



## Important Prescribing Information

October 9, 2017

### Subject: Temporary importation of intravenous drug products to address drug shortages

Dear Healthcare Professional,

In order to address shortages of critical drug products from the aftermath of Hurricane Maria, Baxter Healthcare Corporation (Baxter) is coordinating with the U.S. Food and Drug Administration (FDA) to increase the availability of products from Baxter's manufacturing facility in Ireland.

Baxter has initiated temporary importation of the products tabulated below. These products are manufactured by Baxter's manufacturing facility in Ireland and marketed in Europe. The information contained in this letter pertains only to the products listed below. You may be provided with additional letters depending on the products you receive. Please read each letter in its entirety because the letters may contain different information. At this time, no other entity except Baxter is authorized by the FDA to import or distribute these products in the United States. FDA has not approved the listed products manufactured by Baxter's manufacturing facility in Ireland.

Effective immediately, and during this temporary period, Baxter will offer the following:

Product name and description	Size	Product code	NDC
Sodium Chloride 0.9% w/v Intravenous Infusion, BP, MINI-BAG Plus in VIAFLEX plastic container	50 mL	FPB0042G	0338-9613-30
	100 mL	FPB0043G	0338-9616-30
Sodium Chloride 0.9% w/v Intravenous Infusion, BP, in VIAFLO container	50 mL	FE1306G	0338-9546-50
	100 mL	FE1307	0338-9550-50
Glucose 5% w/v Intravenous Infusion BP* in VIAFLO container	50 mL	FE0086G	0338-9547-50
	100 mL	FE0087	0338-9551-50
Metronidazole Injection 500mg Isotonic Saline in VIAFLO container	100 mL	FE3400G	0338-9554-50

BP = British Pharmacopoeia

\* dextrose monohydrate (or glucose monohydrate) = anhydrous dextrose (or anhydrous glucose)

There are some key differences in the labeling between the U.S. marketed products and the European products. Please see the product comparison tables at the end of this letter for:

- Table 1. Key differences in 0.9% Sodium Chloride Injections
- Table 2. Key differences in 5% Dextrose/Glucose Injections
- Table 3. Key differences in Metronidazole Injections

Dosage and administration instructions provided in the FDA package insert should be followed when administering the products. It is also important to note the following:

- **The barcode may not register accurately on the U.S. scanning systems.** Institutions should manually input the product into their systems and confirm that barcode systems do not provide incorrect information when the product is scanned. Alternative procedures should be followed to assure that the correct drug product is being used and administered to individual patients.
- **While the injection or medication ports are similar** across the FDA-approved products in the VIAFLEX (PVC) container and the imported products in the VIAFLO (non-PVC) containers, **the administration port for the imported VIAFLO (non-PVC) containers needs to be twisted off rather than pulled off.** See photos of each port in tables below.
- The imported VIAFLO (non-PVC) container's administration port system is fully compatible with IV set spike heads that meet the International Organization of Standardization (ISO) standards and with Baxter IV sets marketed in the United States.
- **Prior to use, it is important to check for leaks** by squeezing the inner bag firmly. If leaks are found, discard solution as sterility may be impaired. Additionally, check to see that solution is clear and free of foreign matter. Discard the solution if solution is not clear.

The U.S. approved products are only available by prescription.

**Please refer to the FDA-approved package insert for the full prescribing information of each drug product** as follows:

- 0.9% Sodium Chloride Injection, USP, MINI-BAG Plus Container in Viaflex plastic container (click [here](#))
- 0.9% Sodium Chloride Injection, USP, in Viaflex plastic container (click [here](#))
- 5% Dextrose Injection, USP, in Viaflex plastic container (click [here](#))
- Metronidazole Injection, USP, 500mg/100 mL, in Viaflex plastic container (click [here](#))

If you have any questions about the information contained in this letter or the use of the imported products, please contact Baxter's Medical Information Service at 1-800-933-0303.

To place an order, please contact Baxter's Center for Service by calling 1-888-229-0001.

To report product quality issues please contact Baxter Product Surveillance at 1-800-437-5176.

To report adverse events associated with these imported products, please call Baxter at 1-866-888-2472, or fax: 1-800-759-1801. Adverse events or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax:

- Complete and submit the report **Online:** [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)
- **Regular mail or Fax:** Download form [www.fda.gov/MedWatch/getforms.htm](http://www.fda.gov/MedWatch/getforms.htm) or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.



