ZADA PHARMACEUTICALS

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

RHINOZAD 2,5 mg + 60 mg tablets

triprolidine, pseudoephedrine

2. Qualitative and quantitative composition

Each tablet contains:-

Triprolidine hydrochloride 2.5 mg

Pseudoephedrine hydrochloride 60.0 mg

3. Pharmaceutical form

Tablets for oral administration.

4. Clinical particulars

4.1 Therapeutic indications

For the symptomatic relief of upper respiratory tract disorders which are benefited by a combination of a nasal decongestant and histamine H1-receptor antagonist, for example:

Allergic Rhinitis

Vasomotor Rhinitis

The Common Cold and Influenza

4.2 Posology and method of administration

Adults and children over 12 years

One tablet every 4-6 hours up to 4 times a day

Use in the Elderly

No specific studies have been carried out in the elderly, but triprolidine and pseudoephedrine have been widely used in older people.

Hepatic Impairment

Caution should be exercised when administering RHINOZAD Tablets to patients with severe hepatic impairment.

Renal Impairment

Caution should be exercised when administering RHINOZAD Tablets to patients with moderate to severe renal impairment.

4.3 Contraindications

RHINOZAD is contraindicated in individuals who have previously exhibited intolerance to it or to pseudoephedrine or triprolidine.

RHINOZAD is contraindicated in patients who are taking or have taken monoamine oxidase inhibitors within the preceding two weeks. The concomitant use of pseudoephedrine and this type of product may occasionally cause a rise in blood pressure.

RHINOZAD is contraindicated in patients with severe hypertension or severe coronary artery disease.

The antibacterial agent furazolidone, is known to cause a dose-related inhibition of monoamine oxidase. Although there are no reports of hypertensive crises caused by the concurrent administration of RHINOZAD Tablets and furazolidone they should not be taken together.

4.4 Special warnings and precautions for use

RHINOZAD Tablets may cause drowsiness and impair performance in tests of auditory vigilance. Patients should not drive or operate machinery until they have determined their own response.

Although there are no objective data, users of RHINOZAD Tablets should avoid the concomitant use of alcohol or other centrally acting sedatives.

Although pseudoephedrine has virtually no pressor effect in normotensive patients, RHINOZAD Tablets should be used with caution in patients taking anti-hypertensive agents, tricyclic antidepressants or other sympathomimetic agents, such as decongestants, appetite suppressants and amfetamine-like psychostimulants. The effects of a single dose of RHINOZAD Tablets on the blood pressure of these patients should be observed before recommending repeated or unsupervised treatment.

As with other sympathomimetic agents RHINOZAD Tablets should be used with caution in patients with hypertension, heart disease, diabetes, hyperthyroidism, elevated intraocular pressure and prostatic enlargement.

There have been no specific studies of RHINOZAD Tablets in patients with hepatic and/or renal dysfunction. Caution should be exercised in the presence of severe renal or hepatic impairment.

There is insufficient information available to determine whether triprolidine or pseudoephedrine have mutagenic or carcinogenic potential.

Systemic administration of pseudoephedrine in rats, up to 7 times the human daily dosage in females and 35 times the human daily dosage in males, did not impair fertility nor alter foetal morphological development and survival.

No studies have been conducted in animals to determine if triprolidine has the potential to impair fertility.

There is no information on the effects of RHINOZAD on human fertility.

As with all medicines if you are pregnant, or currently taking any other medicine, consult your doctor or pharmacist before taking this product.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of RHINOZAD Tablets with sympathomimetic agents, such as decongestants, tricyclic antidepressants, appetite suppressants and amfetamine-like psychostimulants, or with monoamine oxidase inhibitors which interfere with the catabolism of sympathomimetic amines, may occasionally cause a rise in blood pressure.

Because of its pseudoephedrine content, RHINOZAD may partially reverse the hypotensive action of drugs which interfere with sympathetic activity including bretylium, betanidine, guanethidine, debrisoquine, methyldopa, alpha-and beta-adrenergic blocking agents.

4.6 Pregnancy and lactation

Although pseudoephedrine, and triprolidine have been in widespread use for many years without apparent ill consequence, there are no specific data on their use during pregnancy. Caution should therefore be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus.

