Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

FLAGEN IV 0.5% w/v

2. Qualitative and quantitative composition

Each ml of solution contains 5 mg of metronidazole.
Each 100 ml of solution contains 500 mg of metronidazole.
Excipient(s) with known effect
Sodium Chloride USP 0.9gm per 100ml bottle

For full list of excipients see 6.1

3. Pharmaceutical form

Solution for intravenous infusion
Clear to pale-yellow solution.

4. Clinical particulars

4.1 Therapeutic indications

Metronidazole Injection USP 0.5% w/v is indicated in adults and children when oral medication is not possible for the following indications:
The prophylaxis and treatment of postoperative infections due to sensitive anaerobic bacteria particularly species of Bacteroides and anaerobic Streptococci, during abdominal, gynaecological gastrointestinal or colorectal surgery which carries a high risk of occurrence of this type of infection.
The treatment of peritonitis, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, and post-operative wound infections from which pathogenic anaerobes have been isolated.
Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

4.2 Posology and method of administration

Method of Administration
Metronidazole Injection USP 0.5% w/v should be infused intravenously at an approximate rate of 5 ml/minute (or one bag infused over 20 to 60 minutes). Oral medication should be substituted as soon as feasible.
Prophylaxis against postoperative infections caused by anaerobic bacteria:
Primarily in the context of abdominal, (especially colorectal) and gynaecological surgery.

Antibiotic prophylaxis duration should be short, mostly limited to the post operative period (24 hours but never more than 48 hours). Various schedules are possible.
Adults: Intra-venous injection of single dose of 1000mg-1500mg, 30-60 minutes preoperatively or alternatively 500mg immediately before, during or after operation, then 500mg 8 hourly.
Children < 12 years: 20-30 mg/kg as a single dose given 1-2 hours before surgery.
New-borns with a gestation age <40 weeks: 10 mg/kg body weight as a single dose before operation.
Anaerobic infections:
Intravenous route is to be used initially if patient symptoms preclude oral therapy. Various schedules are possible.
Adults: 1000mg – 1500mg daily as a single dose or alternatively 500mg every 8 hours.
Children > 8 weeks to 12 years of age: The usual daily dose is 20-30mg/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 new-borns 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 preferably be monitored after a few days of therapy.
Oral medication could be given, at the same dose regimen. Oral medication should be substituted as soon as feasible.
Duration of Treatment
Treatment for seven to ten 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.

Elderly Population

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

Patients with renal failure

Routine adjustments of the dosage of Metronidazole are not considered necessary in the presence of renal failure.
No routine adjustment in the dosage of Metronidazole needs to be made in patients with renal failure undergoing intermittent peritoneal dialysis (IDP) or continuous ambulatory peritoneal dialysis (CAPD). However, dosage reduction may be necessary when excessive concentrations of metabolites are found.
In patients undergoing haemodialysis, Metronidazole should be re-administered immediately after haemodialysis

Patients with advanced hepatic insufficiency

In patients with advanced hepatic insufficiency a dosage reduction with serum level monitoring is necessary.

4.3 Contraindication

Hypersensitivity to the active substance metronidazole or other nitroimidazole derivatives or to any of the excipients listed in section 6.1
Pregnancy - metronidazole should not be used in the first trimester in patients with trichomoniasis or bacterial vaginosis (see section 4.6).
Breast feeding should be discontinued for 12-24 hours when single high dose (e.g., 2g) therapy is used (see section 4.6).

