	METRONIDAZOLE	Tinidazole	Emetine and dehydroemetine	**Chloroquine**
	• **Tissue amoebicide.** • **Acts on trophozoites.** • **Metronidazole inhibits DNA replication.** • **Does not eradicate cysts from intestines** • **Drug of choice for treating invasive amebic infections (intestinal & extra-intestinal).**	**Tinidazole** has similar activity to metronidazole but better potency **Advantages of tinidazole** -has longer duration of action (12-14h) -a simpler dosing regimen -a better toxicity profile than metronidazole.	**Emetine is an alkaloid derived from ipeca while dehydroemetine is a synthetic analog.** **-Both are effective against tissue trophozoites of E. histolytica causing irreversible block of protein synthesis.** **-Because of major toxicity concerns they have been almost completely replaced by metronidazole**	
Pharmacokinetics	**Given orally or IV.** **Absorption is rapid and complete.** **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 (consider drug interactions).** **Excreted in urine.** ***Clearance is decreased in liver impairment**		▪ **Have erratic oral absorption.** ▪ **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.** • **Should not be used for more than 10 days (usually 3-5 days).**	
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-450 (2C9 & 3A4) so increases anticoagulant effect of warfarin.** **Increases lithium toxicity.**			
CONTRAINDICATIONS / PRECAUTIONS: ▪	**Pregnancy and breast feeding women.** ▪ **Alcohol intake** ▪ **CNS diseases** ▪ **Severe renal disease** **Severe hepatic disease**		**the drug should not be used in patients with cardiac or renal disease, in young children,or in pregnancy.**	

cont	METRONIDAZOLE	Tinidazole	Emetine and dehydroemetine	**Chloroquine**
uses	**Extra-luminal amoebiasis:** **is the drug of choice in all tissue amebiasis** **N.B. *should be followed by luminal amebicides*.** **Giardiasis** **-Trichomoniasis** **-Broad spectrum of anaerobic bacterial infections** **e.g.** **Peptic ulcer *(Helicobacter pylori)*** **Pseudo-membranous colitis *(Clostridium difficile).***		• **Amoebic liver abscess.** • **Intestinal wall infections.** • **Severe forms of amebiasis acute amoebic dysentery** **dehydroemetine is preferable due to less toxicity (3-5 days).**	• **Anti-malarial drug** **Used in combination with metronidazole or dehydroemetine for amebic liver diseases**
adrs	**G**IT: • Dry mouth, **metallic taste** • Nausea, vomiting, diarrhea (*NVD*) • Oral Thrush (Moniliasis, yeast infection). CNS: Neurotoxicological effect • Insomnia, dizziness • Peripheral neuropathy, paresthesia • **Encephalopathy, convulsion** (*IV infusion, rare*). **Dysuria, dark urine.** **Neutropenia** **Disulfiram-like effect if taken with alcohol.**		**-Because of major toxicity concerns they have been almost completely replaced by metronidazole** **Dehydroemetine is less toxic than emetine** • **GIT: nausea, vomiting, diarrhea.** • **Serious toxicities: cardiotoxicity** **Hypotension, cardiac arrhythmias, heart failure**	• **pruritus is common** • **Nausea, vomiting, abdominal pain, anorexia.** • **Blurring of vision.** • **Hemolysis in G6PD deficient patients**

Luminal amoebicides

Include

- **Diloxanide furoate**
- **Iodoquinol**
- **Antibiotics**
  - **Paromomycin**
  - **Tetracycline**
- used to eradicate cysts of *E histolytica* after treatment of invasive disease.

	Diloxanide furoate	Iodoquinol	Paromomycin Sulphate
	-Ester of diloxanide + furoic acid . -Given orally. -It splits in the intestine, diloxanide is absorbed, conjugated to form a glucoronide which is excreted in urine . -The unabsorbed diloxanide is the amoebicidal agent . -Mechanism of action is unknown -Direct amoebicidal action against luminal forms *-Not active against trophozoites in intestinal wall or extra-intestinal tissues*.	Is given orally Poorly absorbed, excreted in feces. Mechanism of action is unknown effective against the luminal forms of amebiasis	Aminoglycoside antibiotic. Given orally Not significantly absorbed from GIT Effective only against luminal forms of ameba Has direct amebicidal action *(causes leakage by its action on cell membrane of parasite).* Indirect killing of bacterial flora essential for proliferation of pathogenic amoebae. Small amount absorbed is excreted unchanged in urine *(may accumulate with renal insufficiency).*
uses	Drug of choice for asymptomatic intestinal infection (cysts passers). to eradicate cysts of E histolytica after treatment of invasive disease with systemic amebicides.	luminal amoebicide for asymptomatic amebiasis.	Use in chronic amebiasis to eliminate cysts (in cysts passers).
adrs	Flatulence Nausea, vomiting, abdominal cramps.	GIT: Nausea, vomiting, diarrhea. Peripheral neuropathy including optic neuritis Enlargement of the thyroid gland. Iodine sensitivity interference with thyroid function tests (increase protein-bound serum iodine, decrease in measured *(^{131}I uptake).* Iodoquinol should be used with caution in patients with optic neuropathy, renal or thyroid disease. discontinued if it produces persistent diarrhea or signs of iodine toxicity *(dermatitis, urticaria, pruritus, fever).*	Gastrointestinal distress and diarrhea.
contraindications	Pregnancy - Children (less than 2 years)		Severe renal disease patients with GIT ulceration

Bacillary dysentery
Treated by:

- **Fluoroquinolones such as ciprofloxacin**
- **Cotrimoxazole (trimethoprim- sulfamethoxazole)**
- **Children or patient allergic to sulpha drugs parenetral ceftriaxone or oral cefixime (3dr gen cephalosporin) are safe and effective.**
- **Cotrimoxazole is commonly used in traveler's diarrhea.**

Ceftriaxone

- **Third-generation cephalosporin with broad-spectrum, gram-negative activity. It acts by inhibiting cell wall synthesis**

Cefixime

- **Third-generation oral cephalosporin with broad activity against gram-negative bacteria.**

Ciprofloxacin

active against a variety of gram-positive and gram-negative bacteria.

block bacterial DNA synthesis.

Used in treatment of

1. Bacterial diarrhea (caused by shigella, salmonella, and E coli).

2. Urinary tract infections

3. Respiratory tract infections

4. Soft tissues, bones, and joint infections

Adverse effects

Arthropathy (damage of growing cartilage).

GIT disorders (nausea, vomiting, diarrhea).

CNS disorders (headache, dizziness).

CVS disorder (prolonged QT interval)

Phototoxicity.

Liver toxicity.

Contraindicated:

Children, pregnancy, nursing mother

Epilepsy

Arrhythmias.

Should not be combined with antacids, divalent cations

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