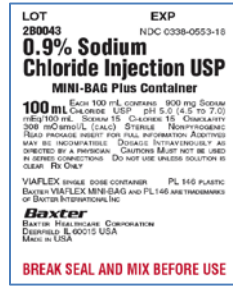
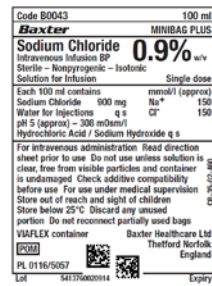




Sincerely,

Scott P. Luce  
General Manager, US Hospital Products  
Baxter Healthcare Corporation

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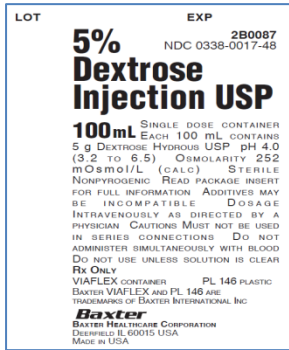



# Product Comparison Tables

**Table 1. Key differences in 0.9% Sodium Chloride Injections**

	US FDA approved product	Import product	USA FDA approved product	Import product
				
<b>Product name</b>	<b>0.9% Sodium Chloride Injection, USP</b>	<b>Sodium Chloride 0.9% w/v Intravenous Infusion, BP</b>	<b>0.9% Sodium Chloride Injection, USP MINI-BAG Plus</b>	<b>Sodium Chloride 0.9% w/v Intravenous Infusion, BP MINI-BAG Plus</b>
<b>Indications</b>	Sodium Chloride Injection, USP is indicated as a source of water and electrolytes.  0.9% Sodium Chloride Injection, USP is also indicated for use as a priming solution in hemodialysis procedures.	Sodium Chloride 0.9% Intravenous Infusion, BP is used to treat: <ul style="list-style-type: none"> <li>• a loss of body water (dehydration),</li> <li>• a loss of sodium from the body (sodium depletion)</li> </ul> Sodium Chloride 0.9% Intravenous Infusion, BP may also be used to deliver or to dilute other medicines for infusion.	0.9% Sodium Chloride Injection, USP is indicated as a source of water and electrolytes and may also be used as diluent for reconstitution of a powdered drug product packaged in a vial with a 20 mm closure.	Sodium Chloride 0.9% Intravenous Infusion, BP is used to treat: <ul style="list-style-type: none"> <li>• a loss of body water (dehydration),</li> <li>• a loss of sodium from the body (sodium depletion)</li> </ul> Sodium Chloride 0.9% Intravenous Infusion, BP may also be used to deliver or to dilute other medicines for infusion.
<b>Active ingredients*</b>	Each 100 mL contains 900 mg Sodium Chloride, USP Sodium 154 mEq/L Chloride 154 mEq/L	Each 100 mL contains 900mg Sodium Chloride, USP mmol per 100 mL (approx.): Sodium 15.4 Chloride 15.4	Each 100 mL contains 900 mg Sodium Chloride, USP Sodium 154 mEq/L Chloride 154 mEq/L	Each 100 mL contains 900 mg Sodium Chloride, USP mmol per L (approx.): Sodium 150 Chloride 150
<b>Additional information</b>	pH is 5.0 (4.5 to 7.0) Osmolarity 308 mOsm/L (calc)	pH 5.5 (approx) Osmolarity 308 mOsm/l (approx)	pH is 5.0 (4.5 to 7.0) Osmolarity 308 mOsmol/L (calc)	pH 5 (approx) Osmolarity 308 mOsm/l (approx)
<b>Storage conditions</b>	Room temperature (25°C/77°F); brief exposure up to 40°C/(104°F) does not adversely affect the product	Do not store above 30°C	Room temperature (25°C/77°F)	Store below 25°C
<b>Container type</b>	VIAFLEX Container (PVC)	VIAFLO container (non-PVC)	MINI-BAG Plus in VIAFLEX (PVC)	MINI-BAG Plus in VIAFLEX (PVC)
<b>Administration ports</b>	<b>Pull off port protector (blue color)</b> 	<b>Twist off port protector (white)</b> 	<b>Pull off port protector (blue color) with same adapter</b> 	<b>Twist off port protector (blue color) with same adapter</b> 

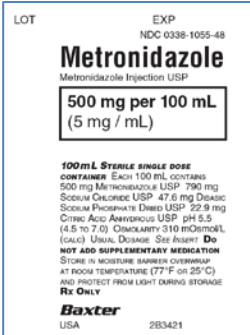



\* For monovalent ions, such as sodium and chloride, the numeric value of the millimole and milliequivalent are identical