4.4 Special warnings and precautions for use

Patients with hepatic impairment

In patients with severe liver damage metronidazole should only be used if its expected benefits clearly outweigh potential hazards.
Metronidazole is mainly metabolized 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 the encephalopathy. Metronidazole should therefore be administered with caution to patients with hepatic encephalopathy. (see section 4.2).
Due to the risk of aggravation, metronidazole should also be used in patients with active or chronic severe peripheral and central nervous system diseases only if its expected benefits clearly outweigh potential hazards.
Convulsive seizures, myoclonus and peripheral neuropathy, the latter mainly characterized by numbness or paresthesia of an extremity, have been reported in patients treated with metronidazole. The appearance of abnormal neurological signs demands the prompt evaluation of the benefit/risk ratio of the continuation of therapy.
Patients should be advised not to take alcohol during Metronidazole therapy and at least 48 hours afterwards because of a disulfram-like effect (flushing, vomiting, tachycardia).
In the case of severe hypersensitivity reactions (e.g. anaphylactic shock), treatment with Metronidazole 500 mg/100 ml Solution for Infusion must be discontinued immediately and established emergency treatment must be initiated by qualified healthcare professionals.
Severe persistent diarrhoea occurring during treatment or during the subsequent weeks may be due to pseudomembranous colitis (in most cases caused by *clostridium difficile*), see section 4.8. This intestinal disease, precipitated by the antibiotic treatment, may be life-threatening and requires immediate appropriate treatment. Anti-peristaltic medicinal products must not be given.
The duration of therapy with metronidazole or drugs containing other nitroimidazoles should not exceed 10 days. Only in specific elective cases and if definitely needed, the treatment period may be extended, accompanied by appropriate clinical and laboratory monitoring. Repeat

therapy should be restricted as much as possible and to specific elective cases only. These restrictions must be observed strictly because the possibility of metronidazole developing mutagenic activity cannot be safely excluded and because in animal experiments an increase of the incidence of certain tumours has been noted.

Active Central Nervous System disease:

Metronidazole should be used with caution in patients with active disease of the Peripheral and Central Nervous System. Severe neurological disturbances (including seizures and peripheral and optic neuropathies) have been reported in patients treated with metronidazole. Stop metronidazole treatment if any abnormal neurologic symptoms occur such as ataxia, dizziness, confusion or any other CNS adverse reaction. The risk of aggravation of the neurological state should be considered in patients with fixed or progressive paraesthesia, epilepsy and active disease of the central nervous system except for brain abscess.

Encephalopathy has been reported in association with cerebellar toxicity characterized by ataxia, dizziness, dysarthria, and accompanied by CNS lesions seen on magnetic resonance imaging (MRI). CNS symptoms and CNS lesions, are generally reversible within days to weeks upon discontinuation of metronidazole.

Aseptic meningitis can occur with metronidazole. Symptoms can start within hours of dose administration and generally resolve after metronidazole therapy is discontinued.

Hepatotoxicity in patients with Cockayne Syndrome

Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome with very rapid onset after treatment initiation in patients with Cockayne syndrome have been reported with products containing metronidazole for systemic use. In this population, metronidazole should not be used unless the benefit is considered to outweigh the risk and if no alternative treatment is available.

Liver function tests must be performed just prior to the start of therapy, throughout and after end of treatment until liver function is within normal ranges, or until the baseline values are reached. If the liver function tests become markedly elevated during treatment, the drug should be discontinued.

Patients with Cockayne syndrome should be advised to immediately report any symptoms of potential liver injury to their physician and stop taking metronidazole.

Renal Disease:

Metronidazole is removed during hemodialysis and should be administered after the procedure is finished.

Patients with renal impairment, including patients receiving peritoneal dialysis, should be monitored for signs of toxicity due to the potential accumulation of toxic metronidazole metabolites.

Blood Dyscrasias

Metronidazole should be used with caution in patients with evidence or history of blood dyscrasia as agranulocytosis, leukopenia and neutropenia have been observed following metronidazole administration.
Blood cell counts should be carefully monitored during prolonged therapy.
Special warnings / precautions regarding excipients
This medicinal product contains 322 mg sodium per 100 ml, equivalent to 16% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
Interference with laboratory tests

Metronidazole interferes with the enzymatic-spectrophotometric determination of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), triglycerides and glucose hexokinase resulting in decreased values (possibly down to zero).

Metronidazole has a high absorbance at the wavelength at which nicotinamide-adenine dinucleotide (NADH) is determined. Therefore, elevated liver enzyme concentrations may be masked by metronidazole when measured by continuous-flow methods based on endpoint decrease in reduced NADH. Unusually low liver enzyme concentrations, including zero values, have been reported.

Patients should be warned that Metronidazole may darken urine.

