SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1 NAME OF THE MEDICINAL PRODUCT

Amibagyl Suspension

2 QUALITATIVEAND QUANTITATIVECOMPOSITION

Each 5ml contains 200mg of Metronidazole

For a full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Oral Suspension

A viscous golden-yellow suspension with a characteristic bitter taste.

4 CLINICALPARTICULARS

4.1 Therapeutic indications

Metronidazole is indicated in adults and children for the following indications:

In the treatment of urogenital trichomonaisis.
In the treatment of acute ulcerative gingivitis.
In the treatment of infections due to E. histolytica (including carrier states).
In the treatment of infections due to G. Lamblia (including carrier states).
In the prevention and treatment of infections due to anaerobic bacteria, particularly species of Bacteroides, anaerobic Streptococci, fusobacteria, clostridia, etc.
In the treatment of acute dental infections.
In the treatment of non-specific vaginitis.

4.2 Posology and method of administration

	Children		
Indications	**1-3 years**	**4-10years**	**Duration**
Intestinal amoebiasis	2.5ml four times daily	5-10ml four times daily	5-10 days
Acute ulcerative gingivitis	2.5ml three times daily	5ml three times daily	7days

Anaerobic infection	2.5ml three times daily	5ml three times daily	7days
Or as directed by the doctor			

4.3 Contra-indications

Hypersensitivity to metronidazole or to imidazoles or to any of the excipients listed in Section 6.1.

4.4. Special warnings and precautions for use

Hypersensitivity / Skin and appendages Allergic reactions, including anaphylactic shock, can occur and be life-threatening (see Section 4.8). In this case, treatment with metronidazole must be discontinued and appropriate medical treatment initiated. If, at the start of treatment, patients experience generalized erythema with fever and pustules, acute generalized exanthematous pustulosis should be suspected (see Section 4.8). If this occurs, treatment must be discontinued and any further administration of metronidazole alone or in combination with other agents is contraindicated. Severe skin reactions have been reported with metronidazole, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, or Lyell syndrome) and acute generalized exanthematous pustulosis. Patients must be informed of the signs and symptoms of these conditions and the skin should be closely monitored. If any signs or symptoms of Stevens-Johnson syndrome, toxic epidermal necrolysis (e.g. progressive skin rash often with blisters or mucosal lesions) or acute generalized exanthematous pustulosis (see Section 4.8) occur, treatment must be discontinued and any further administration of metronidazole alone or in combination with other agents is contraindicated. Central nervous system If symptoms indicative of encephalopathy or cerebellar syndrome appear, patient management should be immediately reassessed and metronidazole treatment discontinued. Cases of encephalopathy have been reported as part of post-marketing surveillance of the drug. Cases of MRI changes associated with encephalopathy have also been observed (see Section 4.8). Damage is most often located in the cerebellum (particularly in the dentate nucleus) and in the splenium of the corpus callosum. Most cases of encephalopathy and MRI changes are reversible on treatment discontinuation. Very rare cases of fatal outcome have been reported. 3 | P a g e Patients should be monitored for warning signs of encephalopathy, and exacerbation of symptoms in

patients with CNS disorders. If aseptic meningitis occurs during treatment, rechallenge with metronidazole is not recommended, and an assessment of the benefit/risk ratio should be done for patients with serious infection. Peripheral nervous system Patients should be monitored for warning signs of peripheral neuropathy, particularly in long-term treatment or in patients with severe, chronic or progressive peripheral neurological disorders. Psychiatric disorders From administration of the first doses, patients may experience psychotic reactions, including self endangering behavior, particularly if they have a history of psychiatric disorders (see Section 4.8). If this happens, metronidazole must be discontinued, the physician informed and appropriate therapeutic measures instituted immediately. Hematological effects In patients who have a history of hematological disorders or who are receiving high-dose and/or longterm treatment, regular blood tests, and particularly leukocyte counts, should be performed. In patients with leukopenia, continued treatment will depend on how serious the infection is. Interaction with other medicinal products Concomitant use of metronidazole and alcohol is not recommended (see Section 4.5). Concomitant use of metronidazole and busulfan is not recommended (see Section 4.5). Concomitant use of metronidazole and disulfiram is not recommended (see Section 4.5). Interactions with laboratory tests Metronidazole may immobilize treponemes, and thus lead to false positive results for the Nelson test. Cases of severe hepatotoxicity/acute liver failure of very rapid onset after treatment initiation, including cases with fatal outcome, have occurred in patients with Cockayne syndrome who were administered medicinal products containing metronidazole intended for systemic use. In this population, metronidazole must therefore be used after thorough evaluation of the benefit/risk ratio and only if no alternative treatment is available. Liver function tests must be performed just before treatment initiation, during treatment and after treatment discontinuation, until liver function values are within the normal range, or until baseline values are reached. If the liver function test values markedly increase during treatment, the medicinal product should be discontinued. Patients with Cockayne syndrome must be instructed to immediately report any symptoms of potential liver damage to their doctor and to stop taking metronidazole.