Systemic administration of triprolidine in rats and rabbits up to 75 times the human dose did not produce teratogenic effects.

Systemic administration of pseudoephedrine, up to 50 times the human daily dosage in rats and up to 35 times the human daily dosage in rabbits, did not produce teratogenic effects.

Pseudoephedrine and triprolidine are excreted in breast-milk in small amounts but the effect of this on breast-fed infants is not known. It has been estimated that approximately 0.5 to 0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in the breast-milk over 24 hours.

4.7 Effects on ability to drive and use machines

RHINOZAD may cause drowsiness and impair performance in tests of auditory vigilance. Patients should not drive or operate machinery until they have determined their own response.

4.8 Undesirable effects

Central nervous system depression or excitation may occur, drowsiness being reported most frequently. Sleep disturbance and, rarely, hallucinations have been reported.

Skin rashes, with or without irritation, tachycardia, dryness of mouth, nose and throat, have occasionally been reported.

Urinary retention has been reported occasionally in men receiving pseudoephedrine; prostatic enlargement could have been an important predisposing factor.

4.9 Overdose

The effects of acute toxicity from RHINOZAD may include drowsiness, lethargy, dizziness, ataxia, weakness, hypotonicity, respiratory depression, dryness of the skin and mucous membranes, tachycardia, hypertension, hyperpyrexia, hyperactivity, irritability, convulsions, and difficulty with micturition.

Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed up to 3 hours after ingestion if indicated. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Triprolidine provides symptomatic relief in conditions believed to depend wholly or partly upon the triggered release of histamine. It is a potent competitive histamine H1-receptor antagonist of the pyrrolidine class with mild central nervous system depressant properties which may cause drowsiness. Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.

After oral administration of a single dose of 2.5mg triprolidine to adults the onset of action, as determined by the ability to antagonise histamine-induced weals and flares in the skin, is within 1 to 2 hours. Peak effects occur at about 3 hours and, although activity declines thereafter, significant inhibition of histamine-induced weals and flares still occurs 8 hours after the dose. Pseudoephedrine produces its decongestant effect within 30 minutes, persisting for at least 4 hours.

5.2 Pharmacokinetic properties

After the administration of one RHINOZAD Tablet (containing 2.5 mg triprolidine hydrochloride and 60 mg pseudoephedrine hydrochloride) in healthy adult volunteers, the peak plasma concentration (Cmax) of triprolidine is approximately 5.5 ng/ml - 6.0 ng/nl, occurring at about 2.0 hours (Tmax) after drug administration. The plasma half life of triprolidine is approximately 3.2 hours. The Cmax of pseudoephedrine is approximately 180 ng/ml with Tmax approximately 2.0 hours after drug administration. The plasma half life of pseudoephedrine is approximately 5.5 hours (urine pH maintained between 5.0-7.0). The plasma half life of pseudoephedrine is markedly decreased by acidification of urine and increased by alkalinisation.

5.3 Preclinical safety data

There is insufficient information available to determine whether Triprolidine pseudoephedrine have mutagenic or carcinogenic potential.

Systematic administration of pseudoephedrine in rats, up to 7 times the human daily dosage in females and 35 times the human daily dosage in males, did not impair fertility nor alter foetal morphological development and survival.

No studies have been conducted in animal to determine if Triprolidine has the potential to impair fertility.

Systemic administration of Triprolidine in rats and rabbits up to 75 times the human dose did not produce teratogenic effects.

Systemic administration of pseudoephedrine, up to 50 times the human daily dosage in rats and up to 35 times the human daily dosage in rabbits, did not produce teratogenic effects.

6. Pharmaceutical particulars

6.1 List of excipients:

Lactose monohydrate, pregelatinised maize starch, povidone and magnesium stearate.

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C.

Store in the original package to protect from light and moisture.

Keep the product out of the reach and sight of children.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6.5 Nature and contents of container

Box of 1000 (100 x 10) tablets, each containing 2,5 mg of triprolidine and 60 mg of pseudoephedrine, in a blister packs.

6.6 Special precautions for disposal and other handling

None.

7. Marketing authorisation holder and manufacturer

ZADA Pharmaceuticals Ltd.

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75 300 Lukavac, Bosnia and Herzegovina