This package insert is continually updated: please read carefully before using a new pack. In case of any question, please contact your physician or pharmacist.

Composition:
Flagyl 200mg Tablet: Each film coated tablet contains 200mg of Metronidazole B.P.
Flagyl 400mg Tablet: Each film coated tablet contains 400mg of Metronidazole B.P.
Flagyl Suspension: Each 5ml of suspension contains Metronidazole Benzoate equivalent to 200mg of Metronidazole B.P.
Flagyl Infusion: Each 100ml bottle contains 500mg of Metronidazole B.P. (0.5%W/V).

Pharmaco-therapeutic class:
Antiamoebic, Anti-infective

Therapeutic indications:

Intravenous Infusion
Flagyl is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria have been identified or are suspected to be the cause.
Flagyl is active against a wide range of pathogenic micro-organisms notably species of Bacteroides, Fusobacteria, Clostridia, Eubacteria, anaerobic cocci and Gardnerella vaginalis.

It is indicated in
-- The prevention of postoperative infections due to anaerobic bacteria, particularly species of Bacteroides and anaerobic Streptococci.
-- The treatment of septicaemia, bacteraemia, peritonitis, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis, and post-operative wound infections from which pathogenic anaerobes have been isolated.

Oral route of Administration:
Flagyl is indicated in the prophylaxis and treatment of infections in which anaerobic bacteria have been identified or are suspected to be the cause.
Flagyl is active against a wide range of pathogenic micro-organisms notably species of Bacteroides, Fusobacteria, Clostridia, Eubacteria, anaerobic cocci and Gardnerella vaginalis. It is also active against Trichomonas, Entamoeba histolytica, Giardia lamblia and Balantidium coli.

If it is indicated in
1. The prevention of post-operative infections due to anaerobic bacteria, particularly species of Bacteroides and anaerobic Streptococci.
2. The treatment of septicaemia, bacteraemia, peritonitis, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis, and post-operative wound infections from which pathogenic anaerobes have been isolated.
3. Urogenital trichomoniases in the female (trichomonal vaginitis) and in the male.
4. Bacterial vaginosis (also known as non-specific vaginitis, anaerobic vaginosis or Gardnerella vaginitis).
5. All forms of amoebiasis (intestinal and extra-intestinal disease and that of...
6. Giardiasis.
7. Acute ulcerative gingivitis.
8. Anaerobically-infected leg ulcers and pressure sores.
9. Acute dental infections (e.g. acute pericoronitis and acute apical infections).

**Dosage and administration:**

**Intravenous Infusion**

Flagyl injection should be infused intravenously at an approximate rate of 5ml/min. Oral medication should be substituted as soon as feasible.

**Anaerobic Infections:** Treatment for seven days should be satisfactory for most patients but, depending upon clinical and bacteriological assessments, the physician might decide to prolong treatment e.g. for the eradication of infection from sites which cannot be drained or are liable to endogenous recontamination by anaerobic pathogens from the gut, oropharynx or genital tract.

**Prophylaxis against anaerobic infection:** Chiefly in the context of abdominal (especially colorectal) and gynaecological surgery.

**Adults**

500mg shortly before operation, repeated 8 hourly. Oral doses of 200 mg or 400 mg 8 hourly to be started as soon as feasible.

**Children**

7.5 mg/kg (1.5 ml/kg) 8 hourly.

**Treatment of established anaerobic infections:** Intravenous route is to be used initially if patient’s symptoms preclude oral therapy.

**Adults**

500 mg 8 hourly.

**Children**

7.5mg/kg 8 hourly.

- Initial loading dose, 15 mg/kg IV infused over 60 minutes
- Term infants, maintenance, 7.5 mg/kg IV every 24hrs, starting 48 hrs after initial dose
- Term infants, (1-4 weeks of age) maintenance, 7.5 mg/kg IV every 12 hrs starting 24 hrs after the initial dose
- Infants and children, maintenance, 30 mg/kg/day IV divided every 6 hr; maximum 4 g/day

**Elderly**

Caution is advised in the elderly. Particularly at high doses although there is limited information available on modification of dosage.

**Oral route of administration:**

Flagyl tablets should be swallowed with water (not chewed). It is recommended that the tablets be taken during or after a meal.

**Anaerobic infections:** The duration of a course of Flagyl treatment is about 7 days but it will depend upon the seriousness of the patient’s conditions assessed clinically and bacteriologically.

**Prophylaxis against anaerobic infection:** Chiefly in the context of abdominal (especially colorectal) and gynaecological surgery.

**Adults**

400 mg 8 hourly intervals during 24 hours immediately preceding operation followed by postoperative intravenous or rectal administration until the patient is able to take tablets.
**Children**
7.5 mg/kg - 8 hourly.

**Treatment of established anaerobic infection**

**Adults**
800 mg followed by 400 mg 8 hourly.

**Children**
7.5 mg/kg 8 hourly

**Protozoal and other infections**

<table>
<thead>
<tr>
<th>Dosage is given in terms of metronidazole or metronidazole equivalent</th>
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<tbody>
<tr>
<td><strong>Duration of dosage in days</strong></td>
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<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td><strong>7 to 10 years</strong></td>
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<tr>
<td><strong>Mucocutaneous</strong></td>
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<td><strong>Trichomoniasis</strong></td>
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<td><strong>Where re-infection is likely, in adults</strong></td>
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<td><strong>Bacterial vaginosis</strong></td>
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<td><strong>Amoebiasis</strong></td>
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<tr>
<td><strong>(a) Invasive intestinal disease in susceptible subjects</strong></td>
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<tr>
<td><strong>(b) Intestinal disease in less susceptible subjects and chronic amoebic hepatitis</strong></td>
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<tr>
<td><strong>(c) Amoebic liver abscess also other forms of extra-intestinal amoebiasis</strong></td>
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<tr>
<td><strong>(d) Symptomatic cyst passers</strong></td>
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**Product:** Flagyl (Tablet, Susp. & Infusion)

