METRONIDAZOLE (Systemic)

Category

Antibacterial (systemic); antiprotozoal; bowel disease (inflammatory) suppressant; anthelmintic (systemic).

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Amebiasis, extraintestinal (treatment)¾Metronidazole is indicated in the treatment of extraintestinal amebiasis, including amebic liver abscess, caused by Entamoeba histolytica. When used in the treatment of invasive amebiasis, metronidazole should be administered concurrently or sequentially with a luminal amebicide (e.g., iodoquinol, paromomycin, tetracycline, diloxanide furoate). 11 When used in the treatment of amebic liver abscesses, metronidazole therapy does not obviate the need for aspiration of the abscess. 62 64

Amebiasis, intestinal (treatment)¾Oral metronidazole is indicated in the treatment of acute intestinal amebiasis caused by Entamoeba histolytica. Metronidazole may not eradicate intestinal amebic infections, requiring treatment with a luminal amebicide.

Bone and joint infections (treatment)¾Metronidazole is indicated in the treatment of bone and joint infections caused by Bacteroides species, including the B. fragilis group (B. fragilis , B. distasonis , B. ovatus , B. thetaiotaomicron , B. vulgatus).

Brain abscess (treatment)¾Metronidazole is indicated in the treatment of brain abscess caused by Bacteroides species, including the B. fragilis group.

Central nervous system (CNS) infections (treatment)¾Metronidazole is indicated in the treatment of CNS infections, including meningitis, caused by Bacteroides species, including the B. fragilis group.

Endocarditis, bacterial (treatment)¾Metronidazole is indicated in the treatment of endocarditis caused by Bacteroides species, including the B. fragilis group.

Intra-abdominal infections (treatment)¾Metronidazole is indicated in the treatment of intra-abdominal infections, including peritonitis, intra-abdominal abscess, and liver abscess, caused by Bacteroides species, including the B. fragilis group, Clostridium species, Eubacterium species, Peptococcus species, and Peptostreptococcus species.

Pelvic infections, female (treatment)¾Metronidazole is indicated in the treatment of female pelvic infections, including endometritis, endomyometritis, tubo-ovarian abscess, and postsurgical vaginal cuff infections, caused by Bacteroides species, including the B. fragilis group, Clostridium species, Peptococcus species, and Peptostreptococcus species.

Perioperative infections, colorectal (prophylaxis)¾Intravenous metronidazole is indicated for the prophylaxis of perioperative infections during colorectal surgery.

Pneumonia, Bacteroides species (treatment) ¾Metronidazole is indicated in the treatment of lower respiratory tract infections, including pneumonia, empyema, and lung abscess, caused by Bacteroides species, including the B. fragilis group.

Septicemia, bacterial (treatment)¾Metronidazole is indicated in the treatment of bacterial septicemia caused by Bacteroides species, including the B. fragilis group, and Clostridium species.

Skin and soft tissue infections (treatment)¾Metronidazole is indicated in the treatment of skin and soft tissue infections caused by Bacteroides species, including the B. fragilis group, Clostridium species, Fusobacterium species, Peptococcus species, and Peptostreptococcus species.

Trichomoniasis (treatment)¾Oral metronidazole is indicated in the treatment of symptomatic and asymptomatic trichomoniasis, in males and females, caused by Trichomonas vaginalis .

Vaginosis, bacterial (treatment)¾Oral metronidazole (extended release formulation) is indicated in the treatment of bacterial vaginosis caused byGardnerella vaginalis,Mobiluncus spp, mycoplasma hominisand anaerobes (Peptostreptococcus spp and Bacteroidesspp).. 45, 63

[Balantidiasis (treatment)] *¾Metronidazole is used in the treatment of Balantidium coli infection. 45

[Bowel disease, inflammatory (treatment)] *¾Metronidazole is used in the treatment of inflammatory bowel disease.

