1.3.1 Summary of Product Characteristics (SmPC)

1. PRODUCT INFORMATION FOR HEALTH PROFESSIONALS

1. NAME OF MEDICINAL PRODUCT

LOXAGYL 200mg Tablet (Metronidazole)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Loxagyl Suspension contains metronidazole 200mg tablet

3. PHARMACOLOGICAL FORM:

Oral

4. CLINICAL PARTICULARS:

4.1 THERAPEUTIC INDICATIONS:

Loxagyl Tablet is particularly recommended for children and adults.

Loxagyl is indicated in the treatment of all forms;

Amoebiasis

(a) Invasive intestinal disease in susceptible subjects.
(b) Intestinal disease in less susceptible subjects and chronic amoebic hepatitis
(c) Symptomless cyst passers

Uro-genital Trichomoniasis

Where re-infection is likely, the consort should receive a similar course of treatment concurrently.

Giardiasis

A second course of treatment may be necessary for some patients two weeks after the end of the first course.

Acute ulcerative gingivitis

Bacterial Viginosis

4.2 DOSAGE AND ADMINISTRATION:

Prophylaxis against anaerobic infection:

Chiefly in the context of abdominal (especially colorectal) and gynaecological surgery.

Adults: 400 mg 8 hourly during 24 hours immediately preceding operation followed by postoperative intravenous or rectal administration until the patient is able to take tablets.

Children < 12 years: 20-30mg/kg as a single dose given 1-2 hours before surgery

Newborns with a gestation age < 40 weeks: 10mg/kg body weight as a single dose before operation

Anaerobic infections:

The duration of a course of metronidazole treatment is about 7 days but it will depend upon the seriousness of the patient's condition as assessed clinically and bacteriologically.

Treatment of established anaerobic infection:

Adults: 800 mg followed by 400 mg 8 hourly.

Children > 8 weeks to 12 years of age: The usual daily dose is 20-30 mg/kg/day as a single dose or divided into 7.5 mg/kg every 8 hours. The daily dose may be increased to 40 mg/kg, depending on the severity of the infection. Duration of treatment is usually 7 days.

Children < 8 weeks of age: 15 mg/kg as a single dose daily or divided into 7.5 mg/kg every 12 hours.

In newborns with a gestation age <40 weeks, accumulation of metronidazole can occur during the first week of life, therefore the concentrations of metronidazole in serum should preferable be monitored after a few days therapy.

Prophylaxis against postoperative infections caused by anaerobic bacteria:

*Adults:*400 mg 8 hourly during 24 hours immediately preceding operation followed by postoperative intravenous or rectal administration until the patient is able to take tablets. *Children < 12 years:* 20-30 mg/kg as a single dose given 1-2 hours before surgery *Newborns with a gestation age <40 weeks:* 10 mg/kg body weight as a single dose before operation

Protozoal and other infections

Dosage is given in terms of metronidazole or metronidazole equivalent					
	Duration of dosage in days	Adults and children over 10 years	**Children**		
			7 to 10 years	**3 to 7 years**	**1 to 3 years**
Urogenital trichomoniasis Where re-infection is likely, in adults the consort should receive a similar course of treatment concurrently	7 or	2000mg as a single dose or 200 mg three times daily or	40mg/kg orally as a single dose or 15-30 mg/kg/day divided in 2-3 doses; not to exceed 2000mg/dose		
	5-7	400mg twice daily			
Bacterial vaginosis	5-7 or	400 mg twice daily			
	1	2000mg as a single dose			
Amoebiasis *(a) Invasive intestinal disease in susceptible subjects* *(b) Intestinal disease in less susceptible subjects and chronic amoebic hepatitis*	5 5-10	800 mg three times daily 400 mg three times a day	400 mg three times daily 200 mg three times daily	200 mg four times daily 100 mg four times daily	200 mg three times daily 100 mg three times daily
c) Amoebic liver abscess also other forms of extra-intestinal amoebiasis	5	400 mg three times daily	200 mg three times daily	100 mg four times daily	100 mg three times daily
(d) Symptomless cyst passers	5-10	400-800 mg three times daily	200-400 mg three times daily	100-200 mg four times daily	100-200 mg three times daily
	Alternatively, doses may be expressed by body weight 35 to 50mg/kg daily in 3 divided doses for 5 to 10 days, not to exceed 2400mg/day				
Giardiasis	3	2000mg once daily or	1000mg once daily	600-800 mg once daily	500 mg once daily
	5	400mg three times daily or			