4.5 Interaction with other medicinal products and other forms of interaction

Not recommended concomitant therapy:
Disulfiram: Concurrent use of metronidazole and disulfiram may result in psychotic reactions and confusion. Metronidazole should not be given to patients who have taken disulfiram within the last two weeks.
Alcohol: Disulfiram-like effect (warmth, redness, vomiting, tachycardia). Alcohol beverage and drugs containing alcohol should be avoided. Patients should be advised not to take alcohol during Metronidazole therapy and at least 72 hours afterwards because of a disulfram-like (antabuse effect) reaction (flushing, vomiting, tachycardia).
Concomitant therapy requiring special precautions:
Oral anticoagulants (warfarin): metronidazole may increase the anticoagulant effects of warfarin and other oral anticoagulants, resulting in a prolongation of the prothrombin time and increased risk of haemorrhage (decrease in its liver catabolism). Patients taking metronidazole and warfarin or other oral coumarins concomitantly should have their prothrombin time and international normalized ratio (INR) monitored more frequently. Patients should be monitored for signs and symptoms of bleeding.
A large number of patients have been reported showing an increase in oral anticoagulant activity whilst receiving concomitant antibiotic therapy. The infectious and inflammatory status of the patient, together

with their age and general well-being are all risk factors in this context. However, in these circumstances it is not clear as to the part played by the disease itself or its treatment in the occurrence of prothrombin time disorders. Some classes of antibiotics are more likely to result in this interaction, notably fluoroquinolones, macrolides, cyclines, cotrimoxazole and some cephalosporins.
Vecuronium (non depolarising curaremimetic): Metronidazole can potentialise the effects of vecuronium.
Combinations to be considered:
5 Fluoro-uracile: increase in the toxicity of 5 fluoro-uracile due to a decrease of its clearance.
Lithium: 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 concentrations of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive Metronidazole.
Cholestyramine may delay or reduce the absorption of Metronidazole.
Phenytoin, barbiturates (phenobarbital): concomitant administration of drugs that induce microsomal liver enzyme activity, such as phenytoin or phenobarbital, may accelerate the elimination of metronidazole and therefore decrease its efficacy.
Cimetidine: concomitant administration of drugs that decrease microsomal liver enzyme activity, such as cimetidine, may cause decreased metabolism and reduced plasma clearance of metronidazole which may result in metronidazole toxicity.
Concomitant use of metronidazole and CYP3A4 substrates (e.g., amiodarone, tacrolimus, cyclosporine, carbamazepine, and quinidine) may increase respective CYP3A4-substrate plasma levels. Monitoring of plasma concentrations of CYP3A4 substrates may be necessary.
Amiodarone
QT interval prolongation and torsade de pointes have been reported with the coadministration of metronidazole and amiodarone. It may be appropriate to monitor QT interval on the ECG if amiodarone is used in combination with metronidazole. Patients treated on an outpatient basis should be advised to seek medical attention if they experience symptoms that could indicate the occurrence of torsade de pointes such as dizziness, palpitations, or syncope.
Busulfan: Plasma concentrations of busulfan may increase during concomitant treatment with metronidazole, which can result in serious busulfan toxicity such as sinusoidal obstruction syndrome, gastrointestinal mucositis, and hepatic veno-occlusive disease.
Contraceptive drugs
Some antibiotics can, in some exceptional cases, decrease the effect of contraceptive pills by interfering with the bacterial hydrolysis of steroid conjugates in the intestine and hereby reduce the re-absorption of unconjugated steroid. Therefore, the plasma levels of the active steroid decrease. This unusual interaction can occur in women with a high excretion of steroid conjugates through the bile. There are case reports

of oral contraceptive failure in association with different antibiotics, e.g. ampicillin, amoxicillin, tetracyclines and also metronidazole.

Mycophenolate mofetil

Substances that alter the gastrointestinal flora (e.g., antibiotics) may reduce the oral bioavailability of mycophenolic acid products. Close clinical and laboratory monitoring for evidence of diminished immunosuppressive effect of mycophenolic acid is recommended during concomitant therapy with anti-infective agents.

