

**Treatment of bacillary dysentery by: Fluoroquinolones such as ciprofloxacin. Cotrimoxazole (trimethoprim- sulfamethoxazole)**

Drug	MOA	Pharmacokinetics	ADRs
<b>Ciprofloxacin:</b> <b>Contraindicated:</b> <ul style="list-style-type: none"> <li>Children, pregnancy, nursing mother</li> <li>Epilepsy</li> <li>Arrhythmias.</li> </ul> Should not be combined with antacids, divalent cations.	Block bacterial DNA synthesis <b>Uses</b> <ul style="list-style-type: none"> <li>Bacterial diarrhea (caused by <i>shigella</i>, <i>salmonella</i> and <i>E coli</i>).</li> <li>Urinary tract infections</li> <li>Respiratory tract infections</li> <li>Soft tissues, bones, and joint infections</li> </ul>	Active against a variety of gram-positive and gram-negative bacteria.	<ul style="list-style-type: none"> <li>Arthropathy (damage of growing cartilage).</li> <li>GIT disorders (nausea, vomiting, diarrhea).</li> <li>CNS disorders (headache, dizziness).</li> <li>CVS disorder (prolonged QT interval)</li> <li>Phototoxicity.</li> <li>Liver toxicity</li> </ul> <b>TOXICITY:</b> GIT, CNS and Tendon related

**Treatment of dysentery and amebiasis :**

Drug	MOA+Uses	Pharmacokinetics	ADRs
<b>1] Luminal Amebicides:</b>			
<b>A) Diloxanide furoate:</b> Drug of choice for <u>asymptomatic intestinal infection</u> .  <b>Contraindications:</b> <ul style="list-style-type: none"> <li><b>Pregnancy.</b></li> <li>Children (less than 2 years).</li> </ul>	Mechanism of action is <u>unknown</u>	-Ester of diloxanide + furoic acid . -Given <b>orally</b> . -It splits in the <b>intestine</b> , <u>most of diloxanide is absorbed</u> , conjugated to form a <b>glucuronide</b> which is <b>excreted in urine (90%)</b> . -The unabsorbed diloxanide <b>is the amoebicidal agent (10%)</b> .	(GIT as all luminal amebicides) <ul style="list-style-type: none"> <li>Flatulence</li> <li>Nausea, vomiting, abdominal cramps.</li> <li>No serious adverse effects</li> </ul>
<b>B) Iodoquinol:</b> <b>Precautions:</b> -Iodoquinol should be used with caution in patients with <b>optic neuropathy, renal or thyroid disease</b> . -discontinued if it produces persistent diarrhea or signs of iodine toxicity ( <i>dermatitis, urticaria, pruritus, fever</i> ).	Mechanism of action is <u>unknown</u>	<ul style="list-style-type: none"> <li>Is given <b>orally</b></li> <li>Not absorbed (90%), excreted in feces.</li> <li><b>10% enter circulation</b>, excreted as <b>glucouronide</b> in urine. (Same as Diloxanide furoate)</li> </ul>	<ul style="list-style-type: none"> <li>GIT: Nausea, vomiting, diarrhea.</li> <li><b>Peripheral neuropathy including optic neuritis</b></li> <li><b>Enlargement of the thyroid gland.</b></li> <li><b>Iodine sensitivity.</b></li> <li><b>Interference with thyroid function tests</b> (increase protein-bound serum iodine, decrease in measured <sup>131</sup>I uptake).</li> </ul>
<b>C) Antibiotics</b>			
<b>1- Paromomycin Sulphate:</b>  <b>2- Tetracyclines:</b> Used in <b>severe cases</b> of amoebic dysentery not responding to <b>metronidazole combined with dehydroemetine</b> . - <u>Very weak</u> direct amoebicidal action.	-Has <u>direct amoebicidal</u> action ( <i>causes leakage by its action on cell membrane of parasite</i> ). - <u>Indirect killing of bacterial flora</u> essential for proliferation of pathogenic amoebae.	<ul style="list-style-type: none"> <li><u>Aminoglycoside</u> antibiotic.</li> <li>It is given <b>orally</b></li> <li><u>Not significantly absorbed</u> from GIT</li> </ul> Small amount absorbed is <b>excreted unchanged in urine</b> ( <i>may accumulate with renal insufficiency</i> ).	Gastrointestinal distress and diarrhea.  <b>Contraindications:</b> <ul style="list-style-type: none"> <li>Severe <b>renal disease</b></li> <li>patients with <b>GIT ulceration</b></li> </ul>

## 2-Tissue (Systemic) Amebicides:

### A) Emetine & Dehydroemetine:

Emetine is an alkaloid derived from ipecac, while dehydroemetine is a synthetic analog.