[Colitis, antibiotic-associated (treatment)] *¾Metronidazole is used in the treatment of antibiotic-associated diarrhea and colitis caused by C. difficile. 47

[Dracunculiasis (treatment)] *¾Metronidazole is used in the treatment of dracunculiasis (guinea worm infection) caused by Dracunculus medinensis. It decreases the inflammation around the ulcer, increasing the ease of removing the worm. 45

[Gastritis, Helicobacter pylori -associated (treatment adjunct)] * or

[Ulcer, duodenal, Helicobacter pylori -associated (treatment adjunct)] *¾Some studies indicate that metronidazole may be effective, in combination with bismuth subsalicylate or colloidal bismuth subcitrate, and other oral antibiotic therapy, such as ampicillin or amoxicillin, in the treatment of Helicobacter pylori -associated gastritis and duodenal ulcer. However, metronidazole resistance may occur, especially in patients who have been previously exposed to metronidazole. 54, 55, 58, 59, 60, 61

[Giardiasis (treatment)] *¾Oral metronidazole is used in the treatment of giardiasis caused by Giardia lamblia. 45

[Periodontal infections (treatment)] *¾Metronidazole is used in the treatment of periodontal infections caused by Bacteroides species.

Not all species or strains of a particular organism may be equally susceptible to metronidazole.

Unaccepted

Metronidazole is not effective against facultative anaerobes, obligate aerobes, Propionibacterium acnes , Actinomyces species, or Candida albicans .

* Not included in Canadian product labeling.

Pharmacology

Mechanism of action/Effect:

Antibacterial (systemic); antiprotozoal¾Microbicidal; active against most obligate anaerobic bacteria and protozoa 6 by undergoing intracellular chemical reduction via mechanisms unique to anaerobic metabolism. Reduced metronidazole, which is cytotoxic but short-lived, interacts with DNA to cause a loss of helical structure, strand breakage, and resultant inhibition of nucleic acid synthesis and cell death. 34

Precautions to Consider

Carcinogenicity/Tumorigenicity

Metronidazole has been shown to be carcinogenic in a number of studies in mice. Pulmonary tumorigenesis has been reported in six studies in mice, including one study in which the animals were dosed on an intermittent schedule (every four weeks). Malignant hepatic tumors have also been reported in male mice given very high doses (approximately 500 mg/kg/day). Malignant lymphomas have been reported in one lifetime feeding study in mice. 2, 16

Metronidazole has also been shown to be carcinogenic in rats. Several long-term, oral-dosing studies in rats have shown that metronidazole causes a statistically significant increase in the incidence of various neoplasms, especially mammary and hepatic tumors, in female rats. 2, 16

Two lifetime tumorigenicity studies in hamsters have given negative results. 2, 16

Metronidazole has not been shown to be carcinogenic or tumorigenic in humans. 11

Mutagenicity

Studies have shown that metronidazole is mutagenic in bacteria and fungi, although this has not been confirmed in mammals. 16

Pregnancy/Reproduction

Pregnancy¾Fertility; pregnancy

Metronidazole crosses the placenta and enters the fetal circulation rapidly. Adequate and well-controlled studies in humans have not been done. Studies in rats, given doses of up to 5 times the human dose, have not shown that metronidazole causes impaired fertility or birth defects in the fetus. Metronidazole, administered intraperitoneally to pregnant mice at approximately the human dose, has been shown to cause fetotoxicity. When administered orally, no fetotoxicity was seen in pregnant mice. 9, 16 However, the use of metronidazole in the treatment of trichomoniasis is not recommended during the first trimester. If metronidazole is used during the second and third trimesters for trichomoniasis, it is recommended that its use be limited to those patients whose symptoms are not controlled by local palliative treatment. Also, the 1-day course of therapy should not be used since this results in higher maternal and fetal serum concentrations. 16

Studies in rats given doses of up to 5 times the usual human dose have not shown that metronidazole causes impaired fertility or birth defects in the fetus. Metronidazole, administered intraperitoneally to pregnant mice at approximately the human dose, has been shown to cause fetotoxicity. When metronidazole was administered orally, no fetotoxicity was seen in pregnant mice. 9, 16

FDA Pregnancy Category B.

