SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

FOR

UNIGYL® (Metronidazole Injection)

1. NAME OF THE MEDICINAL PRODUCT

UNIGYL®
Metronidazole Injection
For Intravenous Infusion U.S.P (500 mg / 100 ml)

Strength

Each 100 ml contains:

Metronidazole U.S.P ……. 500 mg
Sodium Chloride B.P……..806.6mg
Water for injection BP...qs……..100ml

Pharmaceutical/Dosage form

Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 ml contains:

Metronidazole U.S.P ……. 500 mg
Sodium Chloride B.P……..806.6mg
Water for injection BP... qs…….100ml

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Infusion
A clear, almost colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Unigyl® Metronidazole Injection is indicated in adults and children when oral medication is not possible for the following indications:
- The prophylaxis 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 solution may also be used in combination with an antibiotic active against aerobic bacteria.
- The treatment of severe intraabdominal and gynaecological infections in which sensitive anaerobic bacteria particularly Bacteriodes and anaerobic Streptococci have been identified or are suspected to be the cause.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Method of Administration
Unigyl® Metronidazole Injection 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.
Newborns 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. The 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 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.
Bacterial vaginosis:
Adolescents: 400 mg twice daily for 5-7 days or 2000 mg as a single dose
Urogenital trichomoniasis
Adults and adolescents: 2000 mg as a single dose or 200 mg 3 times daily for 7 days or 400 mg twice daily for 5-7 days
Children < 10 years: 40 mg/kg orally as a single dose or 15 – 30 mg/kg/day divided in 2-3 doses for 7 days; not to exceed 2000 mg/dose
Giardiasis:
> 10 years: 2000 mg once daily for 3 days, or 400 mg three times daily for 5 days, or 500 mg twice daily for 7 to 10 days
Children 7 to 10 years: 1000 mg once daily for 3 days
Children 3 to 7 years: 600 to 800 mg once daily for 3 days
Children 1 to 3 years: 500 mg once daily for 3 days
Alternatively, as expressed in mg per kg of body weight: 15-40 mg/kg/day divided in 2-3 doses.
Amoebiasis:
> 10 years: 400 to 800 mg 3 times daily for 5-10 days

Children 7 to 10 years: 200 to 400 mg 3 times daily for 5-10 days
Children 3 to 7 years: 100 to 200 mg 4 times daily for 5-10 days
Children 1 to 3 years: 100 to 200 mg 3 times daily for 5-10 days
Alternatively, doses may be expressed by body weight 35 to 50 mg/kg daily in 3 divided doses for 5 to 10 days, not to exceed 2400 mg/day
Eradication of Helicobacter pylori in paediatric patients:
As a part of a combination therapy, 20 mg/kg/day does not exceed 500 mg twice daily for 7-14 days.
Official guidelines should be consulted before initiating therapy
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 Contraindications