Because of major toxicity concerns they have been almost completely replaced by metronidazole.

irreversible block of protein synthesis.

#### Uses:

- Amoebic liver abscess.
- Intestinal wall infections.
- Severe forms of amebiasis, acute amoebic dysentery dehydroemetine is preferable due to less toxicity (3-5 days).

- Have erratic oral absorption. (Not preferred)
- Given preferably subcutaneously but could be given by IM, **NEVER I.V.** Has long plasma half life about 5 days.
- Metabolized & Excreted slowly via kidney so they have a cumulative effect.
- Trace amounts could be detected in urine 1-2 month after last dose.
- Should not be used for more than 10 days (usually 3-5 days).

- **Dehydroemetine is less toxic than emetine**
- Pain at site of injection, abscesses.
- GIT: nausea, vomiting, diarrhea.
- Serious toxicities: **Cardiotoxicity, Hypotension, cardiac arrhythmias, heart failure**

#### Contraindications:

- **Cardiac Disease.**
- **Renal Disease.**
- **Pregnancy.**
- **Young children**

### B) Chloroquine: (Anti-malarial drug.)

Used in combination with metronidazole or dehydroemetine and luminal amebicide for amebic liver diseases.

**B) Tinidazole:** has similar activity to metronidazole BUT has longer duration of action (12-14h), a simpler dosing regimen (once a day) and a better toxicity profile than metronidazole.

- **Pruritus** is common
- Nausea, vomiting, abdominal pain, anorexia.
- Blurring of vision.
- Hemolysis in G6PD deficient patients
- Agranulocytosis

## 3-Mixed Amebicides:

Effective against both luminal and systemic forms of the disease. Although luminal concentration is too low for single drug-treatment.

### A) Metronidazole:

Drug of choice for treating amebic infections (intestinal & Extra-intestinal).

#### Drug Interactions:

**Enzyme inhibitors** (*cimetidine, ketoconazole*). increase duration of action of metronidazole

**Inducers** (*phenytoin and phenobarbitone*): decrease duration of action of metronidazole

Metronidazole **inhibits CYP family 2C9 & 3A4**  
\*increases **anticoagulant effect of warfarin.**  
\*Increases **lithium toxicity**

Nitro group of metronidazole is reduced by protozoan leading to cytotoxic reduced product that binds to DNA and proteins resulting into parasite death.

#### Uses:

- **Extra-luminal amoebiasis:** is the drug of choice in all tissue amebiasis (**should be combined with luminal amebicide**).
- Giardiasis
- Trichomoniasis
- Broad spectrum of anaerobic bacteria e.g., *Helicobacter pylori* infection + **Pseudo-membranous colitis**

#### Contraindications:

**Pregnancy and nursing women.**  
**Alcohol intake**  
CNS diseases  
**Severe hepatic disease**  
**Severe renal disease**

- **Acts on trophozoites,** has no effect on cysts.
- Given **orally or IV.**
- Absorption is rapid and complete (Due to rapid absorption from GIT, ***not reliably effective against luminal parasites***)
- **Wide distribution to all tissues and body fluids (CSF, saliva, milk).**
- Plasma half life is 8 h
- Metabolized in liver by mixed function oxidase followed by glucuronidation.
- Excreted in urine.
- Clearance is decreased in liver impairment

#### GIT:

- **Dry mouth, metallic taste**
- Nausea, vomiting, diarrhea (***N/D***)
- **Oral Thrush** (Moniliasis, yeast infection).

#### CNS: Neurotoxicological effect

- Insomnia, dizziness
- peripheral neuropathy, paresthesia
- **encephalopathy, convulsion** (***IV infusion, rare***).

#### Other:

- **Dysuria**, dark urine.
- **Neutropenia** (Abnormally low neutrophils)
- **Disulfiram-like effect if taken with alcohol.**