**Table 2. Key differences in 5% Dextrose Injection**

	US FDA approved product	Import product
		
<b>Product name</b>	<b>5% Dextrose Injection USP</b>	<b>Glucose 5% w/v Intravenous Infusion BP</b>
<b>Indications</b>	Dextrose Injection, USP is indicated as a source of water and calories.	Glucose 5% Infusion is used: <ul style="list-style-type: none"> <li>• as a source of fluid and sugar (carbohydrate )</li> <li>• to dilute or to deliver other medicines that can be given by infusion.</li> </ul>
<b>Active ingredients*</b>	Each 100 mL contains 5 g Dextrose Hydrous USP	Formula per 100 ml: Glucose (as monohydrate) 5.0 g
<b>Additional information</b>	pH 4.0 (3.2 to 6.5) Osmolarity 252 mOsm/L (calculated)	pH 4.2 (approx) Osmolarity 278 mOsm/L (approx)
<b>Storage conditions</b>	Room temperature (25°C/77°F); brief exposure up to 40°C/(104°F) does not adversely affect the product.	Do not store above 30°C.
<b>Container type</b>	VIAFLEX Container (PVC)	VIAFLO container (non-PVC)
<b>Administration port images</b>	<p><b>Pull off port protector (blue color)</b></p> 	<p><b>Twist off port protector (white)</b></p> 

\* dextrose monohydrate (or glucose monohydrate) = anhydrous dextrose (or anhydrous glucose)

**Table 3. Key differences in Metronidazole Injection, USP**

	US FDA approved product	Import product
	Metronidazole Injection, USP, 500 mg/100 mL	Metronidazole 500 mg/100 ml Intravenous Infusion
		
<b>Ingredients</b>	Each 100 mL contains: 500 mg Metronidazole USP, 790 mg Sodium Chloride USP, 47.6 mg Dibasic Sodium Phosphate Dried USP, 22.9 mg Citric Acid Anhydrous USP.	Each 100 ml consists of: Metronidazole 500 mg. The other inactive ingredients (excipients) are Disodium phosphate dodecahydrate, Citric acid monohydrate, Sodium chloride and Water for injections.
<b>Additional information</b>	Each container contains 14 mEq of sodium. pH 5.5 (4.5 to 7.0) Osmolarity 310 mOsm/L (calc)	Method of Administration: Metronidazole 500 mg/100 ml should be infused intravenously at an approximate rate of 5 ml/minute (or one bag infused over 20 to 60 minutes). pH 4.5 – 6.0 (approx) Osmolarity 308 mOsmol/L (approx)
<b>Description</b>	Metronidazole Injection, USP, in 100 mL VIAFLEX Plus single dose plastic container, is a sterile, nonpyrogenic, iso-osmotic, buffered solution. Metronidazole Injection, USP is a ready-to-use iso-osmotic solution. <b>No dilution or buffering is required.</b>	The active ingredient in your medicine is metronidazole. It is an antimicrobial agent (an agent that kills micro-organisms or suppresses their multiplication and growth). Your medicine contains metronidazole 500 mg per 100 ml (5 mg per ml). This is a sterile solution for intravenous infusion free from bacterial endotoxin (substances causing fever reactions).
<b>Indications</b>	<p><b>Treatment of Anaerobic Bacterial Infections</b> Metronidazole Injection, USP is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria. Indicated surgical procedures should be performed in conjunction with Metronidazole Injection, USP therapy. In a mixed aerobic and anaerobic infection, antibiotics appropriate for the treatment of the aerobic infection should be used in addition to Metronidazole Injection, USP. Metronidazole Injection, USP is effective in <i>Bacteroides fragilis</i> infections resistant to clindamycin, chloramphenicol and penicillin.</p> <p><b>Intra-Abdominal Infections</b>, including peritonitis, intra-abdominal abscess and liver abscess, caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group (<i>B. fragilis</i>, <i>B. distans</i>, <i>B. ovatus</i>, <i>B. thetaiotaomicron</i>, <i>B. vulgatus</i>), <i>Clostridium</i> species, <i>Eubacterium</i> species, <i>Peptococcus</i> species and <i>Peptostreptococcus</i> species.</p> <p><b>Skin and Skin Structure Infections</b> caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group, <i>Clostridium</i> species, <i>Peptococcus</i> species, <i>Peptostreptococcus</i> species and <i>Fusobacterium</i> species.</p> <p><b>Gynecologic Infections</b>, including endometritis, endomyometritis, tubo-ovarian abscess and postsurgical vaginal cuff infection, caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group, <i>Clostridium</i> species, <i>Peptococcus</i> species, <i>Peptostreptococcus</i> species and <i>Fusobacterium</i> species.</p> <p><b>Bacterial Septicemia</b> caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group and <i>Clostridium</i> species.</p> <p><b>Bone and Joint Infections</b>, as adjunctive therapy, caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group.</p> <p><b>Central Nervous System (CNS) Infections</b>, including meningitis and brain abscess, caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group.</p> <p><b>Lower Respiratory Tract Infections</b>, including pneumonia, empyema and lung abscess, caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group.</p> <p><b>Endocarditis</b> caused by <i>Bacteroides</i> species including the <i>B. fragilis</i> group.</p> <p><b>Prophylaxis</b> – Please refer to full prescribing information.</p>	<p>This medicine is used when oral medication is not possible, for the prevention and treatment of infections caused by certain species of bacteria.</p> <p>It is used in adults and children for:</p> <ul style="list-style-type: none"> <li>the prevention of postoperative infections due to sensitive bacteria in surgical procedure with a high risk of occurrence of this type of infection</li> <li>the treatment of severe established abdominal and gynaecological infections where sensitive bacteria have been identified as the cause or are suspected to be the cause.</li> </ul>
<b>Administration port images</b>	<p><b>Pull off port protector (blue color)</b></p> 	<p><b>Twist off port protector (white)</b></p> 

