SCHEDULING STATUS: S4

PROPRIETARY NAMES AND DOSAGE FORM:

SANDOZ® ETHAMBUTOL HCl 100 (tablets)

SANDOZ® ETHAMBUTOL HCl 400 (tablets)

COMPOSITION:

SANDOZ ETHAMBUTOL HCl 100:

Each tablet contains: 100 mg ethambutol hydrochloride.

Excipients:

Acacia, hydroxypropylmethylcellulose, lactose 200 mesh, magnesium stearate, maize starch, sucrose fine, purified talc.

Contains sugar (215,00 mg lactose and 20,00 mg sucrose).

SANDOZ ETHAMBUTOL HCl 400:

Each tablet contains: 400 mg ethambutol hydrochloride.

Excipients:

Black TF powder, lactose 200 mesh, magnesium stearate, maize starch, povidone K30.

Contains sugar (148,18 mg lactose).

PHARMACOLOGICAL CLASSIFICATION:

A 20.2.3 Tuberculostatics

PHARMACOLOGICAL ACTION:

Pharmacodynamic Properties:

Ethambutol is bacteriostatic. It is effective against *Mycobacterium tuberculosis* and *M. bovis* with an MIC of 0,5 to 8 µg/ml. While it has activity against some atypical mycobacteria including *M. Kansarii*, activity against other microorganisms has not yet been reported. It is effective against *tubercle bacilli* resistant to other tuberculostatics. Cross-resistance has not yet been reported.

Primary resistance to ethambutol is uncommon but resistant strains of *M. tuberculosis* are readily produced if ethambutol is used alone.

Pharmacokinetic Properties:

Absorption:

After single oral administration, ethambutol hydrochloride was rapidly absorbed. Blood concentrations reached a respective peak of 1,8 micrograms/ml at 3 hours with a dose of 15 mg/kg and 5,7 micrograms/ml at 2 hours with a dose of 25 mg/kg (healthy adults).

Distribution:

Drug concentrations were higher in lung tissue than in blood after single oral administration of 0,5 g ethambutol hydrochloride (patients with pulmonary tuberculosis).

Metabolism and excretion:

After single oral administration of 25 mg/kg ethambutol hydrochloride, cumulative excretion in urine and faeces was 54 to 67 % at 24 hours, 72 to 86 % at 48 hours and 79 to 94 % at 144 hours.

Within 24 hours of administration, 54 % of the dose was excreted in the urine. Urinary excretion consisted of the unchanged substance and its metabolites (aldehyde and butyric acid derivative) at a ratio of approximately 2:1 (patients with pulmonary tuberculosis in the United States).

INDICATIONS:

SANDOZ ETHAMBUTOL HCl is indicated for the treatment of tuberculosis in conjunction with other antituberculous medicines.

CONTRAINDICATIONS:

SANDOZ ETHAMBUTOL HCl is contraindicated in patients who are known to be hypersensitive to the active substance or any of the excipients.

SANDOZ ETHAMBUTOL HCl is also contraindicated in patients with known optic neuritis and poor vision unless clinical judgement determines that it may be used.

WARNINGS AND SPECIAL PRECAUTIONS:

SANDOZ ETHAMBUTOL HCl has a unique effect on the eye. It is recommended that patients undergo a full ophthalmic examination before starting treatment. This should include visual acuity, colour vision, perimetry and ophthalmoscopy. Many physicians consider that routine ophthalmological examination for adults is not thereafter necessary, but patients should be informed of the importance of reporting any change in vision and SANDOZ ETHAMBUTOL HCl should be withdrawn if vision deteriorates.

However, routine ophthalmological examinations may be considered desirable when treating young children.

Serum concentrations of ethambutol should not exceed 5 µg/ml. Teratogenic effects have been seen in animals but not in man.

Renal function should be checked before treatment with antituberculous medicines and appropriate dosage adjustments made. SANDOZ ETHAMBUTOL HCl should preferably be avoided in patients with renal impairment, but if used the dose should be reduced and the plasma-drug concentration monitored. Toxic effects are more common if renal function is impaired.

Precautions relating to excipients:

SANDOZ ETHAMBUTOL HCl contains lactose and sucrose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption, fructose intolerance or sucrase-isomaltase insufficiency should not take SANDOZ ETHAMBUTOL HCl.

