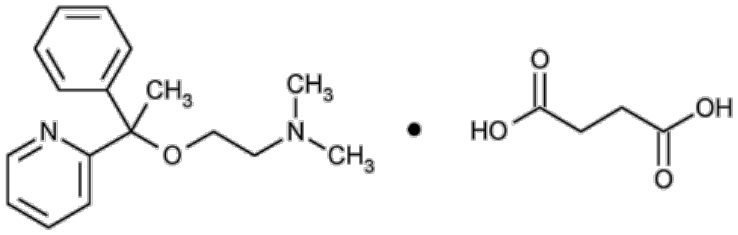
TONIGHT TABLETS

NAME OF THE MEDICINE

Doxylamine Succinate

Chemical name: 2-[(alpha}- 2-diethylaminethocy) (alpha)- methylbenzyl]pyridine succinate.

Structural Formula:



Molecular formula: C17H22N2O.C4H6O4

MW: 388.5

CAS: 562-10-7

DESCRIPTION

TONIGHT Tablets contain 25mg doxylamine succinate as the active ingredient.

PHARMACOLOGY

Doxylamine succinate is an H_1-receptor antagonist antihistamine belonging to the ethanolamine group. This group characteristically produces 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.

PHARMACOKINETICS

Absorption:

Following oral administration of a 25mg dose therapeutic effects start within 15 to 30 minutes and are fully developed within one hour, Peak plasma concentrations of 100 nanogram/mL occurs between two and four hours. The duration of action is six to eight hours. After 24 hours the mean plasma level is 21 nanogram/mL.

Distribution:

The drug is well absorbed from the gastrointestinal tract and it's distributed widely throughout the body.

Metabolism:

Metabolism occurs in the liver by microsomal oxidation. 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. More detailed pharmacokinetic studies have not been performed.

Elimination:

The elimination half-life has been reported at 10.1 and 12 hours. It is prolonged in geriatric males at 15.5 +/- 2.1 hours.

CLINICAL TRAILS

Not applicable

INDICATIONS

TONIGHT tablets is indicated as an aid to the relief of temporary sleep disturbance.

CONTRAINDICATIONS

Hypersensitivity to doxylamine, other antihistamines in the ethanolamine class, or any of the excipients listed.

Doxylamine should not to be given to premature or newborn infants due to their heightened susceptibility to antimuscarinic effects.

PRECAUTIONS

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 in caution in patients with asthma, bladder neck obstruction, urinary retention, chronic bronchitis, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy and epilepsy.

Use in pregnancy (Category A)

Do not use during pregnancy.

Use in lactation

Do not use if breastfeeding. Doxylamine may be excreted into breast milk in small amounts and cause unusual excitement or irritability in infants. Anticholinergic effects may inhibit lactation.

Paediatric Use

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

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.

Carcinogenesis, mutagenesis, impairment of fertility

Long-term animal studies to evaluate the carcinogenic and mutagenic potential have not been performed.

Effect on laboratory tests

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

Impaired renal function

Use with caution. Dosage reduction may be necessary.

Impaired hepatic function

Use in caution. Dosage reduction may be necessary.

Effects on ability to drive or operate machinery

Drowsiness and hangover effects may affect ability to drive or operate machinery the day following use.

INTERACTIONS WITH OTHER MEDICINES

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.

ADVERSE 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 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

DOSAGE AND ADMINISTRATION

Adults

half a tablet to one tablet about half an hour before bedtime.
TONIGHT tablets should not be used for more than ten days consecutively.

Children

Do not give to children under 12 years of age.

OVERDOSAGE

Symptoms

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).

LIST OF EXCIPIENTS

Microcrystalline Cellulose, Dibasic Calcium Phosphate Dihydrate, Sodium Starch Glycolate, Magnesium Stearate.

PRESENTATION AND STORAGE CONDITIONS

TONIGHT tablets are oval cream-white tablet, with a score line on one side.

Storage

Store below 25^{o}C

HOLDER AND MANUFACTURER

CTS CHEMICAL INDUSTRIES LTD

POB 385, KIRYAT-MALACHI, ISRAEL

This leaflet format has been determined by the Ministry of Health and the content has been updated in 11/2020.