Summary of product characteristics

Summary of product characteristics

1. Name of the medicinal product

Amtiba 500mg Film-coated Tablets

2. Qualitative and quantitative composition

Active substance: Tinidazole

Each tablet contains Tindiazole equivalent to 500mg.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coatedtablets

Yellow colored, smooth capsules shaped biconvex film coated tablets, plain on both sides.

4. Clinical particulars

4.1. Therapeutic indications

Treatment of the following infections:

1. Eradication of Helicobacter pylori associated with duodenal ulcer, in the presence of antibiotic and acid suppressant therapy (see section 4.2)
2. Anaerobic infections such as:

- Intraperitoneal infections: peritonitis, abscess
- Gynaecological infections: endometristis, endomyometritis, tube-ovarian abscess
- Bacterial septicaemia
- Post-operative wound infections
- Skin and soft tissue infections
- Upper and lower respiratory tract infections: pneumonia, empyema, lung abscess

3. Non –specific vaginitis
4. Acute ulcerative gingivitis
5. Urogenital trichomoniasis in both male and female patients
6. Giardiasis
7. Intestinal amoebiasis
8. Amoebic involvement of the liver
9. Prophylaxis: the prevention of post-operative infections caused by anaerobic bacterial, especially those associated with colonic, gastro-interstinal and gynaecological surgery.

4.2. Posology and method of administration

Route: Oral administration during or after a meal.

Posology:

Eradication of H.Pylori associated with duodenal ulcers:

Adults: the usual dose of Amitiba is 500mg twice daily coaministered with omeprazole 20mg twice daily and clarithromycin 250mg twice daily for 7days.For the control of intestinal amoebiasis and amoebic liver abscess, four tablet of 500mg a day for 2 to 5 days.

Clinical studies using this 7 days regimen have shown similar H.Pylori eradication rates when omeprazole 20mg once daily was used.

Non-specific vaginitis:

Adults: non-specific vaginitis has been successfully treated with single oral dose of 2gm. Higher cure rates have been achieved with 2 gm single doses on 2 days consecutive days (total dose 4 gm). Simultaneous treatment of male partner is recommended.

For the control of giardiasis:

Adults: 4 tablets of 500mg straight as single dose.
Children: a single dose of 50 to 75 mg/kg of body weight. It may be necessary to repeat this dose.

Anaerobic infections:

Adults: an initial dose of 2gm the first day followed by 1g daily given as a single dose or as 500mg twice daily. Treatment for 5 to 6days will generally be adequate but clinical judgment must be used in determining the duration of therapy, particularly when eradication of infection from certain sites may be difficult. Routine clinical and laboratory observation is recommended if it is considered necessary to continue therapy for more than 7 days.
Children: <12 years- there is no data available.

Acute Ulcerative Gingivitis:

Adults: a single oral dose of 2gm.

Urogenital trichomoniasis:

(when infection with Trichomonas Vaginalis is confirmed, simultaneous treatment of the consort is recommended).

Adults: a single dose of 2gm.
Children: a single dose of 50 to 75mg/kg of body weight. It may be necessary to repeat this dose.

Intestinal Amoebiasis:

Adults: a single dose of 2gm for 2 to 3 days.

Children: a single dose of 50 to 60mg/kg of body weight on each of 3 successive days.

Amoebic involvement in the liver:
Adults: total dosage varies from 4.5 to 12g, depending on the virulence of the *Entamoeba histolytica.*
For amoebic involvement of the liver, the aspiration of pus may be required in addition to therapy with Amtiba.
Initial treatment with 1.5 to 2 gm as a single oral daily dose for three days. Occasionally when a three day course is ineffective, treatment may be continued for up to six days.

Children: a single dose of 50 to 60 mg/kg of body weight per day for five successive days.

Use in Renal impairment:
Dosage adjustments in patients with impaired renal function are generally not necessary. However, because tinidazole is easily removed by haemodialysis, patient may require additional doses of tinidazole to compensate.

Prevention of post-operative infection:
Adults: a single dose of 2gm approximately 12 hours before surgery.
Children: < 12 years- there is no data available.

It is recommended that tinidazole be taken during or after a meal.

Use in the elderly: there are no special recommendations for this age group.

Method of administration
Oral administration. Swallow tablets with a glass of water during or after a meal.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

As with other drugs of similar structure, tinidazole is contraindicated in patients having, or with a history of, blood dyscrasia, although no persistent haematological abnormalities have been noted in clinical or animal studies.

Tinidazole should be avoided in patients with organic neurological disorders.

Tinidazole, other 5-nitroimidazole derivatives or any of the components of this product should not be administered to patients with known hypersensitivity to the drug.

Use of tinidazole is contraindicated during the first trimester of pregnancy and in nursing mothers (see section 4.6).

4.4. Special warnings and special precautions for use

As with related compounds, alcoholic beverages should be avoided during Amitiba therapy because of the possibility of a disulfiram-like reaction (flushing, abdominal cramps, vomiting, tachycardia). Alcohol should be avoided until 72 hours after discontinuing Amitiba.

Drugs of similar chemical structure have also produced various neurological disturbances such as dizziness, vertigo, incoordination and ataxia. If during therapy with Amtiba abnormal neurological signs develop, therapy should be discontinued.

Carcinogenicity has been seen in mice and rats treated chronically with metronidazole, another nitroimidazole agent. Although carcingencity data is not available for tinidazole, the two drugs are structurally related and therefore there is a potential for similar biologic effects. Mutagenicity results with tinidazole were mixed (positive and negative) (see

section 5.3). The use of tinidazole for longer treatment than usually required should be carefully considered.