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

Antabuse reaction Many medicinal products trigger an antabuse effect with alcohol and their concomitant use with alcohol is not advisable. Inadvisable combinations + Alcohol (beverage or excipient) An antabuse effect (hot flushes, erythema, vomiting, tachycardia) may occur. Patients should not consume alcoholic beverages or medicinal products containing alcohol. Alcoholic beverages or medicinal products containing alcohol should not be ingested again until medicinal products have been completely

eliminated from the body. The half-life should be used as a reference. + Busulfan when co-administered with high busulfan doses, metronidazole causes a two-fold increase in plasma busulfan concentrations. + Disulfiram There is a risk of acute psychotic episodes or confusion, reversible on discontinuation of the drug combination. Combinations requiring precautions for use + Enzyme-inducing anticonvulsants Decreased plasma concentrations of metronidazole can occur due to increased liver metabolism by the inducer. Clinical monitoring is required and the metronidazole dose may need to be adjusted during and after treatment with the inducer. + Rifampicin Decreased plasma concentrations of metronidazole can occur due to increased liver metabolism by rifampicin. Clinical monitoring is required and the metronidazole dose may need to be adjusted during and after treatment with rifampicin. + Lithium increased blood lithium levels can occur, which can reach toxic levels with signs of lithium overdose. Strict monitoring of blood lithium levels should be performed and the lithium dose adjusted if necessary. Combinations to be taken into consideration + Fluorouracil (and by extrapolation, tegafur and capecitabine) Increased fluorouracil toxicity can occur due to decreased clearance. Specific issue: INR imbalance: Numerous cases of increased oral anticoagulant activity have been reported in patients receiving antibiotics. The severity of the infection or inflammation, age and general health status of the patient appear to be risk factors. Under these circumstances, it seems difficult to determine to what extent the infection itself or its treatment play a role in the INR imbalance. However, certain classes of antibiotics are more involved particularly fluoroquinolones, macrolides, cyclines, cotrimoxazole and certain cephalosporins.

4.6. Fertility, pregnancy and lactation Pregnancy

There is no evidence from animal studies that metronidazole is teratogenic. Therefore, no malformative effect is expected in humans. To date, substances causing malformations in humans have been shown to be teratogenic in animals during well-conducted studies in two species. In man, analysis of a large number of exposed pregnancies did not seem to show any particular teratogenic or fetotoxic effects of metronidazole. However, only epidemiological studies would make it possible to rule out any risk. Therefore, metronidazole may be prescribed during pregnancy if necessary. Lactation Since metronidazole is excreted in breast milk; administration should be avoided in breast-feeding women.

4.7. Effects on ability to drive or use machines

Patients should be warned of the potential risk of dizziness, confusion, hallucinations and seizures or vision disorders, and should be advised not to drive or operate machines if they experience such symptoms.

4.8. Undesirable effects

Blood and lymphatic system disorders
• neutropenia, agranulocytosis, thrombocytopenia.
Psychiatric disorders
• hallucinations
• psychotic reactions with paranoia and/or delirium possibly accompanied by suicidal ideation or suicide attempts in some isolated cases.
• depressed mood.
Nervous system disorders
• peripheral sensory neuropathy,
• headache,
• dizziness,
• confusion,
• seizures,
• neuropathy / optic neuritis.
Gastrointestinal disorders
• minor gastrointestinal disorders (epigastric pain, nausea, vomiting, diarrhea),
• glossitis with dry mouth, stomatitis, taste disorders, anorexia, reported. Isolated cases of hepatocellular insufficiency possibly requiring liver transplantation have been reported. Skin and subcutaneous tissue disorders • hot flushes, pruritus, skin rash occasionally with fever, • urticaria, angioedema, anaphylactic shock.

4.9. Overdose

Administration of up to 12 g as a single dose has been reported in cases of attempted suicide and accidental overdose. The symptoms were limited to vomiting, ataxia and mild disorientation. There is no specific antidote to metronidazole overdose. If massive overdose occurs, symptomatic treatment should be instituted.

5 PHARMACOLOGICALPROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: antibacterial, antiparasitic antibiotics belonging to the 5nitroimidazole group, ATC code: J01XD01 — P01AB01 (J: Antiinfectives for systemic use, other antibacterials - imidazole derivatives - P: Antiprotozoals, agents against amebiasis and other protozoal diseases - nitroimidazole derivatives). The MIC breakpoints differentiating susceptible from intermediate strains, and intermediate from resistant strains are as follows: S ≤ 4 mg/L and R > 4 mg/L The prevalence of acquired resistance in certain species can vary geographically and over time. It is therefore useful to have local information on the prevalence of resistance, especially in treating severe infections. These data are only guidelines indicating the probability of susceptibility of a bacterial strain to this antibiotic

5.2. Pharmacokinetic Properties

Absorption

Metronidazole benzoate is gradually hydrolyzed as it passes through the gastrointestinal tract. The absorption of metronidazole benzoate is 30% less (area under the curve) than that of metronidazole. Peak plasma concentrations are obtained after four hours following oral administration of the product. At identical doses, metronidazole and metronidazole benzoate do not have significantly different therapeutic results. The plasma half-life is 6.9 hours by HPLC.

Distribution

• Plasma protein binding is below 10%.

• The drug is rapidly and widely distributed in the lungs, kidneys, liver, skin, bile, CSF, saliva, semen and vaginal secretions. Metronidazole crosses the placental barrier and is excreted in breast milk.

Biotransformation

Two unconjugated metabolites with antibacterial activity are formed (10%). Elimination High concentrations of metronidazole can be found in the liver and bile. Low concentrations of the drug are found in the colon.

Metronidazole is poorly excreted in the feces. It is mainly excreted in the urine (40 to 70%, with approximately 20% in unchanged form) causing reddish or brown coloration of the urine.

5.3 Preclinical Safety Data
Not applicable in humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parabens,Propyl parabens, Sugar,Sorbitol Liquid 70%, Propylene glycol, Xanthan gum, Banan flavour, Tartrazine orange, Tween 80, TTutti fruitti flavor, Bronopol,Tartrazine yellow,Alcohol ,Sodium saccharine,

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3years.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

60ml white PET bottle with cap.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER / Manufacturer

Afrab Chem Limited

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