SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TINAZOL® tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains tinidazole 500 mg.
Excipients with know effect : this drug contains sodium methylparahydroxybenzoate and sodium propylparahydroxybenzoate, see section 4.4.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.
White, round, biconvex & film-caoted tablets, with imprints « TINAZOL 500 » on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Tinidazole 500 mg tablets is indicated for oral treatment of:
Trichomonas vaginalis infections of the genito-urinary tract in botch female and male patients. When infection with *Trichomonas vaginalis* has been confirmed or is suspected, similtaneous treatment of the consort is recommended.

Intestinal and liver infections caused by Entamoeba histolytica and *Giardia lamblia* intestinal infections.

Vaginitis caused by *Gardnerella vaginalis*. (non-specific vaginitis)
Tinidazole can also be used for treatment of vaginitis caused by *Gardnerella vaginalis*

Infections caused by anaerobic bacteria.
Tinidazole is still indicated for the treatment of infections in which anaerobic bacteria nave been confirmed or are suspected. Amond these, the most important germs are: *Bacteroides fragilis*, others *Bacteroides* and *Fusobacteria spp.*

Tinidazole exhibits also bactericidal activity on strains of *Peptococcus spp., Peptostreptococcus spp., Clostridium spp , Eubacteria spp.* and *Veillonella spp.*

Tinidazole has been succesfully administered for the treatment of infections caused by one or several of the anearobic microorganisms mentionned above particularly in certain cases of septicaemia, chronic sinusitis, pneumonia , emphysema, lung abscess, osteomyelytis caused by *Bacteroides,* septic abortion, peritonitis, abdominal (gastro-intestinal) phlegmon post-operative infections and post-operative infections.

4.2 Posology and method of administration

Posology
Tinazol is to be administered by oral route during or after a meal.

1) Urogenital Trichomoniasis

When infection with Trichononiasis vaginalis is confirmed, simultaneous treatment of the consort is recommended.
Adults: a single oral of 2 g (4 x 500 mg tablets as a single dose).
Children: single dose of 50 to 75mg/kg of body weight. It may be necessary to repeat this dose.

2) Amoebiasis

a) Acute Amoebic Dysentery (Intestinal Amoebiasis)

Adults: The recommended dosage is 2 g orally as a single dose for two to three days. In the occasional instance when a three days course is ineffective, treatment may be continued for six days.
Children: 50 to 60 mg/kg of body weight given as a single daily dose on each of three successive days.

b) Amoebic Liver Abscess

Total dosage varies according to the virulence of the pathogenic agent between 4.5 to 12 g.
Initiate treatment with 1.5 to 2g as a single oral daily dose for three days.
Occasionally when a three days course is ineffective, treatment may be continued for up to six days.
Children: 50 to 60 mg/kg of body weight given as a single daily dose on each of five successive days.
In amoebic involvement of the liver the aspiration of pus may be required in addition to therapy with tinidazole.

3) Giardiasis

Adults: 4 tablets of Tinazol as a single dose (a single dose of 2g).
Children: a single dose of 50 to 75mg/kg of body weight. It may be necessary to repeat this dose.
Les selles d'un patient atteint de giardiase doivent être contrôlées 7 à 10 jours après le traitement pour déceler la présence éventuelle de Giardia lamblia.

4) Gardnerella vaginalis vaginitis (non-specific vaginitis)

Adults: non-specific vaginitis has been successfully treated with a single oral dose of 2 g, 4 tablets of Tinazol, higher cure rates have been achieced with 2 g single doses on 2 consecutive days (total dose 4g).

5) Anaerobic infections

Adults: an initial dose of 2 g the first day followed by 1 g daily as a single dose or as 500 mg twice daily.
Treatment for 5 to 6 days 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.

Table of dosage summary:

Indications	Quantity of tablets or mg/kg of body weight daily (in one intake during a meal)	Duration of treatment In days
Urinary-genital Trichomoniasis		
In men and women	4 tablets of 500 mg	1
In children above 12 years	50 to 75 mg/kg	1 (repeat one time if necessary)
Gardnerella vaginalis vaginitis	4 tablets of 500 mg	1 to 2
Amoebic infections		
In adults	4 tablets of 500 mg	2 to 3 (up to 6 days if necessary)
In children	50 to 60 mg/kg	3
Hepatic amoebiasis		
In adults	3 to 4 tablets of 500 mg	3 to 6
In children	50 to 60 mg/kg	5
Giardiasis		
In adults	4 tablets of 500 mg	1
In children	50 to 75 mg/kg	1(repeat one time if necessary)
Anaerobic bacterial infections	4 tablets of 500 mg	1
In adults	Followed by 2 tablets of 500 mg	4 to 5

The maximum posology in adults should not be exceeded in children.

Paediatric use
There is no data available to allow dosage recommendations for children below the age of 12 in the prophylaxis of anaerobic infections.

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

4.3 Contraindications

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 (active organic diseases of the central nervous system).
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.

4.4 Special warnings and precautions for use

Unjustified use of tinidazole is to be banned (should be avoided). Carcinogenicity has been seen in certain animal species. Until now there is no proof of a carcinogenic effect in human.
Neurological disturbances such as dizziness, vertigo, incoordination and ataxia can occur. If suspicious neurological symptoms occur during tinidazole treatment, the treatment should be discontinued.
Concomitant use of alcohol should be avoided during tinidazole theray and until three days after discontinuing tinidazole (see section 4.5, Interaction with other medicinal products and other forms of interaction).
This drug contains sodium methylparahydroxybenzoate and sodium propylparahydroxybenzoate that may cause allergic reactions (including delayed reactions).

