or retention.

Other: Hypersensitivity reactions, blood disorders, hypotension, tinnitus and paraesthesia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Overdose produces signs and symptoms of anticholinergic toxicity. Acute overdose may cause various reactions including dry mouth, fixed and dilated pupils, flushing, gastrointestinal symptoms, insomnia, nervousness, euphoria, irritability, tremors, nightmares, hallucinations, CNS depression or stimulation, impaired consciousness, seizures, tachycardia, mydriasis and a psychosis similar to that in catatonic stupor. Rhabdomyolysis with impairment of renal function and acute renal failure has been observed. However, in one series of cases of overdose, 39% of patients studied had no symptoms. Stimulation is particularly likely in children.

Fatalities have been reported from doxylamine overdose. These have been characterized by coma, grand mal seizures and cardiorespiratory arrest. Children appear to be at a high risk for cardiorespiratory arrest. A toxic dose for children of more than 1.8 mg/kg has been reported. A 3 year old child died 18 hours after ingesting 1,000 mg doxylamine succinate. There is no correlation between the amount of doxylamine ingested, the doxylamine plasma level and clinical symptomatology.

Treatment

As overdosage may produce potentially fatal cardiovascular or CNS reactions, patients should be monitored for any abnormalities of vital signs. Adequacy of ventilation and blood pressure should be assessed and full supportive care, including oxygen and assisted ventilation, be provided if required. The patient should be observed for evidence of rhabdomyolysis. Laboratory tests on admission should include a determination of creatine kinase. If this is elevated, a test for myoglobin in the urine should be done and, if present, is a contraindication to acid diuresis. Adequate fluid replacement must be provided and good urine output maintained.

Most patients recover with symptomatic and supportive care. Gastric lavage should be considered if it can be performed soon after ingestion, generally within 60 minutes. Another method of preventing absorption is charcoal administration, which again is most effective when administered within 60 minutes of ingestion. Whole bowel irrigation with polyethylene glycol electrolyte lavage solution may be considered in patients with extremely large ingestions.

Haemodialysis, haemofiltration and peritoneal dialysis have not been studied in the treatment of doxylamine overdose but are unlikely to be effective in view of the high volume of distribution. The efficacy of forced diuresis has not been established.

In case of accidental overdosage, symptomatic treatments and supportive care are suggested. For information on the management of overdose, contact the National Poisons Centre on 0800 764 766.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Systemic antihistamines- aminoalkyl ethers, ATC code: R06AA59.

Doxylamine succinate is a white or creamy white powder with a characteristic odour and has solubilities of approximately 1 g/mL in water and 500 mg/mL in alcohol at 25°C. It has a pKa of 5.8 and 9.3. A 1% aqueous solution has a pH of 4.8 - 5.2.

Doxylamine succinate is an ethanolamine derivative antihistamine. Because of its sedative effect, it is used for the temporary relief of sleeplessness. The drug is also used in combination with antitussives and decongestants for the temporary relief of cold and cough symptoms. It is not structurally related to the cyclic antidepressants.

It is an antihistamine with hypnotic, anticholinergic, antimuscarinic and local anaesthetic effects.

Duration of action is 6-8 hours.

5.2 Pharmacokinetic properties

Following oral administration of a single 25 mg dose of doxylamine succinate in healthy adults, mean peak plasma concentrations of about 100 ng/mL occur within 2-3 hours after administration. The drug has an elimination half-life of about 10 hours in healthy adults.

Absorption
It is easily absorbed from the gastrointestinal tract. Following an oral dose of 25 mg the mean peak plasma level is 99 ng/mL 2.4 hours after ingestion. This level declines to 28 ng/mL at 24 hours and 10 ng/mL at 36 hours.

Distribution
The apparent volume of distribution is 2.5 L/kg.

Metabolism
The major metabolic pathways are N-demethylation, N-oxidation, hydroxylation, N-acetylation, N-desalkylation and ether cleavage.

Elimination
The elimination half life is 10.1 hours. Oral plasma clearance is 217 mL/min the drug is excreted in the urine as unchanged doxylamine (60%), nordoxylamine and dinordoxylamine.

5.3 Preclinical safety data

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The capsules also contain the following inactive ingredients: butylated hydroxyanisole, propylene glycol, macrogol 400, gelatin, amaranth, patent blue V, sorbitol special - glycerin blend, and purified water.

6.2 Incompatibilities

None are known.

6.3 Shelf life

2 years (24 months).

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container
Dozile is available in a blister pack of 10 capsules.

7 MEDICINE SCHEDULE
Pharmacist-only-medicine.

8 SPONSOR
Wilson Consumer Products
AUCKLAND
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9 DATE OF FIRST APPROVAL
27 March 1997

10 DATE OF REVISION OF THE TEXT
13 May 2019

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Update to SPC format
4.8	Reporting of adverse events added
4.9	Poison centre details added