	7-10	500mg twice daily			
	Alternatively, as expressed in mg per kg of body weight: 15-40mg/kg/day divided in 2-3 doses.				
Acute ulcerative gingivitis	3	200 mg three times daily	100 mg three times daily	100 mg twice daily	50 mg three times daily
Acute dental infections	3-7	200 mg three times daily			
Leg ulcers and pressure sores	7	400 mg three times daily			
Children and infants weighing less than 10 kg should receive proportionally smaller dosages. *Elderly:* Metronidazole is well tolerated by the elderly but a pharmacokinetic study suggests cautious use of high dosage regimens in this age group					

Eradication of Helicobacter pylori in paediatric patients:

As a part of a combination therapy, 20 mg/kg/day not to exceed 500 mg twice daily for 7-14 days. Official guidelines should be consulted before initiating therapy

Method of administration

For oral use.

Metronidazole Tablets should be taken during or after meals, swallowed with water and NOT CHEWED.

4.3 CONTRA-INDICATION:

Loxagyl is contraindicated in patients with a prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Convulsive Seizures and Peripheral Neuropathy: The latter characterized mainly by numbness or paresthesia of an extremity, have been reported in patients treated with metronidazole. The appearance of abnormal neurologic signs demands the prompt discontinuation of Loxagyl therapy. Loxagyl should be administered with caution to patients with central nervous system diseases.

Regular clinical and laboratory monitoring (especially leucocyte count) are advised if administration of Metronidazole for more than 10 days is considered to be necessary and patients should be monitored for adverse reactions such as peripheral or central neuropathy (such as paraesthesia, ataxia, dizziness, convulsive seizures).

There is the possibility that after Trichomonas vaginalis has been eliminated a gonococcal infection might persist.

The elimination half-life of metronidazole remains unchanged in the presence of renal failure. The dosage of metronidazole therefore needs no reduction. Such patients however, retain the metabolites of metronidazole. The clinical significance of this is not known at present.

In patients undergoing haemodialysis, metronidazole and metabolites are efficiently removed during an eight-hour period of dialysis. Metronidazole should therefore, be re-administered immediately after haemodialysis.

No routine adjustment in the dosage of Metronidazole need be made in patients with renal failure undergoing intermittent peritoneal dialysis (IPD) or continuous ambulatory peritoneal dialysis (CAPD).

Metronidazole is mainly metabolised by hepatic oxidation. Substantial impairment of metronidazole clearance may occur in the presence of advanced hepatic insufficiency.

Significant cumulation may occur in patients with hepatic encephalopathy and the resulting high plasma concentrations of metronidazole may contribute to the symptoms of encephalopathy.

Metronidazole should be administered with caution to patients with hepatic encephalopathy. The daily dosage may be reduced to one third and may be administered once daily.

Metronidazole should be used with caution in patients with active or chronic severe peripheral and central nervous system disease due to the risk of neurological aggravation.

Methyl, ethyl and propyl hydroxybenzoates are contained in this product which may cause allergic reactions (possibly delayed).

4.5 DRUG INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

As with many other drugs, alcohol should be avoided during treatment with Loxagyl. Rare instances of slight and transient fall in blood pressure have been reported, it may therefore be advisable to lower the dosage of any anti-hypertensive drug which may be given concurrently.

Psychotic reactions have been reported in patients who were using metronidazole and disulfiram concurrently.

Some potentiation of anticoagulant therapy has been reported when metronidazole has been used with the warfarin type oral anti-coagulants. Dosage of the anticoagulant may require reducing. Prothrombin time should be monitored. No interactions have been reported of the heparin type.