	US FDA approved product	Import product
	Metronidazole Injection, USP, 500 mg/100 mL	Metronidazole 500 mg/100 ml Intravenous Infusion
<b>Dosage and administration</b>	<p><b>Treatment of Anaerobic Bacterial Infections</b> The recommended dosage schedule for adults is:</p> <ul style="list-style-type: none"> <li>Loading Dose 15 mg/kg infused over one hour (approximately 1 g for a 70-kg adult).</li> <li>Maintenance Dose 7.5 mg/kg infused over one hour every six hours (approximately 500 mg for a 70-kg adult). The first maintenance dose should be instituted six hours following the initiation of the loading dose.</li> </ul> <p>Parenteral therapy may be changed to oral metronidazole when conditions warrant, based upon the severity of the disease and the response of the patient to Metronidazole Injection, USP treatment. The usual adult oral dosage is 7.5 mg/kg every six hours (approximately 500 mg for a 7-kg adult). A maximum of 4 g should not be exceeded during a 24-hour period.</p> <p>The usual duration of therapy is 7 to 10 days; however, infections of the bone and joint, lower respiratory tract and endocardium may require longer treatment.</p> <p><b>Prophylaxis</b> For surgical prophylactic use, to prevent postoperative infection in contaminated or potentially contaminated colorectal surgery, the recommended dosage schedule for adults is:</p> <ol style="list-style-type: none"> <li>15 mg/kg infused over 30 to 60 minutes and completed approximately one hour before surgery; followed by</li> <li>7.5 mg/kg infused over 30 to 60 minutes at 6 and 12 hours after the initial dose. It is important that (1) administration of the initial preoperative dose be completed approximately one hour before surgery so that adequate drug levels are present in the serum and tissues at the time of initial incision, and (2) Metronidazole Injection, USP be administered, if necessary, at 6-hour intervals to maintain effective drug levels.</li> </ol> <p>Prophylactic use of Metronidazole Injection, USP should be limited to the day of surgery only, following the above guidelines.</p>	<p><b>Prophylaxis against postoperative infections caused by anaerobic bacteria:</b> Primarily in the context of abdominal, (especially colorectal) and gynaecological surgery. Antibiotic prophylaxis duration should be short, mostly limited to the postoperative period (24 hours but never more than 48 hours). Various schedules are possible.</p> <ul style="list-style-type: none"> <li>Adults: Intravenous injection of single dose of 1000 mg – 1500 mg, 30 – 60 minutes preoperatively or alternatively 500 mg immediately before, during or after operation, then 500 mg 8 hourly.</li> <li>Children &lt; 12 years: 20 – 30 mg/kg as a single dose given 1 – 2 hours before surgery.</li> <li>Newborns with a gestation age &lt; 40 weeks: 10 mg/kg body weight as a single dose before operation.</li> </ul> <p><b>Anaerobic infections:</b> Intravenous route is to be used initially if patients symptoms preclude oral therapy. Various schedules are possible.</p> <ul style="list-style-type: none"> <li>Adults: 1000 mg – 1500 mg daily as a single dose or alternatively 500 mg every 8 hours.</li> <li>Children &gt; 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.</li> <li>Children &lt; 8 weeks of age: 15 mg/kg as a single dose daily or divided into 7.5 mg/kg every 12 hours.</li> </ul> <p>In newborns with a gestation age &lt; 40 weeks, accumulation of metronidazole can occur during the first week of life, therefore the concentrations of metronidazole in serum should preferably be controlled 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.</p> <p><b>Bacterial vaginosis</b> Adolescents: 400 mg twice daily for 5 – 7 days or 2000 mg as a single dose.</p> <p><b>Urogenital trichomoniasis</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>Children &lt; 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.</li> </ul> <p><b>Giardiasis</b></p> <ul style="list-style-type: none"> <li>&gt;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.</li> <li>Children 7 to 10 years: 1000 mg once daily for 3 days.</li> <li>Children 3 to 7 years: 600 to 800 mg once daily for 3 days.</li> <li>Children 1 to 3 years: 500 mg once daily for 3 days.</li> <li>Alternatively, as expressed in mg per kg of body weight: 15 – 40 mg/kg/day divided in 2 – 3 doses.</li> </ul> <p><b>Amoebiasis</b></p> <ul style="list-style-type: none"> <li>&gt;10 years: 400 to 800 mg 3 times daily for 5 – 10 days.</li> <li>Children 7 to 10 years: 200 to 400 mg 3 times daily for 5 – 10 days.</li> <li>Children 3 to 7 years: 100 to 200 mg 4 times daily for 5 – 10 days.</li> <li>Children 1 to 3 years: 100 to 200 mg 3 times daily for 5 – 10 days.</li> <li>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.</li> </ul> <p><b>Eradication of Helicobacter pylori in paediatric patients:</b> 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.</p>
<b>Dosage adjustments</b>	<p><b>Patients with Severe Hepatic Impairment</b> For patients with severe hepatic impairment (Child-Pugh C), the metronidazole dose should be reduced by 50% (see CLINICAL PHARMACOLOGY and PRECAUTIONS).</p> <p><b>Patients Undergoing Hemodialysis</b> Hemodialysis removes significant amounts of metronidazole and its metabolites from systemic circulation. The clearance of metronidazole will depend on the type of dialysis membrane used, the duration of the dialysis session, and other factors. If the administration of metronidazole cannot be separated from a hemodialysis session, supplementation of metronidazole dosage following a hemodialysis session should be considered, depending on the patient’s clinical situation (see CLINICAL PHARMACOLOGY).</p>	<p><b>Elderly population</b> Caution is advised in the elderly, particularly at high doses, although there is limited information available on modification of dosage.</p> <p><b>Patients with renal failure</b> Routine adjustments of the dosage of Metronidazole are not considered necessary in the presence of renal failure.</p> <ul style="list-style-type: none"> <li>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.</li> <li>In patients undergoing haemodialysis, Metronidazole should be re-administered immediately after haemodialysis.</li> </ul> <p><b>Patients with advanced hepatic insufficiency</b> In patients with advanced hepatic insufficiency a dosage reduction with serum level monitoring is necessary.</p>
<b>Contraindications</b>	<p><b>Hypersensitivity</b> Metronidazole Injection, USP is contraindicated in patients with a prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives.</p> <p><b>Psychotic Reaction with Disulfiram</b> Use of oral metronidazole is associated with psychotic reactions in alcoholic patients who were using disulfiram concurrently. Do not administer metronidazole to patients who have taken</p>	<p>You MUST NOT receive Metronidazole 500 mg/100 ml</p> <ul style="list-style-type: none"> <li>If you are sensitive or allergic to metronidazole or any of the other ingredients of this medicine</li> <li>if you are suffering from, or have suffered from any end stage liver disease if you have blood cells disorders</li> </ul>