Breast-feeding

Metronidazole is distributed into breast milk; concentrations are similar to those found in the maternal plasma. 16 Use is not recommended in nursing mothers since some studies in rats and mice have shown that metronidazole is carcinogenic and may cause adverse effects in the infant. However, use in the treatment of anaerobic bacterial infections or a short course of treatment with metronidazole for amebiasis, severe periodontal infections, or trichomoniasis may be necessary in nursing mothers. During treatment with metronidazole, the breast milk should be expressed and discarded. Breast-feeding may be resumed 24 to 48 hours after treatment is completed.

Pediatrics

When used for the treatment of anaerobic infections and amebiasis, metronidazole has not demonstrated any pediatrics-specific problems that would limit its usefulness in children.

Geriatrics

No information is available on the relationship of age to the effects of metronidazole in geriatric patients. However, elderly patients are more likely to have an age-related decrease in hepatic function, which may require an adjustment in dosage in patients receiving metronidazole. 16

Dental

Metronidazole may cause dry mouth, an unpleasant or sharp metallic taste, and alteration of taste sensation. Dry mouth may contribute to the development of caries, periodontal disease, oral candidiasis, and discomfort. 5

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

>> Alcohol

(it is recommended that metronidazole not be used concurrently with, or for at least 3 days following, ingestion of alcohol; accumulation of acetaldehyde by interference with the oxidation of alcohol may occur, resulting in disulfiram-like effects such as abdominal cramps, nausea, vomiting, headache, or flushing; in addition, modifications in the taste of alcoholic beverages have been reported during concurrent use 9, 14, 63, 64)

>> Anticoagulants, coumarin- or indandione-derivative

(effects may be potentiated when these agents are used concurrently with metronidazole, because of inhibition of enzymatic metabolism of anticoagulants; periodic prothrombin time determinations may be required during therapy to determine if dosage adjustments of anticoagulants are necessary 14, 56)

Cimetidine

(hepatic metabolism of metronidazole may be decreased when metronidazole and cimetidine are used concurrently, possibly resulting in delayed elimination and increased serum metronidazole concentrations; monitoring of serum concentrations as a guide to dosage is recommended since dosage adjustments of metronidazole may be necessary during and after cimetidine therapy 9, 28)

>> Disulfiram

(it is recommended that metronidazole not be used concurrently with, or for 2 weeks following, disulfiram in alcoholic patients; such use may result in confusion and psychotic reactions because of combined toxicity 9, 14)

>> Lithium

(lithium concentrations may increase when metronidazole therapy is introduced; serum lithium and serum creatinine levels should be monitored several days after beginning metronidazole in order to detect impending lithium intoxication 62, 63, 64)

Neurotoxic medications, other (See Appendix II)

(concurrent use of metronidazole with other neurotoxic medications may increase the potential for neurotoxicity 3)

Phenobarbital

(phenobarbital may induce microsomal liver enzymes, increasing metronidazole"s metabolism and resulting in a decrease in half-life and plasma concentration 27, 36, 37)

Phenytoin

(metronidazole may impair the clearance of phenytoin, increasing phenytoin"s plasma concentration 14, 38, 39)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]), serum and

Aspartate aminotransferase (AST [SGOT]), serum and

Hexokinase glucose and

Lactate dehydrogenase (LDH) and

Triglycerides

(metronidazole has a high absorbance at the wavelength at which nicotinamide-adenine dinucleotide [NADH] is determined; therefore, elevated liver enzyme concentrations may appear to be suppressed 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 6, 27, 62, 63, 64, 65)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Risk-benefit should be considered when the following medical problems exist

>> Active organic disease of the CNS, including epilepsy

(metronidazole may cause CNS toxicity, including seizures with high doses, and peripheral neuropathy 16)

>> Blood dyscrasias, or history of

(metronidazole may cause leukopenia 16)

Cardiac function impairment

(parenteral dosage forms¾because of sodium content 27)

