AUSTRALIAN PRODUCT INFORMATION-RESTAVIT (DOXYLAMINE SUCCINATE)

1.NAME OF THE MEDICINE

Doxylamine succinate

2.QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 25mg doxylamine succinate.

For the full list of excipients, see Section 6.1 List of excipients

3. PHARMACEUTICAL FORM

White uncoated biconvex tablets with a break bar on one side.

4.CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Temporary relief of insomnia

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults: One or two tablets twenty minutes before bed. Swallow tablets with a glass of water.
Restavit should not be used for more than a few days at a time as insomnia may be symptomatic of a serious underlying medical condition.

Children: Do not give to children under 12 years of age

Impaired hepatic and renal function: Dosage reduction may be necessary.

4.3 CONTRAINDICATIONS

Patients with hypersensitivity to doxylamine, other antihistamines in the ethanolamine class, lactose or any other component should not use this product.
Doxylamine should not be given to premature or newborn infants due to their heightened susceptibility to antimuscarinic effects.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Avoid concurrent use with alcohol and medications which suppress the CNS as the effects of both may be enhanced.
A risk-benefit approach should be adopted for patients with glaucoma. Increased ocular pressure could precipitate an attack of angle closure glaucoma. Use with caution in patients with asthma, bladder neck obstruction, urinary retention, chronic

bronchitis, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy and epilepsy.

Use in hepatic impairment
Use with caution.

Use in renal impairment
Use with caution.

Use in the elderly
Use with caution as studies indicate a longer duration of action especially for elderly men. This and enhanced susceptibility to antimuscarinic side effects suggest dosage reduction may be necessary.

Paediatric Use
Do not give to children under 12 years of age due to heightened sensitivity towards paradoxical stimulation.

Effects on Laboratory Tests
Antihistamines may inhibit the cutaneous histamine response. Discontinue at least 72 hours before skin testing begins

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Doxylamine has additive antimuscarinic effects with atropine like drugs, tricyclic antidepressants and MAOIs. Concurrent use with other drugs and substances which suppress the CNS should be avoided. These include alcohol, sedatives (such as benzodiazepines and barbiturates), tranquillizers (e.g., antipsychotics) and opioid analgesics. Use with ototoxic medications e.g., aminoglycoside antibiotics may mask the symptoms of ototoxicity such as tinnitus, dizziness or vertigo.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No data available

Use in pregnancy
Category A
Doxylamine Succinate has 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 foetus having been observed**.**

Use in lactation
Medical or pharmacist advice is required before use in breastfeeding**.** Doxylamine may be excreted into breast milk in small amounts and cause unusual excitement or irritability in infants. Anticholinergic effects may inhibit lactation.[2]

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Drowsiness and hang-over affects may affect ability to drive or operate machinery the day following use.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

More common reactions: Drowsiness**,** dizziness, lassitude, disturbed coordination, headache, psychomotor impairment and muscular weakness. Antimuscarinic effects include dry mouth, nose and throat and thickened respiratory tract secretions.

Less Common Reactions: Paradoxical stimulation of the CNS with the possibility of insomnia, unusual excitement, tremors, nervousness and restlessness. These effects are more likely to occur in children.

Other adverse reactions include tachycardia, palpitations, hypotension, blurred vision, urinary difficulty or retention, constipation and increased gastric reflux.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at http://www.tga.gov.au/reporting-problems

4.9 OVERDOSE

Symptoms of overdose include severe drowsiness, severe dryness of the mouth, nose and throat, flushing or redness in the face, shortness of breath, tachycardia, CNS stimulation, hallucinations, seizures, insomnia, hypotension, delirium, convulsions and fixed and dilated pupils. Coma progressing to respiratory failure and cardiovascular collapse may occur. Cardiorespiratory collapse and death may occur several days after onset of toxic symptoms. Children are at higher risk for cardiorespiratory arrest. Rhabdomyolysis and subsequent acute renal failure may also occur in certain individuals(adults).

