Summary product characteristics:

1. Name of the medicinal product
Eflaron 125mg Oral Suspension

2. Qualitative and quantitative composition
Metronidazole (as Benzoate) BP 125mg/5ml
For the full list of excipients, see section 6.1

3. Pharmaceutical form
Oral Suspension
Orange coloured, viscous suspension free from visible evidence of contamination.

4. Clinical particulars
4.1 Therapeutic indications
Treatment of urogenital Trichomoniasis, non-specific Vaginitis, All form of Amoebiasis, giardiasis , infections of the CNS, pulmonary infections, septicaemia, endocarditis, Ulcerative gingivitis (Vincent's) ,acute pericoronitis, Anaerobic infections particularly Bacteroides fragilis and Bacteroides species, including B. fragilis group (B. distosonis, B. ovatus, B. thetaiotaomicron, B. vulgatus), Clostridium species, Eubacterium species, Peptococcus species, Peptostreptococcus species.
Pelvic inflammatory disease and post-operative wound infections
The prevention of post-operative infections caused by anaerobic bacteria
Given before and after gynecological surgery, appendectomy, colonic surgery
Helicobacter pylori eradication with other appropriate antibiotics combination

4.2 Posology and method of administration
Anaerobic infections
Treatment of anaerobic infections (usually treated for 7 days and for 10 days in antibiotic – associated colitis), by mouth either 800mg initially then 400mg every 8 hours or 500mg every 8 hours.
Children: 7.5mg / kg every 8 hours.
Preventive treatment: adults and children more than 12 years old: (100ml) administered in slow intravenous drip infusion immediately before, or during operation; the same dose is repeated every 8 hours until oral treatment is possible (200mg to 400mg) 3 times daily. The treatment (intravenous and oral together) should not last more than a week.
Children less than 12 years old: 7.5mg/kg body weight (=1.5ml/kg) administered in slow intravenous drip infusion following the same schedule as in adults.
Orally, a dosage of 3.7 to 7.5 mg/kg body weight is administered 3 times daily. The complete treatment lasts 7 days.
Trichomoniasis
Both partners should be treated simultaneously. Metronidazole is given by mouth either as a single 2-g dose, as a 2-day course of 800 mg in the morning and 1.2 g in the evening, or as a 7-day course of 600 mg to 1 g daily in two or three divided doses. If treatment needs to be repeated, an interval of 4 to 6 weeks between courses has been recommended.
Children with trichomoniasis may be given a 7-day course of metronidazole by mouth as follows: 1 to 3 years, 50 mg three times daily; 3 to 7 years, 100 mg twice daily, and 7 to 10 years, 100 mg three times daily. An alternative children's dose is 15 mg/kg daily in divided doses for 7 days.
Amoebiasis
Metronidazole is given in doses of 400 to 800 mg three times daily by mouth for 5 to 10 days. Children aged 1 to 3 years may be given one-quarter, those aged 3 to 7 years one-third, and those aged 7 to 10 years one-half the total adult daily dose; alternatively 35 to 50 mg/kg daily in divided doses has been used. An alternative adult dose is 1.5 to 2.5 g as a single daily dose for 2 or 3 days.
Lambliasis:
Adults: 800mg daily, divided into two doses for a period of 5 days.
Children: 35mg to 50mg/kg body weight divided into two doses for a period of 5 days
Leg ulcers and pressure sores
400mg every 8 hours for 7 days by mouth.

Bacterial vaginosis
400 – 500mg twice daily for 5 - 7 days or 2g as a single dose by mouth.
Pelvic inflammatory disease
400 mg twice daily for 14 days
Acute ulcerative gingivitis
Adults: 200 - 250mg daily every 8 hours for 3 days
Children 1 – 3 years: 50mg daily every 8 hours for 3 days, 3 – 7 years 100mg every 12 hours and 7-10 years 100mg every 8 hours.
Acute oral infections
Adults: 200mg daily every 8 hours for 3 - 7 days
Children 1 – 3 years: 50mg daily every 8 hours for 3 - 7 days, 3 – 7 years 100mg every 12 hours and 7-10 years 100mg every 8 hours.

