SCHEDULING STATUS: **S2**

PROPRIETARY NAMES AND DOSAGE FORMS:

CINDRID 25 (tablets)

CINDRID 75 (capsules)

COMPOSITION:

Each Cindrid 25 tablet contains: 25 mg cinnarizine.

Each Cindrid 75 capsule contains: 75 mg cinnarizine.

The other excipients are:

Each Cindrid 25 tablet:

Aerosil (colloidal silicon dioxide), erythrosine aluminium lake, explotab (sodium starch glycolate), hydroxypropyl methylcellulose 2910 5cPs, indigo carmine aluminium lake (FD&C blue No 2), lactose 200 mesh, magnesium stearate, maize starch, polyethylene glycol 400, purified talc, starch 1500, sucrose, sunset yellow FCF aluminium lake (FD&C yellow No 6), titanium dioxide.

Each CINDRID 75 capsule:

Erythrosin (CI 45430), explotab (sodium starch glycolate), gelatine, lactose DC, magnesium stearate, maize starch, sunset yellow FCF (CI 15985), talc, titanium dioxide (CI 77891), yellow iron oxide (CI 77492).

Each Cindrid 25 tablet contains sugar (lactose 81,00 mg and sucrose 19,00 mg).

Each Cindrid 75 capsule contains sugar (lactose 125,00 mg).

PHARMACOLOGICAL CLASSIFICATION:

A 5.7.2 Anti-emetics and antivertigo preparation

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Cinnarizine has been shown to be a non-competitive antagonist of the smooth muscle contractions caused by various vasoactive agents including histamine.

Cinnarizine also acts on vascular smooth muscle by selectively inhibiting the calcium influx into depolarised cells, thereby reducing the availability of free Ca^{2+} ions for the induction and maintenance of contraction.

Vestibular eye reflexes induced by caloric stimulation of the labyrinth in guinea pigs are markedly depressed by cinnarizine.

Cinnarizine has been shown to inhibit nystagmus.

Pharmacokinetic properties:

***Absorption*:**

In man, after oral administration, absorption is relatively slow, peak serum concentrations occurring after 2,5 to 4 hours.

Distribution:

The plasma protein binding of cinnarizine is 91 %.

Biotransformation:

Cinnarizine is extensively metabolised mainly via CYP2D6, but there is considerable interindividual variation in the extent of metabolism.

Elimination:

The reported elimination half-life for cinnarizine ranges from 4 to 24 hours.

The elimination of metabolites occurs as follows: one third in the urine (unchanged as metabolites and glucuronide conjugates) and two-thirds in the faeces.

INDICATIONS:

Symptomatic treatment of nausea and vertigo due to Ménière's disease and other labyrinth disturbances.

Prevention and treatment of motion sickness.

CONTRAINDICATIONS:

- CINDRID should not be administered to patients who are hypersensitive to cinnarizine or any of the other ingredients of tablets or capsules (see "COMPOSITION").
- Porphyria.
- Parkinson's disease.
- Safety in pregnancy and lactation has not been established.

WARNINGS AND SPECIAL PRECAUTIONS:

As with other antihistamines, CINDRID may cause epigastric discomfort, taking it after meals may diminish gastric irritation.

Elderly patients are more susceptible to adverse effects of antihistamines, like CINDRID, including antimuscarinic effects, sedation and hypotension.

In patients with Parkinson's disease, CINDRID should only be given if the advantages outweigh the possible risk of aggravating this disease.

Use of CINDRID should be avoided in porphyria.

There have been no specific studies in hepatic or renal dysfunction. CINDRID should be used with caution in patients with hepatic or renal insufficiency.

CINDRID may cause somnolence, especially at the start of treatment. Therefore, caution should be taken when alcohol, central nervous system (CNS) depressants or tricyclic antidepressants are used concomitantly.

Diagnostic interference:

Because of its antihistamine effect, CINDRID may prevent an otherwise positive reaction to dermal reactivity indicators if used within 4 days prior to testing.

Lactose intolerance:

CINDRID contains lactose/fructose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take CINDRID.

CINDRID contains sucrose. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take CINDRID.

CINDRID contains lactose and sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Effects on ability to drive and use machines:

CINDRID may cause drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants especially at the start or treatment. Patients affected in this way should not drive or operate machinery.