>> Hepatic function impairment, severe

(metabolized in the liver; hepatic dysfunction may lead to decreased plasma clearance and accumulation of metronidazole and its metabolites; dosage may need to be reduced with severe hepatic function impairment 27)

Hypersensitivity to metronidazole

>> Known or previously unrecognized candidiasis

(metronidazole may cause more prominent symptoms 62, 63, 64, 65)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):
For giardiasis

>> Stool examinations

(3 stool examinations, taken several days apart, beginning 3 to 4 weeks following treatment are recommended if symptoms persist; however, in some successfully treated patients, the lactose intolerance brought on by the infection may persist for a period of some weeks or months, mimicking the symptoms of giardiasis; in cases of treatment failure, alternate drugs may be used 12)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence less frequent 6, 27

Peripheral neuropathy (numbness, tingling, pain, or weakness in hands or feet)¾ usually with high doses or prolonged use; seizures¾usually with high doses
Incidence rare

CNS toxicity (ataxia¾clumsiness or unsteadiness; encephalopathy¾mood or other mental changes); hypersensitivity (skin rash, hives, redness, or itching); leukopenia (sore throat and fever); pancreatitis 10, 40, 41, 42 (severe abdominal and back pain; anorexia; nausea and vomiting); thrombocytopenia (unusual bleeding or bruising; black, tarry stools; blood in urine or stools; pinpoint red spots on skin)¾reversible 62, 63, 64, 65thrombophlebitis (pain, tenderness, redness, or swelling at site of injection); Urinary tract effects (frequent or painful urination; inability to control urine flow; sense of pelvic pressure) 62, 63, 64, 65vaginal candidiasis (any vaginal irritation, discharge, or dryness not present before therapy)
Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent 27

CNS effects (dizziness or light-headedness ; headache); gastrointestinal disturbance (diarrhea; loss of appetite; nausea or vomiting; stomach pain or cramps)
Incidence less frequent or rare 5, 27

Change in taste sensation ; dryness of mouth; unpleasant or sharp metallic taste
Those not indicating need for medical attention

Incidence less frequent or rare 27

Dark urine

Overdose

For more information on the management of overdose or unintentional ingestion, contact a poison control center (see Poison Control Center Listing).
Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:Ataxia; nausea and vomiting; peripheral neuropathy ; seizures 62, 63, 64, 65

Treatment of overdose

Since there is no specific antidote, treatment for metronidazole overdose should be symptomatic and supportive. Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation. 27, 62, 63, 64, 65

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Metronidazole (Systemic).
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Hypersensitivity to metronidazole
Pregnancy¾Metronidazole crosses the placenta; use is not recommended during the first trimester of pregnancy
Breast-feeding¾Metronidazole is distributed into breast milk; metronidazole is not recommended during breast-feeding
Dental¾Metronidazole may cause dry mouth, an unpleasant or sharp metallic taste, and alteration of taste sensation
Other medications, especially alcohol, coumarin- or indandione-derivative anticoagulants, disulfiram, or lithium
Other medical problems, especially active organic disease of the CNS, a history of blood dyscrasias, known or previously unrecognized candidiasis, or severe hepatic function impairment

Proper use of this medication

Taking with meals or a snack to minimize gastrointestinal irritation

Taking extended-release formulation on an empty stomach to maximize dosage form characteristics

>> Compliance with full course of therapy

>> Importance of not missing doses and taking at evenly spaced times

>> Proper dosing
Taking as soon as possible; not taking if almost time for next dose; not doubling doses
>> Proper storage
Precautions while using this medication

Follow-up visit to physician after treatment for giardiasis to ensure that infection has been eradicated.

Checking with physician if no improvement within a few days

>> Avoiding use of alcoholic beverages or other alcohol-containing preparations while taking and for at least 3 days after discontinuing this medication

Possible dryness of mouth; using sugarless candy or gum, ice, or saliva substitute for relief; checking with dentist if dry mouth continues for more than 2 weeks

>> Caution if dizziness or light-headedness occurs

Prevention of reinfection in trichomoniasis; possible need for concurrent treatment of male sexual partner and use of a condom

Side/adverse effects

Signs of potential side effects, especially CNS toxicity, hypersensitivity, leukopenia, pancreatitis, peripheral neuropathy, seizures, thrombocytopenia, thrombophlebitis, urinary tract effects and vaginal candidiasis.