SANDOZ ETHAMBUTOL HCl 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:

Patients who suffer from visual impairment during treatment with ethambutol should not drive or operate machinery.

INTERACTIONS:

The results of a study of coadministration of ethambutol hydrochloride (50 mg/kg) with an aluminum hydroxide containing antacid to 13 patients with tuberculosis showed a reduction of mean serum concentrations and urinary excretion of ethambutol of approximately 20 % and 13 %, respectively, suggesting that the oral absorption of ethambutol may be reduced by these antacid products. It is recommended to avoid concurrent administration of ethambutol with aluminum hydroxide containing antacids for at least 4 hours following ethambutol administration.

(see 'SIDE EFFECTS - Gastrointestinal disorders and Hepatobiliary disorders for interactions reported in patients on multi-drug anti-tuberculosis therapy including ethambutol'.)

PREGNANCY AND LACTATION:

Pregnancy:

There are no adequate and well-controlled studies from the use of ethambutol in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown.

SANDOZ ETHAMBUTOL HCl should not be used in pregnant women or women of childbearing potential unless the potential benefit to the mother is considered to outweigh any possible risk to the foetus.

Lactation:

Ethambutol hydrochloride is excreted into breast milk. The use of SANDOZ ETHAMBUTOL HCl should be considered only if the expected benefit to the mother outweighs the potential risk to the infant.

DOSAGE AND DIRECTIONS FOR USE:

Adult dose: The dosage must be adjusted according to the body mass of the patient - refer to the table of dosages.

For primary treatment:

SANDOZ ETHAMBUTOL HCl should be administered in a single daily oral dose of 15 mg/kg with concomitant medicines being used at their recommended dosage levels.

For re-treatment:

For the first 60 days of treatment, SANDOZ ETHAMBUTOL HCl should be administered in a single daily oral dose of 25 mg/kg. Thereafter the dosage should be reduced to 15 mg/kg with concomitant medicines being maintained at their recommended dosage levels.

Children dose:

Daily doses for children above three months are 20 (15 to25) mg/kg per body-weight daily.

No dosing recommendation can be made in children less than three months due to the lack of specific data. SANDOZ ETHAMBUTOL HCl is not recommended for children under 13 years of age.

Examples of dosage and administration of SANDOZ ETHAMBUTOL HCl tablets are shown in the table below:

15 mg/kg schedule				***25 mg/kg schedule***			
Mass range (kg)	***Total daily dosage (mg)***	***Number of tablets 100 mg***	***Number of tablets 400 mg***	***Mass range (kg)***	***Total daily dosage (mg)***	***Number of tablets 100 mg***	***Number of tablets 400 mg***
Under 37	500	1	1	Under 38	900	1	2
38 to 42,5	600	2	1	38 to 41,5	1 000	2	2
43 to 49,5	700	3	1	42 to 44,5	1 100	3	2
50 to 56,5	800		2	45 to 49,5	1 200		3
57 to 63,5	900	1	2	50 to 53,5	1 300	1	3
64 to 70,5	1 000	2	2	54 to 57,5	1 400	2	3

71 to 78,5	1 100	3	2	58 to 61,5	1 500	3	3
79 to 83,5	1 200		3	62 to 66,5	1 600		4
84 to 89,5	1 300	1	3	67 to 70,5	1 700	1	4
90 to 96,5	1 400	2	3	71 to 74,5	1 800	2	4
97 and over	1 500	3	3	75 to 78,5	1 900	3	4
				79 to 82,5	2 000		5
				83 to 86,5	2 100	1	5
				87 to 90,5	2 200	2	5
				91 to 94,5	2 300	3	5
				95 to 98,5	2 400		6
				99 and over	2 500	1	6

15 mg/kg schedule				***25 mg/kg schedule***			
Mass range (kg)	***Total daily dosage (mg)***	***Number of tablets***		***Mass range (kg)***	***Total daily dosage (mg)***	***Number of tablets***	
		100 mg	***400 mg***			***100 mg***	***400 mg***
Under 37	500	1	1	Under 38	900	1	2
38 to 42,5	600	2	1	38 to 41,5	1 000	2	2
43 to 49,5	700	3	1	42 to 44,5	1 100	3	2
50 to 56,5	800		2	45 to 49,5	1 200		3
57 to 63,5	900	1	2	50 to 53,5	1 300	1	3
64 to 70,5	1 000	2	2	54 to 57,5	1 400	2	3