INTERACTIONS:

Concurrent use of alcohol, or other central nervous system depressants (including alcohol, barbitones, hypnotics, opioid analgesics, anxiolytics, sedatives and neuroleptics) or tricyclic antidepressants may potentiate the sedative effects of either of these medicines or of CINDRID.

It has been suggested that antihistamines could mask the warning signs of damage caused by ototoxic medicines such as aminoglycoside antibiotics. CINDRID may suppress positive skin test results and should be stopped several days before the test.

Because of its antihistamine effect, CINDRID may prevent an otherwise positive reaction to dermal reactivity indicators if used within 4 days prior to testing.

Monoamine oxidase inhibitors may enhance the anti-muscarinic effects of antihistamines. The side effects of anticholinergic substances such as atropine and tricyclic antidepressants may be enhanced by the concomitant administration of antihistamines.

PREGNANCY AND LACTATION:

Pregnancy:

The safety of CINDRID in human pregnancy has not been established (see “CONTRAINDICATIONS”).

Lactation:

Use of CINDRID is not recommended in nursing mothers (see “CONTRAINDICATIONS”).

DOSAGE AND DIRECTIONS FOR USE:

The initial adult dosage is 1 tablet three times a day, which may be increased to 3 tablets or 1 capsule three times a day.

For the prevention of motion sickness, 1 tablet is administered 1 hour prior to departure followed by 1 tablet every six to eight hours.

SIDE EFFECTS:

Nervous system disorders:

Frequent: Somnolence.

Less frequent: Lethargy.

Frequency not known: Dyskinesia, extrapyramidal disorders, parkinsonism, tremors.

Gastrointestinal disorders:

Frequent: Nausea, dyspepsia.

Less frequent: Vomiting, upper abdominal pain.

Hepatobiliary disorders:

Frequency not known: Cholestatic jaundice.

Skin and subcutaneous tissue disorders:

Less frequent: Hyperhidrosis, lichenoid keratosis including lichen planus.

Frequency not known: Subacute cutaneous lupus erythematosus.

Musculoskeletal and connective tissue disorders:

Frequency not known: Muscle rigidity.

General Disorders and administration site conditions:

Less frequent: Fatigue, headache, dry mouth.

Metabolism and nutrition disorders:

***Frequent*:** Increased weight.

Immune system disorders:

Cases of hypersensitivity reactions.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms:

Overdosage may be fatal especially in infants and children in whom the main symptoms are central nervous system stimulation and anti-muscarinic effects including ataxia, excitement, hallucinations, muscle tremor, convulsions, dilated pupils, dry mouth, flushed face and hyperpyrexia. Deepening coma, cardiorespiratory collapse and death may follow.

In adults, the usual symptoms are central nervous system depression with drowsiness, coma and convulsions, progressing to respiratory failure and possibly cardiovascular collapse.

Treatment:

There is no specific antidote. The treatment is symptomatic and supportive.

Activated charcoal should only be considered in patients presenting within one hour of taking a potentially toxic overdose (i.e. more than 15 mg/kg).

IDENTIFICATION:

Cindrid 25: Round, flat, pale orange to pink, slightly mottled tablet with bevel-edges tablet and a score on one side.

Cindrid 75: Opaque yellow body/orange cap, size 2 capsule containing white powder.

PRESENTATION:

Cindrid 25: Amber glass bottles and securitainers of 100, 250 or 500 tablets and blister strips tristar foil for multiple-unit packs and aluminium laminated foil of 10, 100, 250 or 500 tablets.

Cindrid 75: Securitainers of 30 and 100 capsules and amber glass bottles of 10 capsules in 50 mℓ bottles and 100 capsules in 100 mℓ bottles.

Blister strips: PVC, Tristar foil and aluminium laminated foil of 30, 60,100, 500.

Not all pack sizes may be marketed.

STORAGE INSTRUCTIONS:

Store at or below 25 °C. Protect from light.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBERS:

Cindrid 25: U/5.7.2/8

Cindrid 75: U/5.7.2/9

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:

Sandoz SA (Pty) Ltd[1]

Waterfall 5-Ir

Magwa Crescent West

Waterfall City

Jukskei View

2090

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:

Date of registration: 08 March 1988

Date of most recent approval of professional information: 22 August 2019

[1]Company Reg. No.: 1990/001979/07