Lithium retention accompanied by evidence of possible renal damage has been reported in patients treated simultaneously with lithium and metronidazole. Lithium treatment should be tapered or withdrawn before administering metronidazole. Plasma concentration of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

Patients receiving phenobarbital or phenytoin metabolise metronidazole at a much greater rate than normally, reducing the half-life to approximately three hours.

Increased serum carbamazepine levels and toxicity have been seen in patients given concomitant metronidazole.

Aspartate amino transferase assays may give spuriously low values in patients taking metronidazole, depending on the method used.

Clinicians who contemplate continuous therapy for the relief of chronic conditions, for periods no longer than those recommended, are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Metronidazole reduces the clearance of 5-fluorouracil and can therefore result in increased toxicity of 5-fluorouracil.

Patients receiving cyclosporin or tacrolimus with metronidazole are at risk of elevated cyclosporin / tacrolimus serum levels. Serum cyclosporin / tacrolimus and serum creatinine should be closely monitored when co-administration is necessary.

Plasma levels of busulfan may be increased by metronidazole which may lead to severe busulfan toxicity.

4.6 PREGNANCY AND LACTATION:

Pregnant women tolerate metronidazole well and no adverse effect on their offspring. Loxagyl can thus be given during the first three months of pregnancy and during lactation where the physician considers it essential; in these circumstances, the short high dosage regimens are not recommended.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies of the effect of Loxagyl suspension on the ability to drive and use machines have been performed

4.8 SIDE EFFECTS / ADVERSE EFFECTS

There have been occasional reports of an unpleasant taste in the mouth, furred tongue, nausea, vomiting (very rarely) and gastro-intestinal upset. Drowsiness, headache, skin rashes and pruritus have been reported, but rarely.

4.9 OVER DOSAGE:

Single oral doses of metronidazole, up to 12g have been reported in suicide attempts and accidental overdoses. Symptoms were limited to vomiting, ataxia and slight disorientation. There is no specific antidote for metronidazole over dosage. In cases of suspected massive overdose, symptomatic and supportive treatment should be instituted.

5.0 PHARMACOLOGY PROPERTIES:

5.1 Pharmacodynamics properties

The selective action of this compound against anaerobes and anoxic and hypoxic cells is due to the mode of action. The nitro group of metronidazole acts as electron acceptor and is thus reduced to a chemically reactive drug form. This produces biochemical

lesions in the cells, thus causing death. The major site of action is believed to be DNA, where it causes loss of the helical structure and inhibits synthesis.

5.2 Pharmacokinetic properties

It is readily absorbed from the gastro-intestinal tract and widely distributed in body tissues. Half-life in plasma is about 8-10 hours. About 10% is bound to plasma proteins.

It penetrates well into body tissues and fluids, including vaginal secretions, seminal fluid, saliva and breast milk. Therapeutic concentrations are also achieved in cerebrospinal fluid.

Unchanged metronidazole and several metabolites are excreted in the urine, the liver is the main site of metabolism and the major metabolites are as a result of side chain oxidation, forming glucuronides.

6 PHARMACEUTICAL PARTICULARS:

6.1 LIST OF EXCIPIENTS:

Sodium Dihydrogen Phosphate Dihydrate
Granulated Sugar
Ethanol 96%
Veegum HV
Benzoyl Metronidazole
Methyl Hydroxybenzoate
Propyl Hydroxybenzoate
Lemon Oil
Oil of Orange Terpeneless BP
Purified Water BP

6.2 INCOMPATIBILITIES:

Not applicable

6.3 SHELF LIFE

5 years

6.4 SPECIAL PRECAUTION FOR STORAGE:

Store below 30°C in cool dry place. Protect from light. Keep out of reach of children

6.5 NATURE AND CONTENT OF CONTAINER:

60ml Amber Pet Bottle

6.6 SPECIAL PRECAUTION FOR DISPOSAL:

To be destroyed by NAFDAC enforcement unit.

6. Manufacturer

May & Baker Nigeria Plc.

1, May & Baker Avenue off Idiroko Road

Ota

Ogun State.

7. Marketing Authorization Holder(s)

Same as Manufacturer

8. Date of revision of the text

7th June 2024