	US FDA approved product	Import product
	Metronidazole Injection, USP, 500 mg/100 mL	Metronidazole 500 mg/100 ml Intravenous Infusion
	<p>disulfiram within the last two weeks (see PRECAUTIONS-Drug Interactions).</p> <p><b>Interaction with Alcohol</b> Use of oral metronidazole is associated with a disulfiram-like reaction to alcohol, including abdominal cramps, nausea, vomiting, headaches, and flushing. Discontinue consumption of alcohol or products containing propylene glycol during and for at least three days after therapy with metronidazole (see PRECAUTIONS-Drug Interactions).</p>	<ul style="list-style-type: none"> <li>• if you are suffering from any uncontrolled disease of the nervous system</li> <li>• if you are less than 3 months pregnant or think you may be less than 3 months pregnant.</li> </ul>
<b>Warnings</b>	<p>Metronidazole has been shown to be carcinogenic in mice and rats (see PRECAUTIONS). Unnecessary use of the drug should be avoided. Its use should be reserved for the conditions described in the INDICATIONS AND USAGE section below.</p> <p><b>Central and Peripheral Nervous System Effects</b> Encephalopathy and peripheral neuropathy: Cases of encephalopathy and peripheral neuropathy (including optic neuropathy) have been reported with metronidazole. Encephalopathy has been reported in association with cerebellar toxicity characterized by ataxia, dizziness, and dysarthria. CNS lesions seen on MRI have been described in reports of encephalopathy. CNS symptoms are generally reversible within days to weeks upon discontinuation of metronidazole. CNS lesions seen on MRI have also been described as reversible. Peripheral neuropathy, mainly of sensory type has been reported and is characterized by numbness or paresthesia of an extremity. Convulsive seizures have been reported in patients treated with metronidazole. Aseptic meningitis: Cases of aseptic meningitis have been reported with metronidazole. Symptoms can occur within hours of dose administration and generally resolve after metronidazole therapy is discontinued. The appearance of abnormal neurologic signs and symptoms demands the prompt evaluation of the benefit/risk ratio of the continuation of therapy (see ADVERSE REACTIONS).</p>	<p>Cases of severe liver toxicity/acute liver failure, including cases with a fatal outcome, in patients with Cockayne syndrome have been reported with product containing metronidazole. If you are affected by Cockayne syndrome, your doctor should also monitor your liver function frequently while you are being treated with metronidazole and afterwards. Tell your doctor immediately and stop taking metronidazole if you develop: Stomach pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine, putty or mastic coloured stools or itching.</p> <p><b>Pregnancy and breast-feeding:</b> This medicine should be avoided during pregnancy or breast-feeding unless your doctor considers it essential. It must not be given during the first three months of pregnancy. Ask your doctor or pharmacist for advice before taking any medicine.</p> <p><b>Driving and Using machines</b> You should not drive or use machines while being treated with this medicine.</p>
<b>Adverse Events</b>	<p>The following reactions have been reported during treatment with metronidazole.</p> <p><b>Central Nervous System</b> The most serious adverse reactions reported in patients treated with metronidazole have been convulsive seizures, encephalopathy, aseptic meningitis, optic and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity. Since persistent peripheral neuropathy has been reported in some patients receiving prolonged administration of metronidazole, patients should be specifically warned about these reactions and should be told to stop the drug and report immediately to their physicians if any neurologic symptoms occur. In addition, patients have reported headache, syncope, dizziness, vertigo, incoordination, ataxia, confusion, dysarthria, irritability, depression, weakness, and insomnia (see WARNINGS).</p> <p><b>Gastrointestinal</b> The most common adverse reactions reported have been referable to the gastrointestinal tract, particularly nausea, sometimes accompanied by headache, anorexia and occasionally vomiting, diarrhea; epigastric distress; abdominal cramping; and constipation.</p> <p><b>Mouth</b> A sharp, unpleasant metallic taste is not unusual. Furry tongue, glossitis and stomatitis have occurred; these may be associated with a sudden overgrowth of <i>Candida</i> which may occur during effective therapy.