71 to 78,5	1 100	3	2	58 to 61,5	1 500	3	3
79 to 83,5	1 200		3	62 to 66,5	1 600		4
84 to 89,5	1 300	1	3	67 to 70,5	1 700	1	4
90 to 96,5	1 400	2	3	71 to 74,5	1 800	2	4
97 and over	1 500	3	3	75 to 78,5	1 900	3	4
				79 to 82,5	2 000		5
				83 to 86,5	2 100	1	5
				87 to 90,5	2 200	2	5
				91 to 94,5	2 300	3	5
				95 to 98,5	2 400		6
				99 and over	2 500	1	6

SIDE EFFECTS:

Side effects that have been observed are listed below.

Blood and lymphatic system disorders:

Less Frequent: Thrombocytopenia, leucopenia, neutropenia.

Immune system disorders:

Less Frequent: Hypersensitivity, anaphylactoid reactions, (see also *Skin and subcutaneous tissue disorders*).

Metabolism and nutrition disorders:

Frequency unknown: Hyperuricaemia, Gout.

Psychiatric disorders:

Frequency unknown: Mental confusion, disorientation, hallucinations.

Nervous system disorders:

Less Frequent: Peripheral neuropathy, numbness, paraesthesia of the extremities, Headache, dizziness.

Eye disorders:

Less Frequent: Optic neuritis (decreased visual acuity, loss of vision, scotoma, colour blindness, visual disturbance, visual field defect, eye pain).

Respiratory, thoracic and mediastinal disorders:

Less Frequent: Pneumonitis, pulmonary infiltrates, with or without eosinophilia.

Gastrointestinal disorders:

Less Frequent: Anorexia, nausea, vomiting, abdominal pain and diarrhoea have been noted in patients on multiple-drug anti-tuberculosis therapy including ethambutol although not in test patients receiving ethambutol as sole therapy.

Hepatobiliary disorders:

Less Frequent: Hepatic reactions with hepatitis, jaundice, abnormal liver function test values, and very rarely hepatic failure, have been reported in patients treated with multiple-drug therapy including ethambutol.

Liver function tests should be performed in patients who develop symptoms suggestive of hepatitis or who become generally unwell during treatment.

Skin and subcutaneous tissue disorders:

Less Frequent: Rash, pruritus, urticarial, photosensitive lichenoid eruptions, bullous dermatitis, Stevens-Johnson syndrome, epidermal necrolysis.

Renal and urinary disorders:

Less Frequent: Interstitial nephritis.

General disorders and administration site conditions:

Less Frequent: Malaise, joint pains, pyrexia.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms of overdosage may be any of those listed under “SIDE EFFECTS” above.

Changes in visual acuity should be carefully evaluated and if necessary the administration of the medicament should be discontinued.

There is no specific antidote, but gastric lavage should be employed if necessary followed by supportive and symptomatic treatment.

IDENTIFICATION:

SANDOZ ETHAMBUTOL HCl 100: White to off-white, round, slightly mottled, biconvex tablets.

SANDOZ ETHAMBUTOL HCl 400: Bluish-grey green, round, slightly mottled, biconvex tablets.

PRESENTATIONS:

28, 40, 56, 60, 84, 100 or 500 tablets in securitainers, blisters, or amber glass bottles.

Not all pack sizes may be marketed.

STORAGE INSTRUCTIONS:

Keep well closed and store in a dry place at or below 25 °C.

Store in original packaging in order to protect from moisture.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

SANDOZ ETHAMBUTOL HCl 100: Q/20.2.3/175

SANDOZ ETHAMBUTOL HCl 400: Q/20.2.3/176

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

Sandoz SA (Pty) Ltd[1]

Waterfall 5lr

Magwa Crescent West

Waterfall City

Jukskei view

2090

DATE OF PUBLICATION:

Date of registration: 20 June 1983

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

Additional country registration details:

Country	*Product name*	*Scheduling status (or Category of distribution)*	*Registration number*
Namibia	Sandoz Ethambutol 400	NS2	90/20.2.3/001470

Name and address of manufacturer:

Kiara Health (Pty) Ltd.
72 Steel Road, Spartan

Kempton Park, Johannesburg

1619, South Africa

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