4.5 Interaction with other medicinal products and other forms of interaction

<u>Associations not recommended</u>

- Disulfiram : delirious episode, confusion.
- Alcohol : Alcoholic beverages should be avoided during tinidazole treatment and for at least 72 hours (three days) after discontinuing tinidazole because of the possibility of a disulfiram-like reaction (flushing, abdominal cramps, vomiting, and tachycardia).

<u>Associations with special precautions for use</u>
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 Pregnancy and lactation

Use in pregnancy:
Tinidazole is contraindicated during the first trimester of pregnancy.
There is no evidence that tinidazole is harmful during latter stages of pregnancy, but its use during the second and third trimesters requires that potential benefits be weighed against possible hazard to mother of foetus.

Use in 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 tinidazole.

4.7 Effects on ability to drive and use machines

The effect of tinidazole on the ability to drive or operate heavy machineny has not been studied.
Drivers and machinery operators should be aware of potential risk of vertigo.

4.8 Undesirable effects

Autonomic Nervous System: flushing.
Body as a whole: fever, tiredness.
Central and Peripheral Nervous System: ataxia, convulsions (rarely), dizziness, headache, hypoesthesia, parathesia, peripheral neuropathy, sensory disturbances, and vertigo.
Gastrointestinal: abdominal pain, anorexia, diarrhoea, furry tongue, glossitis, nausea, stomatitis, vomiting.
Haematopoietic: transient leukopenia.
Skin/Appendages: hypersensitivity reactions occasionally sever may occur in rare cases in the form of skin rash, pruritis, urticaria, and angioneurotic oedema.
Special senses: metallic taste.
Urinary system: dark urine.
Other: modifications of biological tests might happen.
During treatment with 5-nitro-imidazole derivatives, as tinidazole, surinfection by *Candida albicans* can happen.

4.9 Overdose

Signs and symptoms of overdosage: there are no reported overdoses in human with tinidazole.
Treatment of overdosage: There is no specific antidote for treatment of overdosage with tinidazole.
Treatment is symptomatic and supportive. Gastric lavage may be useful. Tinidazole is easily dialysable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterial for systemic use, ATC code: J01XD02.

Tinidazoleis a derivative of the substitued imidazole group of compounds. Tinidazole has been shown to be effective against *Trichomonas vaginalis*, *Entamoeba histolytica* and *Giardia lamblia*. Tinidazole has also been shown to be effective against anaerobic bacteria such as *Bacteroides fragilis, Bacteroides spp*., *Fusobacterium spp*., *Peptococcus spp*., *Peptostreptococcus spp*, *Clostridium spp*., *Eubacterium spp*., and *Veillonella spp*.
Tinidazole is also active in vitro against *Gardnerella vaginalis* but it is inactive against *Candida albicans*.
Tinidazole chemical name is: 1-(2-ethylsulfonylethyl)-2-methyl-5-nitro-imidazole
Tinidazole is a pale yellow crystalline solid that is insoluble in water, but soluble in methanol and chloroform.
The mode of action of tinidazole against anaerobic bacteria and protozoa involves penetration of the drug into the cell of the micro-organism and subsequent damage of DNA strands or inhibition of their synthesis.

5.2 Pharmacokinetic properties

Distribution
Tinidazole is rapidly and completely absorbed following oral administration of a single oral dose of 2g of tinidazole. Peak serum levels were obtained 1 to 2 hours post-administration, then plasma levels of tinidazole decreased slowly and tinidazole remains detectable n in serum at 48 hours after oral administration.
The plasmatic half-life of tinidazole is approximately 12.7 ± 0.5 hours.
The peak serum levels following oral administration of a single dose of 2 mg of tinidazole were: 41 ± 5 mcg/ml at 1 hour, 46 ± 4 mcg/ml at 4 hours and 19 ± 2 mcg/ml at 24 hours.
About 12% of plasma tinidazole is bound to plasma proteins.
Biotransformation
Administered dose is excreted by the kidneys with 20-25% of the administered dose excreted as unchanged tinidazole and 12% as metabolites.
Eliminination
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.

Tinidazole is widely distributed in all body tissues and also crosses the blood brains barrier, obtaining clinically effective concentrations in all tissues.

Studies in patients with renal failure indicate that there is no statistically significant change in tinidazole pharmacokinetic parameters in these patients, (see section 4.2 Posology and method of administration).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core: *maize starch, microcristalline cellulose, sodium methylparahydroxybenzoate (E219), sodium propylparahydroxybenzoate (E217), talc, magnesium stearate, colloidal anhydrous silica,*
Film-coating: *talc, hypromellose, titanium dioxide (E171), polyethylene glycol 6000.*

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Sore in the original package, protect from heat, light and moisture
Store below 30°C. Keep out the reach and sight of children.

6.5 Nature and contents of container
Boxe of 4 film-coated tablets packaged in PVC-Aluminium blister.

6.6 Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. CATEGORY OF DISTRIBUTION
☐ Medicinal product not subject to medical prescription ☒ Prescription only medicine

8. MARKETING AUTHORISATION HOLDER
EXPHAR s.a.
Zoning Industriel de Nivelles Sud, zone II – Av. Thomas Edison 105 – 1402 Thines (Belgium).

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9. MANUFACTURER

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10. DATE OF REVISION OF THE TEXT

08/2016