Hypersensitivity to the active substance, to other imidazole derivatives or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Liver disease:
Caution is needed in patients with severe hepatic impairment. The dose of **Unigyl®** Metronidazole Injection should be reduced as necessary. Metronidazole is mainly metabolised by hepatic oxidation. Substantial impairment of Metronidazole clearance may occur in the presence of advanced hepatic insufficiency. The risk/benefit ratio of using **Unigyl®** Metronidazole Injection to treat trichomoniasis in such patients should be carefully considered (for dosage adjustment see section 4.2). Plasma levels of Metronidazole should be closely monitored.
Caution is needed in patients with hepatic encephalopathy. Patients with severe hepatic encephalopathy metabolize metronidazole slowly, with resultant accumulation of metronidazole. This may cause exacerbation of CNS adverse effects. The dose of **Unigyl®** Metronidazole Injection should be reduced as necessary.
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, **Unigyl®** Metronidazole Injection should therefore be used after careful benefit-risk assessment and only 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.
Active Central Nervous System disease:
Metronidazole should be used with caution in patients with active diseases 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 (see section 4.8).
Blood Dyscrasias
Unigyl® Metronidazole Injection 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.
Renal Disease:
Unigyl® Metronidazole Injection is removed during haemodialysis 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.
Sodium restricted patients:
This medicinal product contains 13.5 mmol (310 mg) sodium per 100 mL. To be taken into consideration by patients on a controlled sodium diet.
Alcohol:
Patients should be advised to discontinue consumption of alcoholic beverages or alcohol-containing products before, during, and up to 72hours after taking **Unigyl®** Metronidazole Injection because of a disulfram-like effect (abdominal cramps, nausea, headaches, flushing, vomiting and tachycardia). See section 4.5.
Intensive or prolonged Metronidazole therapy:
As a rule, the usual duration of therapy with i.v Metronidazole or other imidazole derivatives is usually less than 10 days. This period may only be exceeded in individual cases after a very strict benefit-risk assessment. Only in the rarest possible case should the treatment be repeated. Limiting the duration of treatment is necessary because damage to human germ cells cannot be excluded.
Intensive or prolonged Metronidazole therapy should be conducted only under conditions of close surveillance for clinical and biological effects and under specialist direction. If prolonged therapy is required, the physician should bear in mind the possibility of peripheral neuropathy or leucopenia. Both effects are usually reversible.
In case of prolonged treatment, occurrence of undesirable effects such as paraesthesia, ataxia, dizziness and convulsive crises should be checked. High dose regimes have been associated with transient epileptiform seizures.
Monitoring:
Due to increased risk for adverse reactions, regular clinical and laboratory monitoring (including blood count) are advised in cases of high-dose, prolonged or repeated treatment, in case of antecedents of blood dyscrasia, in case of severe infection and in severe hepatic insufficiency.
General:
Patients should be warned that **Unigyl®** Metronidazole Injection may darken urine (due to Metronidazole metabolite).

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. **Unigyl®** Metronidazole Injection 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 **Unigyl®** Metronidazole Injection therapy and at least 72 hours afterwards because of a disulfram-like (antabuse effect) reaction (flushing, vomiting, tachycardia).
Concomitant therapy requires special precautions:
Oral anticoagulants (warfarin): **Unigyl®** Metronidazole Injection 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.
Many 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): **Unigyl®** Metronidazole Injection 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 plasma concentrations of CYP3A4 substrates may be necessary.
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.
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 Fertility, pregnancy and lactation

Pregnancy
Metronidazole crosses the placental barrier.

Clinical data on many 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.
Therefore, Metronidazole should not be given during pregnancy unless clearly necessary.
Lactation
Metronidazole is excreted in breast milk. During the lactation either breast-feeding or Metronidazole should be discontinued.
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 (see section 5.3).

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. Some adverse reactions to metronidazole such as seizure, dizziness, optic neuropathy, may impair the ability to drive or operate machines (see section 4.8).
Therefore, it is recommended that patients should not drive or use machines.

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.

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
Pharmacotherapeutic group: Antiprotozoals: nitroimidazole derivatives
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 tindazol occurs.

5.2 Pharmacokinetic properties

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 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 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 (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

S. No	Composition	Reference
1.	Sodium Chloride	BP
2.	Water for Injections	BP

6.2 Incompatibilities

Do not use equipment containing aluminum (e.g., needles, cannulae) 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 products except for those mentioned in 6.6.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and contents of container

The product is supplied in LDPE (Low-density polyethylene) bottle containing 100ml of sterile solution of Metronidazole 500mg/100ml.

The bottle is overwrapped with nylon wrapper composed of Plain Biaxially Oriented Polypropylene (Plain BOPP). Each bottle is packed into printed inner cartons together with leaflet insert. The bottles are then packed into cardboard cartons to contain 100 x 100ml bottles per carton.

Pack sizes: 100 ml

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.
The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution to 0000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000prevent air entering the system.
In patients maintained on intravenous fluids, **Unigyl®** Metronidazole Injection may 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 (see Section 6.2).
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.

7. APPLICANT/HOLDER OF CERTIFICATE PRODUCT REGISTRATION.

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8. DRUG PRODUCT MANUFACTURER
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9. NAFDAC REGISTRATION NUMBER(S)

04-0373

10. DATE OF REVISION OF THE TEXT

20/12/2028