</p> <p><b>Dermatologic</b> Erythematous rash and pruritus.</p> <p><b>Hematopoietic</b> Reversible neutropenia (leukopenia); rarely, reversible thrombocytopenia.</p> <p><b>Local Reactions</b> Thrombophlebitis after intravenous infusion. This reaction can be minimized or avoided by avoiding prolonged use of indwelling intravenous catheters.</p> <p><b>Cardiovascular</b> Flattening of the T-wave may be seen in electrocardiographic tracings.</p> <p><b>Hypersensitivity</b> Urticaria, erythematous rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, flushing, nasal congestion, dryness of the mouth (or vagina or vulva) and fever.</p> <p><b>Renal</b> Dysuria, cystitis, polyuria, incontinence, and a sense of pelvic pressure. Instances of darkened urine have been reported by approximately one patient in 100,000. Although the pigment which is probably responsible for this phenomenon has not been positively identified, it is almost certainly a metabolite of metronidazole and seems to have no clinical significance.</p> <p><b>Other</b> Proliferation of <i>Candida</i> in the vagina, dyspareunia, decrease of libido, proctitis and fleeting joint pains sometimes resembling "serum sickness". Rare cases of pancreatitis, which abated on withdrawal of the drug, have been reported. Patients with Crohn's disease are known to have an increased incidence of gastrointestinal and certain extraintestinal cancers. There have been some reports in the medical literature of breast and colon cancer in Crohn's disease patients who have been treated with metronidazole at high doses for extended periods of time. A cause and effect relationship has not been established. Crohn's disease is not an approved indication for Metronidazole Injection, USP.</p>	<p>Like all medicines, this medicine can cause side effects, although not everybody gets them.</p> <p><b>Severe side effects:</b> The following severe side effects can occur rarely (less than 1 person out of 1,000 but more than 1 person out of 10,000):</p> <ul style="list-style-type: none"> <li>• severe allergic reaction (which may cause sudden faintness, severe breathlessness, abdominal pain or swelling of the tongue and throat)</li> <li>• severe neurological effects: (convulsion or fits, brain disease, disorder of the nerves which can causes loss of vision, brain fever not caused by bacterials (aseptic meningitis)</li> <li>• inflammation of your pancreas (which may cause pain in your belly with radiation through the back)</li> <li>• severe skin effects (Erythema multiforme, Serious illness with blistering of the skin, mouth, eyes and genitals and skin peeling).</li> </ul> <p>If you experience any of these severe side effects, please tell your doctor immediately. The doctor will stop the infusion.</p> <p><b>Common side effects</b> (less than 1 person out of 10 but more than 1 person out of 100):</p> <ul style="list-style-type: none"> <li>• feeling sick (nausea)</li> <li>• vomiting</li> <li>• unpleasant metallic taste in the mouth</li> <li>• inflammation of the mouth and tongue</li> <li>• dry mouth</li> <li>• pain in the muscles.</li> </ul> <p><b>Uncommon side effects</b> (less than 1 person out of 100 but more than 1 person out of 1,000):</p> <ul style="list-style-type: none"> <li>• Decrease of the number of white blood cells in your blood, headache and feeling of weakness.</li> </ul> <p><b>Rare side effects</b> (less than 1 person out of 1,000 but more than 1 person out of 10,000):</p> <ul style="list-style-type: none"> <li>• Fever itching, inflammation or swelling of the skin, skin eruption or skin rashes all of which may sometimes be severe</li> <li>• face oedema (Quincke oedema: accumulation of fluid in the skin at the level of the face)</li> <li>• pustule</li> <li>• drowsiness, dizziness, or hallucinations</li> <li>• clumsiness, or poor coordination</li> <li>• alteration of your blood that can modify results of your blood tests</li> <li>• abnormal liver test results</li> <li>• yellowing of the skin and eyes (jaundice)</li> <li>• unexpected infections, mouth ulcers, bruising, bleeding gums, sore throat or mouth, upset stomach, cramps, diarrhoea, or loss of appetite (anorexia)</li> <li>• darkening of your urine</li> <li>• double vision or nearsightedness.</li> </ul> <p>If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor. Your doctor will take the appropriate measures according to the side effect you have developed.</p>