**Component:** Leaflet (Page 3 / 8)

**SAP No.:** 513016

**Code No.:** 513016-03

**Version:** 1

**Logo Version:** Brand Name is set in OSAV Bold

**Min. font size:** 8

**Size (W x H):** 420 x 168 mm

**PCM:** PCM 1 (10mm)

**Colour Scheme:** Reflex Blue

**Country:** sanofi-aventis Pakistan limited
Korangi Industrial Area, Karachi.

**Prepared by:** M. Jahangir

**Checked & Reviewed by:**

**QC. Officer:** Mammona F. Naqvi
**DRA Associate:** Dr. Amanullah Khan
**Assist. Medical Manager:** S. Salman Ahmed

**Date:**

**Approved By:**

**Title:** DRA Director
**Date:**

**Title:** Medical Director
**Date:**

**Title:** Head IQC
**Date:**
Contraindications:
Hypersensitivity to imidazoles.

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

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

If for compelling reasons, metronidazole must be administered longer than the usually recommended duration, it is recommended that hematological tests, especially leukocytes count should be carried out regularly and that patients should be monitored for adverse reactions such as peripheral or central neuropathy (such as paresthesia, ataxia, dizziness, convulsive seizures).

Flagyl should be administered with caution to patients with hepatic encephalopathy.

Patients should be warned that metronidazole may darken urine (due to metronidazole metabolite).

Driving a Vehicle or Performing Other Hazardous Tasks:
Patients should be warned about the potential for confusion, dizziness, hallucinations, convulsions or transient visual disorders, and advised not to drive or operate machinery if these symptoms occur.

Interactions:
Disulfiram: psychotic reactions have been reported in patients who were using metronidazole and disulfiram concurrently.

Alcohol: alcoholic beverages and drugs containing alcohol should not be consumed during therapy and for at least one day afterward because of a possibility of a disulfiram like reaction (antabuse effect: flushing, vomiting and tachycardia)

Oral anticoagulant therapy (warfarin type): potentiation of the anticoagulant effect and increased hemorrhagic risk caused by decreased hepatic catabolism. In case of coadministration, prothrombin time should be more frequently monitored and anticoagulant therapy adjusted during treatment with metronidazole.
**Lithium:** Plasma levels of lithium may be increased by metronidazole. Plasma concentration of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

**Cyclosporin:** risk of elevation of cyclosporin serum levels. Serum cyclosporin and serum creatinine should be closely monitored when coadministration is necessary.

**Phenytoin or Phenobarbital:** increased elimination of metronidazole resulting in reduced plasma levels.

**5 Fluorouracil:** reduced clearance of 5 fluorouracil resulting in increased toxicity of 5 fluorouracil.

**Busulfan:** Plasma levels of busulfan may be increased by metronidazole, which may lead to severe busulfan toxicity.

**Pregnancy:**
As metronidazole crosses the placental barrier and as its effects on human fetal organogenesis are not known, its use in pregnancy should be carefully evaluated.

**Lactation:**
As metronidazole is excreted in human milk, unnecessary exposure to the drug should be avoided.

**Adverse Reactions:**

**Gastrointestinal effects**
- Epigastric pain, nausea, vomiting, diarrhea.
- Oral mucositis, taste disorders, anorexia.
- Exceptional and reversible cases of pancreatitis.

**Hypersensitivity reactions**
- Rash, pruritus, flushing, urticaria.
- Fever, angioedema, exceptional anaphylactic shocks.
- Very rare pustular eruptions.

**Peripheral and central nervous system**
- Peripheral sensory neuropathy.
- Headache, convulsions, dizziness.
- Very rare reports of encephalopathy (e.g. confusion) and subacute cerebellar syndrome (e.g. ataxia, dysarthria, gait impairment, nystagmus, and tremor), which may resolve with discontinuation of the drug.

**Psychiatric disorders**
- Psychotic disorders including confusion, hallucinations.
- Vision disorders.
- Transient vision disorders such as diplopia, myopia.

**Haematology**
- Very rare cases of agranulocytosis, neutropenia and thrombocytopenia have been reported.

**Liver**
- Very rare cases of reversible abnormal liver function tests and cholestatic hepatitis sometimes with jaundice have been reported.

**Overdose:**
Symptoms were limited to vomiting, ataxia and slight disorientation. Single oral doses of metronidazole up to 12g have been reported in suicide attempts and accidental overdose.

**Management of Overdose**
There is no specific antidote for metronidazole over dosages. In case of suspected

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**ARTWORK LEGEND**

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massive over dosages, a symptomatic and supportive treatment should be instituted.

Storage and instructions:
For Tablets and Infusion: Store below 30°C.
For Suspension: Store below 25°C.

Keep protect from light.
Keep medicines out of the reach of children.

Special instructions:
Intravenous Infusion: Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
Suspension: Shake well before use

Expiry date:
Do not use later than the date of expiry.

Presentations:
Flagyl Infusion: Solution for intravenous infusion in 100 ml bottle.
Flagyl Suspension: Bottle of 60 ml Suspension.
Flagyl Tablet 200mg: Film-coated tablets of 200 mg, box of 20 x 10.
Flagyl Tablet 400mg: Film-coated tablets of 400 mg, box of 20 x 10.

Manufactured by:
sanofi-aventis Pakistan limited
Plot No. 23, Sector 22, Korangi Industrial Area, Karachi

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