Professional Information for ZYACTIN

SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE

ZYACTIN 4 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 4 mg cyproheptadine (as hydrochloride).

Excipients with known effect:

Contains sugar (40 mg lactose monohydrate per tablet).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

White to off-white, round, flat faced, bevelled edge tablets, bisected on one side and debossed with "11 10" on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZYACTIN is used in the symptomatic treatment of seasonal and perennial rhinitis.

ZYACTIN is also indicated for the symptomatic relief of pruritis.

4.2 Posology and method of administration

For seasonal and perennial allergic rhinitis and pruritis.

Posology:

Adults:

The therapeutic range is from 4 mg to 20 mg per day. The majority of patients require 12 mg to 16 mg a day. It is suggested that the dosage be initiated with 4 mg (1 tablet) three times a day and adjusted according to the weight and response of the patient.

Children (7 to 14 years):

The usual dosage is 4 mg (1 tablet) 2 or 3 times a day. The dosage may be adjusted according to the weight and response of the child. Should an additional dose be required, it should preferably be taken at bedtime. The dosage must not exceed 16 mg per day.

Children (2 to 6 years):

The suggested dosage is 2 mg (½ tablet) 2 or 3 times a day. The dosage may be adjusted according to the weight and response of the child. Should an additional dose be required, it should preferably be taken at bedtime. The daily dosage should not exceed 8 mg.

4.3 Contraindications

- Hypersensitivity to cyproheptadine or to any of the excipients (see section 6.1).
- In patients with closed angle glaucoma.
- In patients with bladder neck obstruction.
- In patients with symptomatic prostatic hypertrophy.
- In patients on monoamine oxidase inhibitor (MAOI) therapy.
- In patients with stenosing peptic ulcer.
- In pyloroduodenal obstruction.
- In the elderly or debilitated patient.

Paediatric use:

Safety and efficacy in children below the age of two years have not been established.

Acute asthmatic attack:

ZYACTIN should not be used for the treatment of an acute asthmatic attack.

Nursing mothers:

Because of the higher risk of antihistamines for infants generally, and for newborns and babies born prematurely in particular, ZYACTIN is contraindicated in nursing mothers.

4.4 Special warnings and precautions for use

Dizziness, sedation and hypotension is more likely to occur in elderly patients.

Prolonged therapy with ZYACTIN may cause blood dyscrasias. Due to the atropine-like action of ZYACTIN, it should be used with caution in patients with a history of bronchial asthma, hyperthyroidism, increased intra-ocular pressure, cardiovascular disease and hypertension.

Lactose monohydrate:

ZYACTIN contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take ZYACTIN.

4.5 Interaction with other medicines and other forms of interaction

Monoamine oxidase inhibitors (MAOIs):

MAOIs may prolong and intensify the anticholinergic effects of ZYACTIN.

Central nervous system (CNS) depressants:

Cyproheptadine may have additive effects when combined with alcohol and other CNS depressants, e.g. hypnotics, sedatives, tranquillisers and anxiolytic medicines.

Antidepressants:

Medicines with anti-serotonin activity, such as ZYACTIN, may interfere with serotonin-enhancing antidepressant medicines.

Drug screening:

ZYACTIN may cause a false positive test result for tricyclic antidepressant medicines when evaluating a drug screen (e.g. urine, serum).

4.6 Fertility, pregnancy and lactation

Safety in pregnancy has not been established.

4.7 Effects on ability to drive and use machines

ZYACTIN may lead to drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of other CNS depressant medicines or alcohol. Hence patients should not operate hazardous machinery or drive motor vehicles while on ZYACTIN.

4.8 Undesirable effects

Summary of the safety profile:

The side effects that present frequently are drowsiness and somnolence. Many patients who complain initially of drowsiness may no longer do so after the first three of four days of continuous administration.