	US FDA approved product	Import product
	Metronidazole Injection, USP, 500 mg/100 mL	Metronidazole 500 mg/100 ml Intravenous Infusion
<b>Drug Interactions</b>	<p><b>Disulfiram</b> Psychotic reactions have been reported in alcoholic patients who are using metronidazole and disulfiram concurrently. Metronidazole should not be given to patients who have taken disulfiram within the last two weeks (see CONTRAINDICATIONS).</p> <p><b>Alcoholic Beverages</b> Abdominal cramps, nausea, vomiting, headaches and flushing may occur if alcoholic beverages or products containing propylene glycol are consumed during or following metronidazole therapy (see CONTRAINDICATIONS).</p> <p><b>Warfarin and other Oral Anticoagulants</b> Metronidazole has been reported to potentiate the anticoagulant effect of warfarin and other oral coumarin anticoagulants, resulting in a prolongation of prothrombin time. When Metronidazole Injection, USP is prescribed for patients on this type of anticoagulant therapy, prothrombin time and INR should be carefully monitored.</p> <p><b>Lithium</b> In patients stabilized on relatively high doses of lithium, short-term metronidazole therapy has been associated with elevation of serum lithium and, in a few cases, signs of lithium toxicity. Serum lithium and serum creatinine levels should be obtained several days after beginning metronidazole to detect any increase that may precede clinical symptoms of lithium intoxication.</p> <p><b>Busulfan</b> Metronidazole has been reported to increase plasma concentrations of busulfan, which can result in an increased risk for serious busulfan toxicity. Metronidazole should not be administered concomitantly with busulfan unless the benefit outweighs the risk. If no therapeutic alternatives to metronidazole are available, and concomitant administration with busulfan is medically needed, frequent monitoring of busulfan plasma concentration should be performed and the busulfan dose should be adjusted accordingly.</p> <p><b>Drugs that Inhibit CYP450 Enzymes</b> The simultaneous administration of drugs that decrease microsomal liver enzyme activity, such as cimetidine, may prolong the half-life and decrease plasma clearance of metronidazole.</p> <p><b>Drugs that Induce CYP450 Enzymes</b> The simultaneous administration of drugs that induce microsomal liver enzyme activity, such as phenytoin or phenobarbital, may accelerate the elimination of metronidazole, resulting in reduced plasma levels; impaired clearance of phenytoin has also been reported.</p> <p><b>Drug/Laboratory Test Interactions</b> Metronidazole may interfere with certain types of determinations of serum chemistry values, such as aspartate aminotransferase (AST, SGOT), alanine aminotransferase (ALT, SGPT), lactate dehydrogenase (LDH), triglycerides and glucose hexokinase. Values of zero may be observed. All of the assays in which interference has been reported involve enzymatic coupling of the assay to oxidation-reduction of nicotinic adenine dinucleotide (NAD<sup>+</sup> ⇌ NADH). Interference is due to the similarity in absorbance peaks of NADH (340nm) and metronidazole (322nm) at pH 7.</p>	<p>Certain medicines are known to change the normal effect of this infusion. Certain medicines can have their effect changed by this infusion. These medicines should not be used at the same time as Metronidazole 500 mg/100 ml Intravenous Infusion. Please tell your doctor if you are taking or have recently taken any of the following medicines:</p> <ul style="list-style-type: none"> <li>• warfarin (oral anticoagulant) as your blood clotting time will need to be monitored more frequently</li> <li>• vecuronium</li> <li>• 5-Fluoro-uracile</li> <li>• Lithium as lithium treatment should be reduced or stopped before you are given Metronidazole</li> <li>• phenobarbital</li> <li>• cholestyramine</li> <li>• phenytoin</li> <li>• cimetidine</li> <li>• ciclosporin</li> <li>• busulfan</li> </ul> <p>Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.</p> <p><b>Using Metronidazole 500 mg/100 ml with food and drink</b> Do not drink any alcohol while receiving your medicine, and for 48 hours afterwards. This might cause unpleasant side effects, such as feeling sick and vomiting, abdominal pain, hot flushes, palpitations, and headache.</p> <p><b>Pregnancy and breast-feeding</b> This medicine should be avoided during pregnancy or breast-feeding unless your doctor considers it essential. It must not be given during the first three months of pregnancy. Ask your doctor or pharmacist for advice before taking any medicine.</p> <p><b>Driving and Using machines</b> You should not drive or use machines while being treated with this medicine.</p>