Surgical prophylaxis
Adults: 400 - 500mg daily every 2 hours before surgery; upto 3 further doses of 400 - 500 mg may be given every 8 hours for high – risk procedures.
Children: 7.5mg / kg 2 hours before surgery; upto 3 further doses of 7.5 mg / kg may be given every 8 hours for high – risk procedures

Treatment of Helicobacte r pylori –associated gastritis and deudenal ulcers
Paediatric patients: As a part of combination therapy, 20mg/kg/day not to exceed 500mg twice daily for 7 – 14 days.
Adult: As a part of combination therapy, 500mg twice daily for 7 – 14 days.

4.3 Contraindications.
Hypersensitivity to metronidazole or other nitro- imidazole derivatives.
The first trimester of pregnancy.
If CNS disorders occur (ataxia, paraesthesia), treatment should be discontinued immediately. Concomitant administration of disulfiram is contraindicated too.

4.4 Special warnings and precautions for use.
Administration of Metronidazole for more than 10 days, patients should be monitored for adverse reactions such as peripheral or central neuropathy (such as paraesthesia, ataxia, dizziness, convulsive seizures) if signs occur treatment should be discontinued
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.
Metronidazole should be administered with caution to patients with liver disease. 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.
Patients should be warned that metronidazole may darken urine.
Due to inadequate evidence on the mutagenicity risk in humans the use of Metronidazole for longer treatment than usually required should be carefully considered.
Patients should abstain from alcoholic beverages during treatment.
The use of metronidazole during pregnancy and lactation is not recommended.
Metronidazole is excreted with human milk and penetrates the placental barrier. Therefore use of metronidazole during pregnancy and lactation is not recommended.

4.5 Interaction with other medicinal products and other forms of interaction

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

Patients should be advised not to take alcohol during metronidazole therapy and for at least 1-3 days afterwards because of the possibility of a disulfiram-like (antabuse effect) reaction.

Potentiation of Oral anticoagulant therapy(warfarin type) has been reported and increases hemorrhagic effects when metronidazole has been used with the warfarin type oral anti-coagulants. Dosage of the warfarin type oral anti-coagulants anticoagulant may require reducing and Prothrombin time should be monitored during therapy.

Lithium Plasma concentration level is increased by metronidazole.

Plasma concentration of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

Phenytoin accelerates the metabolism of metronidazole at a much greater rate than normally, reducing the half -life to approximately three hours, with a consquent reduction in the effectiveness of metronidazole

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

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

Patients receiving ciclosporin or tacrolimus with metronidazole are at risk of elevated ciclosporin / tacrolimus serum levels. Serum ciclosporin / 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

Cimetidine decreases the hepatic metabolism of metronidazole when administered concurrently, thus resulting to delayed elimination and increased serum metronidazole concentrations with an increased risk of neurological side effects

4.6 Pregnancy and lactation.

Safety of metronidazole in pregnancy and lactation has not been established

Metronidazole crosses the placenta barrier and excreted in milk therefore use during pregnancy or lactation should be carefully evaluated

4.7 Effects on ability to drive and use machines.

Patients should be warned about the potential for drowsiness, dizziness, confusion, hallucinations, convulsions or transient visual disorders, and advised not to drive or operate machinery if these symptoms occur.

4.8 Undesirable effects.

Immune system disorders:

Rare: Anaphylaxis

Not known: Urticaria, angioedema and fever

Metabolism and nutrition disorders:

Not known: Anorexia

Psychiatric disorders:

Very rare: Psychotic disorders, including confusion and hallucinations

Not known: Depressed mood

Nervous system disorders:

Very rare: Encephalopathy (e.g. confusion, fever, headache, hallucinations, paralysis, light sensitivity, disturbances in sight and movement, stiff neck) and sub-acute cerebellar syndrome (e.g. ataxia, dysathria, gait impairment, nystagmus and tremor) have been reported very rarely which may resolve on discontinuation of the drug

Drowsiness, dizziness, convulsions, headache, ataxia, inco-ordination of movement

Not known:During intensive and/or prolonged metronidazole therapy a few instances of peripheral neuropathy or transient epileptiform seizures have been reported. In most cases neuropathy disappeared after treatment was stopped or when dosage was reduced.