Adverse reactions which have been reported with the use of cyproheptadine are as follows:

Blood and lymphatic system disorders:

Less frequent: haemolytic anaemia, agranulocytosis, leucopenia, thrombocytopenia

Metabolism and nutrition disorders:

Less frequent: increased appetite / weight gain

Psychiatric disorders:

Frequency unknown: diminished mental alertness, excitability (especially in young children), confusion, hallucinations, restlessness, insomnia, irritability, nervousness, excitation, aggressive behaviour, euphoria

Nervous system disorders:

Frequent: drowsiness and somnolence (the drowsiness effect may subside after the first three or four days of continuous administration)

Less frequent: sedation, disturbed coordination, dizziness, confusion, restlessness, excitation, nervousness, irritability, aggressive behaviour, tremor, paraesthesia, insomnia, convulsions, euphoria, hallucinations, faintness, hysteria, neuritis, vertigo, headache

Eye disorders:

Less frequent: blurred vision, diplopia

Ear and labyrinth disorders:

Less frequent: tinnitus, acute labyrinthitis

Cardiac disorders:

Less frequent: tachycardia, palpitations, extrasystoles

Vascular disorders:

Less frequent: hypotension, anaphylactic shock

Respiratory, thoracic and mediastinal disorders:

Less frequent: thickening of bronchial secretions, dryness of nose and throat, tightness of chest and wheezing, nasal stuffiness, epistaxis

Gastrointestinal disorders:

Less frequent: dryness of the mouth, anorexia, epigastric distress, nausea, vomiting, diarrhoea, constipation

Hepatobiliary disorders:

Less frequent: jaundice, cholestasis, hepatic failure, hepatitis, abnormal hepatic function

Skin and subcutaneous tissue disorders:

Less frequent: allergic manifestations such as a rash and oedema, photosensitivity, excessive perspiration, urticaria

Renal and urinary disorders:

Less frequent: frequency of micturition, difficult micturition, urinary retention

Reproductive system and breast disorders:

Less frequent: early menses

General disorders and administration site conditions:

Less frequent: fatigue, rigors, chills.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of ZYACTIN is important. It allows continued monitoring of the benefit/risk balance of ZYACTIN. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Signs and symptoms of cyproheptadine overdosage may vary from hallucinations and CNS depression or stimulation, to convulsions and death, especially in infants and children. Atropine-like effects (dry mouth, fixed dilated pupils, flushing, etc) as well as gastrointestinal symptoms may occur.

If overdosage occurs, the patient should be monitored, and standard supportive treatment applied as required. If vomiting has not occurred spontaneously, vomiting should be induced if the patient is conscious. Stimulants should not be used. Hypotension may be treated with vasopressors.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 5.7.1 Antihistaminics.

Pharmacotherapeutic group: Antihistamines for systemic use.

ATC code: R06AX02.

Cyproheptadine hydrochloride, a piperidine derivative, is a sedating antihistamine with antimuscarinic, serotonin antagonist and calcium channel blocking actions.

5.2 Pharmacokinetic properties

After a single 4 mg oral dose of ^{14}C-labelled cyproheptadine HCl in normal subjects, given as tablets, 2 – 20 % of the radioactivity was excreted in the stools. Only about 34 % of the stool radioactivity was unchanged medicine, corresponding to less than 5,7 % of the dose.

At least 40 % of the administered radioactivity was excreted in the urine.

The principal metabolite found in human urine has been identified as a quaternary ammonium glucuronide conjugate of cyproheptadine. Elimination is diminished in renal insufficiency.

5.3 Preclinical safety data

No further information of relevance is available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Magnesium stearate (E572)

Microcrystalline cellulose (E460(i))

Sodium starch glycolate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the blister strips in the outer carton until required for use.

6.5 Nature and contents of container

Aluminium/aluminium blister strips of 10 tablets packed in an outer carton containing 30 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Zydus Healthcare SA (Pty) Ltd

Southdowns Office Park

Building B, Ground Floor

22 Karee Street

Centurion, Pretoria

0157

8. REGISTRATION NUMBER

55/5.7.1/0847

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

06 February 2024

10. DATE OF REVISION OF THE TEXT

Not applicable.