Dark urine may be alarming to patient although medically insignificant

General Dosing Information

Patients with severely impaired hepatic function metabolize metronidazole slowly. Close monitoring for toxicity, as well as reduction in dose, may be required. 28, 62

Anuric patients do not generally require a reduction in dose since metabolites of metronidazole may be rapidly removed by hemodialysis. Also, reduced renal function does not significantly affect single-dose pharmacokinetics of metronidazole. 28, 62

Patients with candidiasis may present with more prominent symptoms during metronidazole therapy, requiring treatment with a candidacidal agent. 62, 63, 64, 65

For oral dosage forms only

Metronidazole may be taken with meals or a snack to lessen gastrointestinal irritation.
The extended-release formulation of metronidazole should be taken on an empty stomach, at least one hour before or two hours after meals, in order to ensure maximal performance of the extended-release characteristics. 63

When metronidazole is used in the treatment of trichomoniasis, sexual partners should receive concurrent therapy since asymptomatic trichomoniasis in the male partner is a frequent source of reinfection in the female. The male partner should be advised to use a condom for the duration of treatment. 6

For parenteral dosage forms only

Parenteral metronidazole should be administered by slow intravenous infusion only, either continuously or intermittently over a 1-hour period. 27, 65

If metronidazole is administered concurrently with a primary intravenous solution, the primary solution should be discontinued while metronidazole is being infused. 28

Serum metronidazole concentrations may be lower in patients whose gastric secretions are removed by continuous nasogastric aspiration, since metronidazole may be removed in the gastric aspirate. 65

Oral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

Note: The dosing and dosage forms available are expressed in terms of metronidazole base.

METRONIDAZOLE CAPSULES

Usual adult and adolescent dose

Antibacterial (systemic)¾
Anaerobic infections: Oral, 7.5 mg (base) per kg of body weight, up to a maximum of 1 gram, every six hours for seven days or longer. 16

[Bowel disease, inflammatory] *: Oral, 500 mg (base) four times a day. 11

[Colitis, antibiotic-associated] *: Oral, 500 mg (base) three or four times a day. 11

[Gastritis, Helicobacter pylori -associated (treatment adjunct)] * or

[Ulcer, duodenal, Helicobacter pylori -associated (treatment adjunct)] *¾Oral, 500 mg (base) three times a day, in conjunction with bismuth subsalicylate or colloidal bismuth subcitrate and other oral antibiotic therapy, such as ampicillin or amoxicillin, for one to two weeks. 54, 58

[Vaginosis, bacterial] *: Oral, 500 mg (base) two times a day for seven days. 11

Antiprotozoal¾
Amebiasis: Oral, 500 to 750 mg (base) three times a day for five to ten days. 16

Amebic liver abscess: Oral, 500 to 750 mg (base) three times a day for five to ten days. 62 64

[Balantidiasis] *: Oral, 750 mg (base) three times a day for five or six days.
[Giardiasis] *: Oral, 2 grams (base) once a day for three days; or 250 mg three times a day for five to seven days.
Trichomoniasis: Oral, 2 grams (base) as a single dose; 1 gram two times a day for one day; 375 mg two times a day for seven days; or 250 mg three times a day for seven days. 16, 64

Anthelmintic (systemic)¾
[Dracunculiasis] *: Oral, 250 mg (base) three times a day for ten days.