Laboratory tests:

Metronidazole may immobilise Treponema and thus may lead to falsely positive Nelson's test. Metronidazole may interfere with serum aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), triglycerides, and glucose hexokinase determinations. Metronidazole causes an increase in ultraviolet absorbance at 340 nm resulting in falsely decreased values.

4.6 Pregnancy and Lactation

Pregnancy

Metronidazole crosses the placental barrier.

Clinical data on a large number of exposed pregnancies and animal data did not show a teratogenic or foetotoxic effect. However unrestricted administration of nitroimidazolene to the mother may be associated with a carcinogenic or mutagenic risk for the unborn or newborn child.

During the first trimester, Metronidazole 500 mg/100 ml Solution for Infusion should only be used to treat severe life-threatening infections, if there is no safer alternative. During the second and third trimester, Metronidazole 500 mg/100 ml Solution for Infusion may also be used to treat other infections if its expected benefits clearly outweigh any possible risk.

Lactation:

Metronidazole is excreted in breast milk. During lactation either breast-feeding or Metronidazole should be discontinued. Also after the end of the therapy with metronidazole, nursing should not be resumed before another 2-3 days because of the prolonged half-life period of metronidazole.

Fertility

There are no clinical data relating to the effect of metronidazole on fertility.

Animal studies demonstrated adverse effects on the male reproductive system that are wholly or partially reversible after treatment withdrawal.

4.7 Effects on ability to drive and use machines

No studies have been performed following intravenous treatment with Metronidazole on the ability to drive and use machines. Patients should

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

4.8 Undesirable effects

There are no data available on adverse reactions from Baxter-sponsored clinical trials conducted with Metronidazole. The following adverse reactions have been reported with Metronidazole, listed by MedDRA System Organ Class (SOC), Preferred Term and frequency. The following frequency groupings are used: very common (≥1/10); common (≥1/100 and <1/10); uncommon (≥1/1,000 and <1/100); rare (≥1/10,000 and <1/1,000); very rare (<1/10,000) and not known (cannot be estimated from the available data).

Frequency, type and severity of adverse reactions in children are the same as in adults.

System Organ Class (SOC)	**Preferred MedDRA Term**	**Frequency**
Blood and Lymphatic System Disorders	Leukopenia Agranulocytosis Pancytopenia Neutropenia Thrombocytopenia Eosinophilia	uncommon rare rare rare rare not known
Immune System Disorder	Anaphylactic shock Jarisch-Herxheimer reaction Hypersensitivity	rare rare not known
Metabolism and Nutrition Disorders	Decreased appetite	not known
Psychiatric Disorders	Hallucinations Depression Confusional state Insomnia	rare not known not known not known
Nervous System Disorders	Dysgeusia Headache Encephalopathy Meningitis aseptic Seizure Somnolence Neuropathy peripheral Ataxia DizzinessDysarthria Hypoaesthesia Paraesthesia	common uncommon rare rare rare rare rare rare rare not known not known not known
Eye Disorders	Optic neuropathy Diplopia Myopia	rare rare rare
Cardiac Disorders	Tachycardia Palpitations	not known not known

Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea	not known
Gastrointestinal Disorders	Glossitis Stomatitis Dry mouth Pancreatitis Abdominal pain upper Diarrhoea Nausea Vomiting Constipation Tongue discoloration	common common common rare rare rare rare rare not known not known
Hepatobiliary disorders	Jaundice cholestatic	rare
Skin and Subcutaneous Disorders	Stevens-Johnson syndrome Toxic epidermal necrolysis Angioedema Erythema multiforme Pruritus Swelling face Urticaria Hyperhidrosis Rash	rare rare rare rare not known not known not known not known not known
Musculoskeletal and Connective Tissue Disorders	Myalgia Muscle spasms Arthralgia	common not known not known
Renal and urinary disorders	Chromaturia Dysuria	rare not known
General and Administration Site Conditions	Asthenia Mucosal inflammation Pyrexia Injection site reaction Malaise Face oedema Oedema peripheral Chest pain Chills	uncommon rare rare not known not known not known not known not known not known
Investigations	Hepatic enzyme increased	not known

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme.
Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

Symptoms

In cases of overdose in adults, the clinical symptoms are usually limited to nausea, vomiting and neurotoxic effects, including ataxia, slight disorientation, confusion, seizures and peripheral neurophathy.

