Alert

There are few data from prospective trials on the safety and efficacy of metronidazole in newborn infants.

Indication

Treatment of anaerobic bacterial (including meningitis) and protozoal infections. Treatment of necrotising enterocolitis.

Action

Metronidazole is bactericidal against anaerobic bacteria and an antiprotozoal agent.

Drug Type

Antibacterial — nitroimidazole

Trade Name

Flagyl, Metronidazole Sandoz IV Solution for infusion, DBL Metronidazole Intravenous Infusion, Metronidazole Intravenous Infusion (Baxter) Solution for infusion, Metronidazole-Claris Solution for infusion

Flagyl S Suspension

Presentation

500 mg/100 mL IV solution
200 mg/5 mL Oral Suspension

Dosage/Interval

IV or PO

<table>
<thead>
<tr>
<th>Postmenstrual age/Corrected age</th>
<th>Loading dose</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 27 weeks</td>
<td>15 mg/kg</td>
<td>7.5 mg/kg 24 hourly</td>
</tr>
<tr>
<td>27th–33rd weeks</td>
<td>15 mg/kg</td>
<td>7.5 mg/kg 12 hourly</td>
</tr>
<tr>
<td>34th–40th weeks</td>
<td>15 mg/kg</td>
<td>7.5 mg/kg 8 hourly</td>
</tr>
<tr>
<td>≥ 41st weeks</td>
<td>15 mg/kg</td>
<td>7.5 mg/kg 6 hourly</td>
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Maximum daily dose

Route

IV or PO

Preparation/Dilution

IV: Use undiluted.

Administration

IV Infusion: Over 30 minutes with a syringe pump. Oral: Give 1 hour before feeds preferably.

Monitoring

Full blood count if patient is on therapy > 1 week. Liver and renal function tests.

Contraindications

Hypersensitivity to metronidazole or other nitroimidazoles.

Precautions

Patients with seizures or peripheral neuropathy, blood dyscrasias, renal or hepatic impairment — dose reduction may be required.

Drug Interactions

Co-administration with phenobarbital (phenobarbitone) and phenytoin may reduce metronidazole concentrations and increase phenytoin concentrations. Monitor anticonvulsant concentrations. Concurrent use with QT-prolonging drugs may result in increase of QT interval resulting in arrhythmias (torsades de pointes).

Adverse Reactions

More common: GI upset, stomatitis and candida overgrowth. Drug metabolite may cause brownish discoulouration of urine. Rare: Convulsive seizures and peripheral neuropathy characterised mainly by numbness or paraesthesia of an extremity have been reported in adults. May cause reversible leucopenia and/or thrombocytopenia.

Compatibility

Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%
Drugs via Y-site: Amino acid solution, aciclovir, dopamine, esmolol, fluconazole, labetalol, lipid emulsion, magnesium sulfate, methylprednisolone sodium succinate, midazolam, morphine sulfate, piperacillin-tazobactam (EDTA-free), remifentanil

Incompatibility

Amphotericin, aztreonam, cefepime, ganciclovir

Stability

Once removed from original container, use as soon as practicable

Storage


Special Comments

Metronidazole oral suspension is best absorbed on an empty stomach.
### Evidence summary

**Efficacy and Safety**

There is a lack of data from prospective trials on the safety and efficacy of metronidazole in newborn infants. A retrospective study reported broad-spectrum antibiotics plus metronidazole may not prevent the deterioration of NEC in full-term and near-term infants.¹ (LOE III-3 GOR D)

**Pharmacokinetics**

Metronidazole principally undergoes hepatic metabolism with clearance increasing with weight and post-menstrual age (PMA). Cohen-Wolkowiez et al evaluated the pharmacokinetics of metronidazole in 32 infants born at ≤ 32 weeks’ gestation and less than 120 days old. The study correlated metronidazole clearance with PMA and developed a PK model using nonlinear mixed-effect modeling (NONMEM). Monte Carlo simulations were performed and the study gives dosing recommendations based on PMA separated into < 34 weeks, 34 weeks to 40 weeks, and > 40 weeks.²³ Suyagh et al evaluated the pharmacokinetics of 32 infants born at ≤ 37 weeks gestation and less than 55 days old. A 1-compartment model was developed using NONMEM. Monte Carlo simulations were performed and dose recommendations are given based on PMA separated into < 26 weeks, 26–27 weeks, 28–33 weeks, and ≥ 34 weeks.⁴ (LOE IV GOR C)

### References

5. MIMS Product Information (2014) DBL Metronidazole Intravenous Infusion, Hospira
8. MIMS Product Information (2016) Flagyl S Suspension, Sanofi-Aventis