Usual adult prescribing limits

Antibacterial (systemic)¾
Up to a maximum of 4 grams (base) daily. 16

Usual pediatric dose

Antibacterial (systemic)¾
Anaerobic infections *: Oral, 7.5 mg (base) per kg of body weight every six hours, or 10 mg per kg of body weight every eight hours. 52, 53

Antiprotozoal¾
Amebiasis: Oral, 11.6 to 16.7 mg (base) per kg of body weight three times a day for ten days. 16

[Balantidiasis] *: Oral, 11.6 to 16.7 mg (base) per kg of body weight three times a day for five days. 50

[Giardiasis] *: Oral, 5 mg (base) per kg of body weight three times a day for five to seven days.
Trichomoniasis: Oral, 5 mg (base) per kg of body weight three times a day for seven days. 34

Anthelmintic (systemic)¾
[Dracunculiasis] *: Oral, 8.3 mg (base) per kg of body weight, up to a maximum of 250 mg, three times a day for ten days.

Strength(s) usually available

U.S.¾375 mg (base) (Rx)[Flagyl (Black iron oxide) (corn starch) (D&C Yellow No. 10) (FD&C Green No.3) (gelatin) (magnesium stearate) (titanium dioxide)]

Canada¾500 mg (base) (Rx)[Flagyl (sodium 5.47 mg)] [Trikacide]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Store in a light-resistant container.

Auxiliary labeling:

· Avoid alcoholic beverages.
· May cause dizziness.
· Continue medicine for full time of treatment.

METRONIDAZOLE TABLETS USP

Usual adult and adolescent dose

See Metronidazole Capsules .

Usual adult prescribing limits

See Metronidazole Capsules .

Usual pediatric dose

See Metronidazole Capsules .

Strength(s) usually available

U.S.¾250 mg (base) (Rx)[Flagyl] [Metric 21] [Protostat (scored) (lactose)]

500 mg (base) (Rx)[Flagyl] [Protostat (scored) (lactose)]

Canada¾250 mg (base) (Rx)[Apo-Metronidazole] [Flagyl (sodium 3.1 mg)] [Novonidazol (scored) (sodium 2.2 mg)] [Trikacide]

Packaging and storage:

Store in a dry place at 25 °C (77 °F); excursions permitted between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a well-closed, light-resistant container.

Preparation of dosage form:

For patients who cannot take oral solids¾According to the primary manufacturer, the tablets may be crushed and suspended in Cherry Syrup NF to prepare a pediatric dosage form. The recommended concentration per 5 mL is the dose calculated for a particular pediatric patient. The suspension is stable

for 30 days if stored at ambient room temperature or refrigerated. Dispense with "shake well"" instructions.

Auxiliary labeling:

· Avoid alcoholic beverages.
· May cause dizziness.
· Continue medicine for full time of treatment.

METRONIDAZOLE EXTENDED RELEASE TABLETS

Usual adult and adolescent dose

Antibacterial (systemic)¾
Vaginosis, bacterial: Oral, 750 mg (base) once a day for seven days. 63

Usual pediatric dose

Safety and efficacy have not been established.

Strength(s) usually available
U.S.¾750 mg (base)[Flagyl ER (FD&C Blue No.2 Aluminum Lake) (hydroxpropyl methylcellulose) (lactose) (magnesium stearate) (poly (meth) acrylic acid ester copolymers) (polyethylene glycol) (polysorbate 80) (silicon dioxide) (simethicone emulsion) (talc) (titanium dioxide)]

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Packaging and storage:

Store in a dry place at 25 °C (77 °F); excursions permitted between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a well-closed, light-resistant container. 63

Auxiliary labeling:

· Avoid alcoholic beverages.
· Continue medicine for full time of treatment.
· Take on an empty stomach, at least one hour before or two hours after meals.

Parenteral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

Note: The dosing and dosage forms available are expressed in terms of metronidazole base.