• Aseptic meningitis has been reported

Eye disorders:

Very rare: transient visual disorders such as diplopia and myopia have been reported

Not known: Optic neuropathy/neuritis has been reported

Gastrointestinal disorders:

Not known: Unpleasant taste in the mouth, oral mucositis, furred tongue, nausea, vomiting, gastro-intestinal disturbances such as epigastric pain and diarrhoea.

Hepatobiliary disorders:
Very rare: Abnormal liver function tests, increase in liver enzymes (AST, ALT, alkaline phosphatase), cholestatic or mixed hepatitis, and hepatocellular liver injury, jaundice and pancreatitis, reversible on Cases of liver failure requiring liver transplant have been reported in patients treated with metronidazole in combination with other antibiotic drugs.

Skin and subcutaneous tissue disorders:
Very rare: skin rashes, pustular eruptions, pruritus, flushing
Not known: Erythema multiforme may occur, which may be reversed on drug withdrawal. Stevens-Johnson syndrome or toxic epidermal necrolysis.

Musculoskeletal, connective tissue and bone disorders:
Very rare: myalgia, arthralgia

Renal and urinary disorders:
Very rare: darkening of the urine (due to metronidazole metabolite)
Metronidazole Oral Suspension contains glycerol, which can cause headache, gastro-intestinal disturbance and diarrhoea.

4.9 Overdose
Accidental overdoses. Symptoms were limited to vomiting, ataxia and slight disorientation.
There is no specific antidote for metronidazole overdosage. In cases of suspected massive overdose, symptomatic and supportive treatment should be instituted.

5. Pharmacological properties
5. Pharmacodynamic properties
Metronidazole is a 5-nitroimidazole derivative with activity against anaerobic bacteria and protozoa. It also has a radiosensitising effect on hypoxic tumour cells. Its mechanism of action is thought to involve interference with DNA by a metabolite in which the nitro group of metronidazole has been reduced. Metronidazole is active against several protozoa including Balantidium coli, Blastocystis hominis, Entamoeba histolytica, Giardia intestinalis (Giardia lamblia), and Trichomonas vaginalis. Most obligate anaerobic bacteria, including Bacteroides and Clostridium spp., are sensitive in vitro to metronidazole. It is bactericidal. It also has activity against the facultative anaerobes Gardnerella vaginalis and Helicobacter pylori and against some spirochaetes.
Metronidazole has well-established bactericidal activity against obligate anaerobic bacteria in vitro, including the Gram-negative organisms Bacteroides fragilis and other Bacteroides spp., Fusobacterium spp., and Veillonella spp., and the Gram-positive organisms Clostridium difficile, Cl. perfringens, and other Clostridium spp., Eubacterium spp., Peptococcus spp., and Peptostreptococcus spp.; Propionibacterium and Actinomyces spp. are often resistant. It also has activity against the facultative anaerobe Gardnerella vaginalis, although its bactericidal effect is reported to be much slower than against obligate anaerobes, against some strains of Campylobacter spp. including C. fetus subsp. jejuni, and against Helicobacter pylori.
The oxidative metabolites of metronidazole also have antibacterial activity; the hydroxy metabolite has been reported to be consistently more active than metronidazole against strains of G. vaginalis.

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.

5.3 Preclinical safety data
Epidemiological studies have provided no clear evidence of an increased carcinogenic risk in humans.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium saccharin
Xanthan gum
Sodium CMC
Simethicone (30%)
Colour sunset yellow
Tween 80
Sodium methylparaben
Sodium propyl paraben
Sodium benzoate
Aerosil 200
Strawberry flavor
Citric acid
Bronopol
Monopropylene glycol
Sorbitol
Purified water.

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C. Protect from light.
Keep all medicines out of reach of children.

6.5 Nature and contents of container

Amber coloured 60ml and 100ml PET bottles in a unit box

7. Marketing authorization holder

Dawa Limited,
Plot No.7879/8 Baba Dogo Road, Ruaraka
P.O Box 16633-00620 Nairobi –Kenya

8. Marketing authorization holder

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Plot No.7879/8 Baba Dogo Road, Ruaraka
P.O Box 16633-00620 Nairobi –Kenya

9. Legal category: Prescription only medicine, **(POM)**

10. Date of revision of the text

August 2018.