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Diloxanide (Systemic)

VA CLASSIFICATION
Primary: AP109

Commonly used brand name(s): *Entamide; Furamide.*

Note: For a listing of dosage forms and brand names by country availability, see *Dosage Forms* section(s).

*Not commercially available in the U.S.

†Not commercially available in Canada.

Category:

Antiprotozoal (systemic)—

Indications

Note: Because diloxanide is not commercially available in the U.S. or Canada, the bracketed information and the use of the superscript 1 in this monograph reflect the lack of labeled (approved) indications for this medication in these countries.

Accepted

[Amebiasis, intestinal (treatment)][1]—Diloxanide is used alone as a primary agent in the treatment of asymptomatic (cyst passers) intestinal amebiasis caused by *Entamoeba histolytica* {01} {02} {03} {04} {05} {07} {08} {09} {10} {11} {12} {13} {14} {23} This medication may also be used concurrently, or sequentially, with other agents such as the nitroimidazoles in the treatment of invasive or extraintestinal forms of amebiasis. {03} {09} {11} {12} {14} {20} {24}

Unaccepted

Diloxanide alone is not effective in the treatment of invasive or extraintestinal amebiasis. {04} {07} {11} {13}

[1] Not included in Canadian product labeling.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Source—

Diloxanide furoate is the ester of 2-furoic acid and diloxanide, a dichloroacetamide derivative. {09} {13} The furoate ester is more active than the parent compound, diloxanide {13}

Molecular weight—

Diloxanide: 234.08 {15}

Diloxanide furoate: 328.2 {16}

Mechanism of action/Effect:

Luminal amebicide. {01} {03} {09} {13} {14} The mechanism of action of diloxanide is unknown. {07} {13} This agent destroys the trophozoites of *E. histolytica* that eventually form into cysts. The cysts are then excreted by persons infected with asymptomatic amebiasis. {24} {25}

Absorption:

Diloxanide furoate is slowly absorbed from the gastrointestinal tract {03} {04} {16} and can therefore provide an adequate concentration of the medication in the intestinal lumen for a long period of time. {03} {04} However, the parent compound, diloxanide, is rapidly absorbed and has a bioavailability of approximately 90%. {16} {17}

Biotransformation:

Diloxanide furoate is largely hydrolyzed into diloxanide and furoic acid in the intestinal lumen before being absorbed. The absorbed diloxanide is extensively conjugated with glucuronic acid, this conjugate being inactive. {14} {16} 99% of diloxanide occurs as glucuronide and 1% as free diloxanide in the systemic circulation. {16}

Time to peak concentration:

Approximately 2 hours after oral administration. {07}

Duration of action:

About 6 hours. {07}

Elimination:
Renal—Approximately 90% of diloxanide is rapidly excreted in the urine as the glucuronide metabolite. {07}
Fecal—About 10%, as diloxanide. {14} {16} {17}

Precautions to Consider

Pregnancy/Reproduction

Pregnancy—
Studies in humans have not been done.

According to the manufacturer, studies in New Zealand white rabbits given diloxanide furoate by oral intubation in doses of 120 or 300 mg per kg of body weight per day from the first day to the twenty-ninth day of pregnancy have shown no embryotoxic or teratogenic effects. The same results were obtained in rats given the same dose from the first day to the twentieth day of pregnancy. Some animals that were given a lower dose of diloxanide furoate until term had normal parturition, survival, and development of the young. {03} {14} {16}

Breast-feeding

It is not known whether diloxanide is distributed into breast milk. However, problems in humans have not been documented.

Pediatrics

Appropriate studies on the relationship of age to the effects of diloxanide have not been performed in the pediatric population. However, no pediatrics-specific problems have been documented to date.

Geriatrics

Appropriate studies on the relationship of age to the effects of diloxanide have not been performed in the geriatric population. However, no geriatrics-specific problems have been documented to date.

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):

Fecal examination (may be required prior to treatment to establish the diagnosis; follow-up stool examinations **{03} {06} {11} {14} {16}** should be done no earlier than 2 weeks after the end of treatment to determine efficacy of treatment **{23}**)

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)—not necessarily inclusive:

Those indicating need for medical attention
Incidence rare

Urticarial rash (skin rash)**{01}{07}{09}{11}{14}{23}**

Those indicating need for medical attention only if they continue or are bothersome
Incidence more frequent

Flatulence (full feeling or passing gas)

{01}{03}{09}{11}{14}{23}nausea{03}{11}{23}

Incidence less frequent

Abdominal cramps (stomach pain)

*{03}{09}{11}{23}**anorexia*** (loss of appetite)

*{03}{09}{23}**diarrhea**{03}{09}{11}{23}*

Patient Consultation
As an aid to patient consultation, refer to *Advice for the Patient, Diloxanide (Systemic)*.

In providing consultation, consider emphasizing the following selected information (» = major clinical significance):

Proper use of this medication
» Taking with meals to minimize gastrointestinal irritation

» Compliance with full course of therapy

» Proper dosing
Missed dose: Taking as soon as possible; not taking if almost time for next dose; not doubling doses

» Proper storage

Precautions while using this medication
Checking with physician at the end of treatment

Side/adverse effects
Sign of potential side effects, especially urticarial rash

General Dosing Information

Diloxanide furoate should be taken with meals to minimize possible gastrointestinal irritation. {18}

Compliance with therapy is important since relapse and reinfection are common. {06} {07}

For treatment of adverse effects
Recommended treatment consists of the following:

• Reduction in dose or discontinuation of treatment. {19}

Oral Dosage Forms

Note: Because diloxanide is not commercially available in the U.S. or Canada, the bracketed uses and the use of superscript 1 in the *Dosage Forms* section reflect the lack of labeled (approved) indications for this product in these countries.

DILOXANIDE FUROATE TABLETS

Usual adult and adolescent dose
[Amebiasis, intestinal][1]
Oral, 500 mg three times a day for ten days. {01} {03} {04} {09} {10} {12} {14} {23}

Usual pediatric dose
[Amebiasis, intestinal][1]
Children up to 12 years of age: Oral, 20 mg per kg of body weight per day given in three divided doses for ten days. {01} {03} {04} {05} {08} {09} {12} {14} {23}

Children 12 years of age and over: See ***Usual adult and adolescent dose.*** {01} {03} {04} {05} {08} {09} {12} {14}

Usual pediatric prescribing limits
Up to 1.5 grams a day. {08}

Strength(s) usually available
U.S.—

Not commercially available. {03} {08} {11} {12} {18}

Note: Although diloxanide is not commercially available in the U.S., it can be obtained from the Parasitic Disease Drug Service, Centers for Disease Control and Prevention, Atlanta, Georgia 30333 (telephone nos.: 404-639-3670; 404-639-2888 on evenings, weekends, or holidays [emergencies only]). {12}

Canada—
Not commercially available.

Note: Although diloxanide is not commercially available in Canada, it is made available with authorization from the Bureau of Human Prescription Drugs (BHPD), Health Protection Branch (HPB), Health Canada, Tower B, 3rd Floor, 1600 Scott Street, Ottawa, Ontario K1A 0L2 (telephone nos.: 613-941-2108). {21} {22}

Other (United Kingdom)—

500 mg (Rx) [*Entamide*] [*Furamide{01}*]

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. Protect from light. {14} {16}

Developed: 08/15/1994

References

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22. Panel comment, 6/94.

23. Panel consensus, 6/94.

24. Panel comment, 6/94.

25. Panel comment, 6/94.

Further information

Always consult your healthcare provider to ensure the information displayed on this page applies to your personal circumstances.