Treatment
There is no specific treatment for Metronidazole overdose, Metronidazole infusion should be discontinued. Patients should be treated symptomatically.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Metronidazole is an anti-infectious drug belonging to the pharmacotherapeutic group of nitroimidazole derivatives, which have effect mainly on strict anaerobes. This effect is probably caused by interaction with DNS and different metabolites.
Pharmacotherapeutic group: Antibacterials for systemic use: imidazole derivatives
ATC Code: J01XD01
Pharmacotherapeutic group: Antiprotozoals: nitroimidazole derivatives
ATC Code: P01AB01.
Metronidazole has antibacterial and antiprotozoal actions and is effective against anaerobic bacteria and against Trichomonas vaginalis and other protozoa including Entamoeba histolytica and Giardia lamblia.
Anti-Microbial Spectrum:

The MIC breakpoints separating susceptible from intermediately susceptible and intermediately susceptible from resistant organisms are as following:
S ≤ 4 mg/l and R > 4 mg/l
The prevalence of acquired resistance may vary geographically and with time for selected species and local information is desirable, particularly when treating severe infections. This information gives only approximate guidance on probabilities whether microorganisms will be susceptible to Metronidazole or not.

Categories
SUSCEPTIBLE
Gram negative aerobes
Helicobacter pylori
Anaerobes
Bacteroides fragilis
Bifidobacterium>>resistant (70%)
Bilophila
Clostridium
Clostridium difficile
Clostridium perfringens

Eubacterium
Fusobacterium
Peptostreptococcus
Prevotella
Porphyromonas
Veillonella
RESISTANT
Gram positive aerobes
Actinomyces
Anaerobes
Mobiluncus
Propionibacterium acnes
ANTIPARASITIC ACTIVITY
Entamoeba histolytica
Giardia intestinalis
Trichomonas vaginalis

Cross–resistance with tinidazole occurs.

5.2 Pharmacokinetic properties

Absorption: Metronidazole is readily absorbed from the gastrointestinal tract and the oral bioavailability is > 90%. Consequently, the same mg dose will result in similar exposure (AUC) when switching between intravenous and oral dosing.

Distribution: After administration of a single 500 mg dose, mean Metronidazole peak plasma concentrations of ca. 14 – 18 µg/ml are reached at the end of a 20-minute infusion. 2-hydroxy-metabolite peak plasma concentrations of ca. 3 µg/ml are obtained after a 1 g single i.v. dose. Steady state Metronidazole plasma concentrations of about 17 and 13 µg/ml are reached after administration of Metronidazole every 8 or 12 hours, respectively.

Plasma protein binding is less than 10%, and the volume of distribution 1.1 ± 0.4 l/kg.

Metabolism: Metronidazole is metabolised in the liver by hydroxylation, oxidation and glucuronidation. The major metabolites are a 2-hydroxy- and an acetic acid metabolite.

Elimination: More than 50% of the administered dose is excreted in the urine, as unchanged Metronidazole (ca. 20% of the dose) and its metabolites. About 20% of the dose is excreted with faeces. Clearance is 1.3 ± 0.3 ml/min/kg, while renal clearance is about 0.15 ml/min/kg. The plasma elimination half-life of Metronidazole is ca. 8 hours, and of the 2-hydroxy-metabolite ca. 10 hours.
Special patient groups: The plasma elimination half-life of Metronidazole is not influenced by renal impairment; however, this may be increased for 2-hydroxy- and an acetic acid metabolite. In the case of haemodialysis, Metronidazole is rapidly excreted and the plasma elimination half-life is decreased to ca. 2.5 h. Peritoneal dialysis does not appear to affect the elimination of Metronidazole or its metabolites compared to patients with renal impairment.
In patients with impaired liver function, the metabolism of Metronidazole is expected to decrease, leading to an increase in the plasma elimination half-life. In patients with severe liver impairment, clearance may be decreased up to ca. 65%, resulting in an accumulation of Metronidazole in the body.