<b>Overdosage and treatment</b>	<p>Use of dosages of intravenous metronidazole higher than those recommended has been reported. These include the use of 27 mg/kg three times a day for 20 days, and the use of 75 mg/kg as a single loading dose followed by 7.5 mg/kg maintenance doses. No adverse reactions were reported in either of the two cases. Single oral dose of metronidazole, up to 15 g, have been reported in suicide attempts and accidental overdoses. Symptoms reported included nausea, vomiting and ataxia. Oral metronidazole has been studied as a radiation sensitizer in the treatment of malignant tumors. Neurotoxic effects, including seizures and peripheral neuropathy, have been reported after 5 to 7 days of doses of 6 to 10.4 g every other day.</p> <p><b>Treatment of Overdosage</b> There is no specific antidote for metronidazole overdose; therefore, management of the patient should consist of symptomatic and supportive therapy.</p>	<p>– Symptoms: If you have received more infusion than you should, the following symptoms could appear:</p> <ul style="list-style-type: none"> <li>• feeling sick (nausea)</li> <li>• vomiting</li> <li>• poor coordination (ataxia) and</li> <li>• slight disorientation.</li> </ul> <p>No symptoms developed where too much of this medicine is given to <i>newborn infants born prematurely</i>.</p> <p>– Treatment: Please inform your doctor immediately if any of these symptoms occur. In the event of accidental over-infusion, your doctor will stop the infusion. Your doctor will take the appropriate measures according to the symptoms you have developed.</p>
<b>Storage conditions</b>	<p>Store at controlled room temperature (77°F or 25°C) and protect from light during storage. Do not refrigerate. Do not remove unit from overwrap until ready for use. The overwrap is a moisture barrier. The inner bag maintains the sterility of the product.</p> <p>After removing overwrap, check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution as sterility may be impaired.</p>	<p>Keep out of the reach and sight of children.</p> <p>Do not use this medicine after the expiry date which is stated on the label after Exp.:. The expiry date refers to the last day of that month. You will not be given this medicine if this date has passed.</p> <p>Keep container in the outer carton in order to protect from light.</p> <p>Do not remove the unit from overwrap until ready for use.</p> <p>Do not use if the solution is not clear, or if the unit is damaged in any way. Discard any unused portion.</p>
<b>Directions for use</b>	<p><b>Warning:</b> 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 administration of the fluid from the secondary container is completed.</p> <p><b>To open:</b> Tear overwrap down side at slit and remove solution container. Visually inspect the container. If the outlet port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for leaks. <b>Do not add supplementary medication.</b></p> <p><b>Caution:</b> Metronidazole Injection, USP is to be administered by slow intravenous drip infusion only, either as a continuous or intermittent infusion. Additives should not be introduced into Metronidazole Injection, USP. If used with a primary intravenous fluid system, the primary solution should be discontinued during metronidazole infusion. <b>DO NOT USE EQUIPMENT CONTAINING ALUMINUM (e.g., NEEDLES, CANNULAE) THAT WOULD COME IN CONTACT WITH THE DRUG SOLUTION.</b></p>	<p>Use only if the solution is clear, without visible particles and if the container is undamaged. Administer immediately following the insertion of infusion set.</p> <p>Do not remove unit from overpouch until ready for use. The inner bag maintains the sterility of the product.</p> <p>The product should be used immediately after opening.</p> <p>Discard after single use. Discard any unused portion.</p> <p>Do not reconnect partially used bags.</p>