4.5. Interaction with other medicinal products and other forms of interaction

Alcohol: Concurrent use of tinidazole and alcohol may produce a disulfiram-like reaction and should be avoided, (see section 4.4).

Anticoagulants: Drugs of similar chemical structure have been shown to potentiate the effects of oral anticoagulants. Prothrombin time should be closely monitored and adjustments to the dose of the anticoagulants should be made as necessary.

4.6. Use during pregnancy and lactation

Pregnancy

Animal studies have shown reproductive toxicity (see section 5.3). Tinidazole crosses the placental barrier. Since the effects of compounds of this class on fetal development are unknown, tinidazole is contraindicated in the first trimester of pregnancy.

There is no evidence that tinidazole is harmful during the latter stages of pregnancy, but it should be used in the second and third trimesters only in cases where it is absolutely necessary, when the benefits of therapy outweigh possible risks to both mother and fetus (see section 5.3).

Lactation

Tinidazole is excreted in breast milk. Tinidazole may continue to appear in breast milk for more than 72 hours after administration. Women should not nurse until at least 3 days after having discontinued taking Amtiba.

4.7. Effects on ability to drive and use machines

No special precautions should be necessary. However, drugs of similar chemical structure, including Amtiba, have been associated with various neurological disturbances such as dizziness, vertigo, ataxia, peripheral neuropathy (paraesthesia, sensory disturbances, hypoaesthesia) and rarely convulsions. If any abnormal neurological signs develop during Amtiba therapy, the drug should be discontinued.

4.8. Undesirable effects

Side effects like nausea, vomiting, anorexia, metallic and bitter taste are mild and infrequent. Malaise, pruritus, headache and skin rashes have been reported rare.

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. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9. Overdose

There is no specific reported overdoses in human with Amtiba.

Treatment for overdose: there is no specific antidote for treatment of over dosage with tinidazole. Treatment is symptomatic and supportive. Gastric lavage may be useful. Tinidazole is easily dialyzable.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Antiinfectives for systemic use. ATC code: J 01XD02.

Amtiba is active against both protozoa and obligate anaerobic bacteria. The activity against protozoa involves *Trichomonas vaginalis, Entamoeba histolytica and Giaradia lambia.*

The mode of action of Amtiba against bacteria and protozoa involves peneteration of the drug into the cell of the micro-organism and subsequent damage of DNA strands or inhibition of their synthesis.

Amtiba is active aginist *H.Pylori, Gardnerella vaginalis* and most anaerobic bacteria including *Bacteroides fragilis, Bacteroides melaninogenicus,* Bacteroides spp., Clostridium spp., Fusobacterium spp., Peptococcus spp., Peptostreptococcus spp. And Veillonella spp.

5.2. Pharmacokinetic properties

Absorption

Amtiba is rapidly and completely absorbed following oral administration.

The plasma elimination half-life for tinidazole is between 12-14 hours.

Distribution

The plasma elimination half-life for tinidazole is between 12-14 hours. Tinidazole is widely distributed in all body tissues and also crosses the blood brain barrier, obtaining clinically effective concentrations in all tissues. The apparent volume of distribution is about 50 litres. About 12% of plasma tinidazole is bound to plasma protein.

Excretion

Tinidazole is excreted by the liver and kidneys. Studies in healthy patients have shown that over 5 days, 60-65% of an administered dose is excreted by the kidneys with 20-25%

of the administered dose excreted as unchanged tinidazole. Up to 5% of the administered dose is excreted in the faeces.

Studies in patients with renal failure (creatinine clearance <22ml/min) indicate that there is no statistically significant change in tinidazole pharmacokinetic parameters in these patients, (see section 4.2).

5.3. Preclinical safety data

Genotoxicity/carcinogenicity

Tinidazole showed some evidence of mutagenic potential. Tinidazole carcinogenicity studies in rats, mice or hamsters have not been reported. However, metronidazole, a chemically-related nitroimidazole, has been reported to be carcinogenic in mice and rats but not hamsters. In several studies metronidazole showed evidence of pulmonary, hepatic, and lymphatic tumorigenesis in mice and mammary and hepatic tumors in female rats.

6. Pharmaceutical particulars

6.1. List of Excipients

Core Tablet:
Microcrystalline cellulose (PH 101)
Calcium hydrogen Phosphate
Color tartarazine yellow
Polyvinyl Pyrolidone (PVPK-30)
Starch
Sodium Starch glycollate
Magnesium Stearate
Seal and Film coating:
Ethyl cellulose
Hydroxypropyl Methyl Cellulose (HPMC 5 cps)
Polyethylene Glycol 6000
Titanium dioxided
Purified talc
Isopropyl Alchol
Methylene chloride

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

48 Months.

6.4. Special precautions for storage

Store below 30°C. Protect from light.

6.5. Nature and content of container

Amtiba tablets are packed in blister packs of 0.02mm Aluminum foil and .025mm non-toxic transparent PVC film.

Pack size: 4 tablets in blister

6.6. Instructions for use and handling, and disposal (if appropriate)

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

CADILA PHARMACEUTICALS (ETHIOPIA) PLC
GELAN CITY, OROMIA REGION
ETHIOPIA

8. NUMBER (S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS :

Certificate No: 04430/06693/REN/2018

9. Date of first authorization / renewal of the authorization:

Apr 25, 2019

10. Date of revision of the text:

02/08/2023