METRONIDAZOLE INJECTION USP

Usual adult and adolescent dose

Antibacterial (systemic)¾
Anaerobic infections: Intravenous infusion, 15 mg (base) per kg of body weight initially, then 7.5 mg per kg of body weight, up to a maximum of 1 gram, every six hours for seven days or longer. 27, 65

Perioperative infections, colonic (prophylaxis): Intravenous infusion, 15 mg (base) per kg of body weight one hour prior to the start of surgery; and 7.5 mg per kg of body weight six and twelve hours after the initial dose. 11, 27

[Antiprotozoal¾Amebiasis] *¾
Intravenous infusion, 500 to 750 mg (base) every eight hours for five to ten days. 11

Usual adult prescribing limits

Antibacterial (systemic)¾
Up to a maximum of 4 grams (base) daily. 27

Usual pediatric dose

Antibacterial (systemic)¾Anaerobic infections: 52, 53¾
Preterm infants¾Intravenous infusion, 15 mg per kg of body weight (base) as an initial dose, then 7.5 mg per kg of body weight every twelve hours starting 48 hours after the initial dose.
Term infants¾Intravenous infusion, 15 mg (base) per kg of body weight as an initial dose, then 7.5 mg per kg of body weight every twelve hours starting 24 hours after the initial dose.
Infants greater than 7 days of age and children¾Intravenous infusion, 15 mg (base) per kg of body weight as an initial dose, then 7.5 mg per kg of body weight every six hours.

Strength(s) usually available

U.S.¾500 mg in 100 mL (base) (Rx)[Flagyl I.V. RTU (sodium 14 mEq)] [Metro I.V. (sodium 13.5 mEq)] [Generic]

Canada¾500 mg in 100 mL (base) (Rx)[Flagyl] [Generic]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light during storage. 7, 8 Protect from freezing.

Incompatibilities:

Intravenous admixtures of metronidazole and other medications are not recommended. 27

Additional information:

Metronidazole Injection USP is an isotonic (297 to 310 mOsm per liter), ready-to-use solution, requiring no dilution or buffering prior to administration. 7

Metronidazole Injection USP in prefilled plastic minibags should not be used in series connections. This may result in air embolism because of residual air (approximately 15 mL), which may be drawn from the primary plastic bag before administration of the infusion from the secondary plastic bag is completed.

METRONIDAZOLE HYDROCHLORIDE FOR INJECTION

Usual adult and adolescent dose

See Metronidazole Injection USP .

Usual adult prescribing limits

See Metronidazole Injection USP .

Usual pediatric dose

See Metronidazole Injection USP .

Size(s) usually available:

U.S.¾500 mg (base) (Rx)[Flagyl I.V. (sodium 5 mEq)]

Canada¾Not commercially available.

Packaging and storage:

Prior to reconstitution, store below 30 °C (86 °F), in a light-resistant container, unless otherwise specified by manufacturer.

Preparation of dosage form:

Metronidazole hydrochloride for injection must not be given by direct intravenous injection since the initial dilution has an extremely low pH (0.5 to 2.0). It must be diluted further and neutralized prior to administration. 27

To prepare initial dilution for intravenous infusion, add 4.4 mL of sterile water for injection, bacteriostatic water for injection, 0.9% sodium chloride injection, or bacteriostatic sodium chloride injection to each 500-mg vial to provide a concentration of 100 mg per mL (pH 0.5 to 2.0). The resulting solution should be further diluted in 100 mL of 0.9% sodium chloride injection, 5% dextrose injection, or lactated Ringer"s injection. The final dilution must be neutralized with approximately 5 mEq of sodium bicarbonate injection per 500 mg of metronidazole (final pH 6 to 7). Since carbon dioxide gas is produced during neutralization, it may be necessary to relieve the pressure in the final container. The final concentration should not exceed 8 mg per mL since neutralization decreases the solubility of metronidazole and precipitation may occur. 27

Stability:

After reconstitution, solutions retain their potency for 96 hours if stored below 30 °C (86 °F) in room light. Diluted and neutralized solutions retain their potency for 24 hours. 27

Do not refrigerate neutralized solutions since precipitation may occur. 27

Incompatibilities:

Do not use with aluminum needles or hubs. 27

Intravenous admixtures of metronidazole with other medications are not recommended. 27

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10 Corey WA, et al. Metronidazole-induced acute pancreatitis. Rev Infect Dis 1991; 13: 1213-5.

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