5.3 Preclinical safety data

Metronidazole has been shown to be non-mutagenic in mammalian cells *in vitro* and *in vivo*.
Metronidazole and a metabolite have been shown to be mutagenic is some tests with non-mammalian cells.
Although Metronidazole has been shown to be carcinogenic in certain species of mice, it was not carcinogenic in either rats or guinea pigs. There is no suspicion of carcinogenicity in man.
Daily peroral metronidazole at 5-times the maximum human daily dose for greater than 4 weeks caused testicular toxicity and infertility in male rats. Fertility was restored in most subjects by 8 weeks after cessation of treatment, whereas the lower testicular and epididymal weights and sperm counts had improved but were still observed.
Daily peroral metronidazole at approximately 6-times the maximum human daily dose for ≥2 weeks caused testicular toxicity in male mice. Most indices of testicular toxicity were restored within 2 months after cessation of treatment, whereas the lower testicular and epididymal weights had improved but were still observed.
These studies demonstrate that the adverse effects of metronidazole on the male reproductive system are wholly or partially reversible after treatment withdrawal.

6. Pharmaceutical Particulars

6.1 List of Excipients

Sodium Chloride USP
Water for Injections USP

6.2 Incompatibilities

Do not use equipment containing aluminum (e.g., needles, cannulas) that would come in contact with the drug solution as precipitates may form.

Metronidazole is incompatible with (includes but is not limited to):

- Aztreonam
- Cefamandole nafate
- Cefoxitin
- Penicillin G

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal product except for those mentioned in 6.6.

6.3 Shelf-Life

Unopened

3 years.

After first opening the container

Unused contents must be discarded and not be stored for later use.

6.4 Special Precautions for storage

Keep container in the outer carton in order to protect from light. Store below 30^{o}C

6.5 Nature and Content of container

The product is supplied in Polyethylene bottles, contents: 100ml

6.6 Special precautions for disposal and other handling

Use only if the solution is clear, without visible particles and if the container is undamaged. Administer immediately following the insertion of infusion set.

Do not remove unit from overpouch until ready for use.

The inner bag maintains the sterility of the product.

Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed.

Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

In patients maintained on intravenous fluids, Metronidazole Injection USP 0.5% w/vmay be diluted with appropriate volumes of 0.9% sodium chloride solution, dextrose 5% - 0.9% sodium chloride solution, dextrose 5% w/v or potassium chloride infusions (20 and 40 mmol/litre).
Using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In the case of adverse reaction, infusion must be stopped immediately.
Additives:
Additives known or determined to be incompatible should not be used.
Before adding a substance or medication, verify that it is soluble and stable in metronidazole, and that the pH range of metronidazole is appropriate. Additives may be incompatible. When introducing additives, the instructions for use of the medication to be added and other relevant literature must be consulted.
Mix the solution thoroughly when additives have been introduced.
After addition, if there is a color change and/or the appearance of precipitates, insoluble complexes or crystals, do not use.
Do not store solutions containing additives.
The product should be used immediately after opening.
Discard after single use.
Discard any unused portion.
Do not reconnect partially used bags.
1. Opening
a. Remove the Viaflo container from the overpouch just before use.
b. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution, as sterility may be impaired.
c. Check the solution for limpidity and absence of foreign matters. If solution is not clear or contains foreign matters, discard the solution.
2. Preparation for administration
Use sterile material for preparation and administration.
a. Suspend container from eyelet support.
b. Remove plastic protector from outlet port at bottom of container:
- grip the small wing on the neck of the port with one hand,
- grip the large wing on the cap with the other hand and twist,
- the cap will pop off
c. Use an aseptic method to set up the infusion
d. Attach administration set. Refer to complete directions accompanying set for connection, priming of the set and administration of the solution.

7. Marketing Authorization Holder

GOODMED PHARMACY LTD.
Hass Plaza, lower Hill Road
P.O Box 76337-00508
Nairobi, Kenya.

8. Marketing Authorization Number

CTD10439

9. Date of first authorization/renewal of the authorization
07/02/2025

10. Date of revision of the text
5/5/2025