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia)

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Doxylamine is an H1 receptor antagonist antihistamine belonging to the ethanolamine group. This group characteristically produce pronounced sedative effects with low incidence of gastrointestinal disturbance. The significant sedative properties result from inhibition of histamine N-methyltransferase and blockage of central histaminergic receptors. Antagonism of other CNS receptor sites such as those for

serotonin, acetyl choline and alpha-adrenergic stimulation may be involved. Anticholinergic activity at muscarinic receptors also occurs.

Clinical Trials
No data available

5.2 PHARMACOKINETIC PROPERTIES

Absorption: The drug is well absorbed from the gastrointestinal tract. Following oral administration of a 25mg dose therapeutic effects start within 15 to 30 minutes and are fully developed within one hour. Peak plasma concentration of 100ng/ml[7]occurs between 2 and 4 hours. The duration of action is 6-8 hours. After 24 hours, the mean plasma level is 21ng/ml.
Distribution: The drug is well absorbed from the gastrointestinal tract and is widely distributed throughout the body.
Metabolism: Metabolism occurs in the liver. The major metabolic pathway is N-demethylation to N-desmethyldoxylamine and N, N-didesmethyldoxylamine. N-acetyl conjugates of these metabolites have been identified. The activity of these metabolites is unknown. N-glucuronidation has been identified as a minor metabolic route. Additional metabolic pathways found in animal studies include N-oxidation, aromatic hydroxylation and ether cleavage.
Excretion: The elimination half- life has been reported at 10.1and 12 hours. It is prolonged in geriatric males at 15.5± 2.1 hours.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity
Doxylamine succinate is considered not to be genotoxic

Carcinogenicity
There is inadequate evidence in humans for the carcinogenicity of doxylamine succinate. There is limited evidence in experimental animals for the carcinogenicity of doxylamine succinate

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Lactose, maize starch, microcrystalline cellulose, magnesium stearate

6.2 INCOMPATIBILITIES

Incompatibilities were not assessed as part of the registration of the medicine

6.3 SHELF LIFE

Three years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C in a dry place

6.5 NATURE AND CONTENTS OF CONTAINER

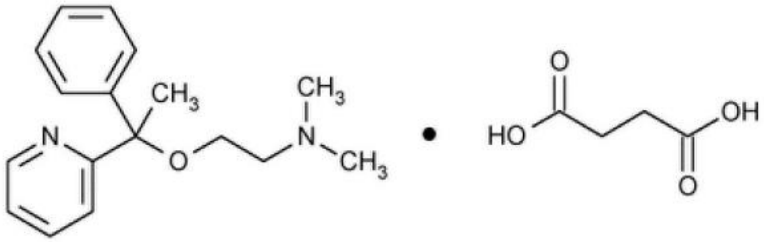
Cartons containing 20 tablets in two PVC/PVDC blister platforms of 10 tablets

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy

6.7 PHYSIOCOCHEMICAL PROPERTIES

Chemical Structure



2-[(alpha)-(2-dimethylaminoethoxy) (alpha)-methylbenzyl] pyridine succinate

Doxylamine succinate is a white or almost white powder, very soluble in water and freely soluble in alcohol.

Chemical Formula:
$C_{17}H_{22}N_2OC_4H_6O_4$

Molecular Weight:
388.5

CAS Number
562-10-7

7.MEDICINES SCHEDULE (POISONS STANDARD)

Schedule 3 (S3)

8.SPONSOR

H.W. Woods Pty. Ltd
8 Clifford Street Huntingdale
Victoria 3166.
03 9544 6466
Email: info@hwwoods.com.au

9. DATE OF FIRST APPROVAL:

20 March 2003

10. DATE OF REVISION

5 October 2023Summary table of changes

Date	Section changed	Summary of new information
19 July 2019	4.2 Dose and method of administration	Updated information on duration of use
19 July 2019	4.6 Fertility, Pregnancy and Lactation	Updated information on use in pregnancy and lactation
19 July 2019	5.2 Pharmacokinetic Properties-Metabolism	Amended information on metabolism
19 July 2019	5.3 Preclinical safety data	Amended information on genotoxicity and carcinogenicity
5 October 2023	4.6 Fertility, Pregnancy and Lactation	Removal of advice on use in pregnancy