INSTRUCTIONS FOR USE — READ CAREFULLY!

FRESENIUS AG
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Metronidazole Fresenius

Infusion solution

Composition

100 ml contain:

Metronidazole	500 mg
Sodium chloride	740 mg
Sodium monohydrogen phosphate, 12 H_2O	150 mg
Citric acid monohydrate	44 mg

Na^+	135 mmol/l
Cl^-	126.6 mmol/l
PO_4^{---}	4.2 mmol/l

Theoretical osmolarity = 297 mosm/l

Indications

Treatment of infections where bacteria, growing under exclusion of air, anaerobic bacteria are known or presumed, such as predominantly Bacteroides fragilis and other strains of anaerobic bacteria as well as further strains sensitive to metronidazole, eg, Fusobacteria, Eubacteria, Clostridia and other cocci growing under exclusion of air.

Metronidazole Fresenius has been successfully used in infections of the gastrointestinal tract, after colon surgery, in peritonitis, purulent diseases of the pelvic cavity (abscesses, phlegmon), infections of the female genital tract (eg, following hysterectomy and other gynecological surgery) as well as puerperal fever.

Metronidazole Fresenius is also used in sepsis, especially in sepsis originating from the gastrointestinal tract or the female genital tract, as well as in pneumonia with histolysis (necrotizing pneumonia), cerebral abscesses, osteomyelitis and endocarditis.

Metronidazole Fresenius is indicated particularly

- in severe infections with bacteria growing under exclusion of air (anerobes),
- if administration of metronidazole tablets is not possible or not indicated,
- for preparing a surgery, notably when infections like peritonitis or purulent diseases located below the diaphragm (subphrenic abscess), or of the pelvis (abscesses), are already known or suspected,
- for preparing a surgery, where a contamination with bacteria growing under exclusion of air (eg, originating from the gastrointestinal tract, the female genital tract as well as the oropharyngeal space), can be expected.

Contraindications

Contraindications for the use of Metronidazole Fresenius do not exist in vital indication. Metronidazole should not be used in the first trimester of pregnancy unless its use is considered essential; in these circumstances Metronidazole should be used in the lowest effective dose in the shortest possible time period. During the second and last third of pregnancy therapy with Metronidazole Fresenius is possible if vital indication is given. During the lactation period, nursing or the treatment should be discontinued.

The following remarks should also be considered:

- A treatment with Metronidazole Fresenius must not exceed 10 days.

The limitation of the treatment period must be strongly observed. Extraordinary circumstances may require a prolonged duration of therapy. The therapy should be repeated as rarely as possible and only if the indication is established (cf also "Period of use").

— In hypersensitivity to nitroimidazole derivatives as well as in granulocytopenia, Metronidazole Fresenius has to be applied with caution.

— In meningitis, metronidazole passes particularly easily into the cerebrospinal liquor and can lead to peripheral neuropathies (cf side effects).

Side effects

Gastrointestinal disturbances (eg eructation, coating of the tongue, pressure of the stomach, and, in extremely rare cases, nausea and vomiting) can occur.

Incidence of somnolence, vertigo, headache and ataxia have been reported in some cases.

A possible occurrence of dark urine (metabolic product of metronidazole) is not dangerous.

In single cases allergic reactions like for instance itching, cutaneous eruptions, and anaphylaxis can occur.

Following an extremely high dosage or long-term therapy, peripheral neuropathy was reported in single cases. After reducing the dosage or discontinuing the therapy, the peripheral neuropathy vanished. Since normally, after a few intravenously administered doses, the treatment is continued with tablets, the side effects, which can occur during intensive or extremely long treatment with tablets do not give cause for concern in intravenous administration. Blood count is advisable in long, high-dosage treatment, since under these circumstances an effect on the white blood count cannot be absolutely excluded.

Interactions with other medication

Metronidazole can influence the serum concentration of drugs influencing anticoagulation. Patients simultaneously treated with such medications, might have to be newly adjusted.
The simultaneous intake of alcohol (ethanol) has to be avoided, since otherwise side reactions like nausea and vomiting might occur.

Interactions with insulin or oral antidiabetics are not known.

Interactions or side effects of metronidazole in combination of metronidazole with sulfonamides (which have to be separately administered), or antibiotics, respectively, have not been clinically reported.

Moderate synergic response of metronidazole to antibiotics (like Tetracycline, Spiramycin, Clindamycin, Acylureido-penicillins and Rifampicin) have been reported.

Nalidixin acid and metronidazole show clear synergic influence.

In vitro tests upon the simultaneous administration of metronidazole and ampicillin, streptomycin, gentamicin and fusidic acid did not show reciprocal effects. There was no evidence of an antagonistic effect. In animal tests with an effective dose of 50% no antagonism of metronidazole and Novobiocin, Cephalexin, Chloramphenicol, Rifampicin, naldixic acid as well as Cotrimoxazol could be observed.

Dosage and application

If not prescribed otherwise, the following dosing applies:
Infections with anerobic causative agents

— Adults and children over 12 years.
Daily dosis: 1x daily 300 ml infusion solution or 3x daily 100 ml Metronidazole Fresenius

for a body weight of ca 70 kg as slow intravenous infusion of 5 ml infusion solution/minute, corresponding to 22.5 mg metronidazole/kg body weight/day.
A change to tablets as early as possible is recommended (3x daily 7.5 mg metronidazole/kg body weight).

— Children under 12 years.
Daily dosis: The dosis according to the calculation basis of 22.5 mg metronidazole/kg body weigth/day is administered 1x daily as slow intravenous solution of 5 ml infusion solution/minute (7.5 mg per kg body-weight thrice daily).

Treatment before or after surgery.
For perioperative treatment a single slow intravenous infusion (5 ml infusion solution/minute) of 300 ml Metronidazole Fresenius corresponding to 1.5 g metronidazole immediately before the onset of surgery is recommended.
In cross-contaminations or in dehiscence of suture or wound areas the same dosis should again be administered 24 hours later.

Remark
In differently strong renal insufficiency metronidazole is increasingly excreted with the stools via the gall.
In case of anuria the dosage should be lowered to 400 — 500 mg metronidazole in 12-hour intervals.

Metronidazole Fresenius should be administered as slow intravenous infusion (5 ml/minute). A concomitant parenteral administration of suitable antibiotics, which have to be administered separately, is possible.

Metronidazole Fresenius can also be administered as intravenous infusion combined with physiological sodium chloride solution, glucose

saline solutions, 5% glucose solution, potassium chloride solutions (20 mmol, 40 mmol) and Ringer solution.

Duration of application

Caution
Treatment with Metronidazole Fresenius must not exceed 10 days. Only in well-founded single cases the duration of application can be prolonged. The therapy should only be repeated in rare instances and only in established indication (cf also contraindications).

The limitation of the duration of application has to be strictly obeyed, since it cannot be excluded that metronidazole may cause a mutagenic and carcinogenic response.

Storage conditions

Store protected from light!

Precautions

Do not use Metronidazole Fresenius after expiry date.

Do not use if the solution is cloudy or if the container is damaged.

Keep out of reach of children!

Presentation

Glass bottle	100 ml
Hospital pack	10 x 100 ml

Fresenius