IVERMECTIN (Systemic)

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Onchocerciasis (treatment)¾Ivermectin is used in the treatment of onchocerciasis (river blindness) caused by the parasite Onchocerca volvulus. 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 16, 33, 34

[Filariasis, Bancroft"s (treatment)] *¾Ivermectin is used in the treatment of bancroftian filariasis caused by Wuchereria bancrofti. 20, 21, 22, 26

[Scabies (treatment)] *¾Ivermectin is used in the treatment of scabies caused by Sarcoptes scabiei. 38

Strongyloidiasis (treatment)¾Ivermectin is used as a secondary agent in the treatment of intestinal strongyloidiasis caused by the nematode parasite Strongyloides stercoralis. 29, 34

Acceptance not established

Ivermectin has been used to treat cutaneous larva migrans caused by Ancylostoma braziliense or Ancylostoma caninum. However, data are limited and further study is required to define the role of ivermectin for this condition. 38

Precautions to Consider

Carcinogenicity

Long-term animal studies have not been performed to evaluate the carcinogenic potential of ivermectin. 34

Mutagenicity

Studies using the in vitro Ames microbial mutagenic assay, the mouse lymphoma cell line L5178Y, and the unscheduled DNA synthesis have not shown ivermectin to be genotoxic. 34

Pregnancy/Reproduction

Fertility¾Studies conducted in rats using repeated doses of up to 3 times the maximum recommended human dose of 200 micrograms (mcg) per kg of body weight have shown no adverse effects on fertility. 34 Other studies in cattle, sheep, horses, swine, dogs, and rats also have not shown that ivermectin has any adverse effects on fertility. 8

Pregnancy¾Although adequate and well-controlled studies in humans have not been done, use is not recommended in pregnant women. However, one study of 203 children born to mothers who had been treated with ivermectin during pregnancy (85% during the first trimester and 36% within the first month

of pregnancy) found that use of ivermectin was not associated with any significant difference in the rate of miscarriage, stillbirth, or major congenital malformations, and was not associated with any difference in developmental status or disease patterns. 31

When given to mice, rats, and rabbits in repeated doses of 0.2, 8.1, and 4.5 times the maximum recommended human dose, respectively, ivermectin was found to be teratogenic. Teratogenicity occurred at or near doses that were maternotoxic in these animals. Therefore, ivermectin does not appear to be selectively fetotoxic to the developing fetus in mice, rats, and rabbits. 34

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Breast-feeding

Ivermectin is distributed into breast milk. In one study, a maximum level of 23 nanograms per mL was found on the day after treatment and dropped below 0.1 nanogram per mL approximately 1 week later. 27

Pediatrics

Appropriate studies on the relationship of age to the effects of ivermectin have not been performed in children weighing less than 15 kg. Safety and efficacy have not been established. 34

Geriatrics

No information is available on the relationship of age to the effects of ivermectin in geriatric patients.

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
With physiology/laboratory values

For the treatment of onchocerciasis

Hemoglobin concentration and

White blood cell count

(may be increased 34)

For the treatment of strongyloidiasis

Alanine aminotransferase (ALT [SGPT]) values, serum and

Aspartate aminotransferase (AST [SGOT]) values, serum

(may be increased 34)

Hemoglobin concentration and

White blood cell count

(may be decreased 34)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Risk-benefit should be considered when the following medical problems exist

Hypersensitivity to ivermectin

Bronchial asthma

(worsening of bronchial asthma has been reported 34)

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):
For onchocerciasis

>> Ophthalmologic examinations

(ophthalmologic examinations, including examinations for visual acuity and slit-lamp examinations to determine the number of microfilariae in the cornea and anterior chamber, are recommended prior to and following treatment with ivermectin; if intraocular microfilariae are noted prior to treatment, slit-lamp examinations should be repeated 3, 6, and 12 months following treatment 2, 3, 7, 8, 9, 14)

>> Skin snips

(skin snips from the lateral sides of one or both scapulae, iliac crests, or calves are recommended prior to and following treatment with ivermectin to determine the number of intradermal microfilariae; skin snips are recommended 3, 6, and 12 months following treatment 2, 3, 6, 7, 8, 9, 14)

For strongyloidiasis

>> Stool examinations

(at least three stool examinations should be done over the 3 months following treatment; concentration techniques, such as a Baermann test, should be used to perform the examination. This technique can detect very low numbers of Strongyloides larvae in feces and should be used if routine stool examinations are negative and for posttherapy examinations 34, 35)

Side/Adverse Effects

Note: No major CNS toxicity has been reported since ivermectin does not cross the blood-brain barrier in humans. 6, 7, 14

The microfilaricidal action of ivermectin is less abrupt than that of diethylcarbamazine, and no serious systemic or ocular toxicity has been reported in humans. 1, 2, 3, 4, 7, 8 However, the frequency and severity of side effects were found to be related to the degree of parasite infection. 19 Side effects usually peak around day 2 or 3. 25

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence less frequent

During treatment of onchocerciasis

Ophthalmologic effects, including limbitis 2, 34 , punctate opacity 2, 3, 34 , conjunctivitis 34 , and eyelid edema 34 (eye or eyelid irritation, pain, redness, or swelling) 34

Note: Ophthalmologic side effects do occur as a result of the disease itself but also have been reported after treatment with ivermectin and are rarely severe or associated with loss of vision. These side effects usually resolve without corticosteroid treatment.

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

Incidence more frequent

During treatment of onchocerciasis

Mazzotti-like reaction, especially arthralgia or myalgia 2, 25, 34 (joint or muscle pain); but also fever 1, 2, 3, 25, 34; lymphadenopathy 2, 3, 25, 34 (painful and tender glands in neck, armpits, or groin); pruritus 2, 3, 6, 25, 34 (itching); or skin rash 2, 3, 25, 34; tachycardia 34 (rapid heartbeat)
Incidence less frequent

During treatment of onchocerciasis

Facial edema 34 (swelling of the face); headache 3, 25, 34; peripheral edema 34 (swelling of the arms, feet, hands, or legs)
During treatment of strongyloidiasis

Diarrhea 34; dizziness 6; skin rash 2, 3, 25, 34 or itching 2, 3, 6, 25, 34¾due to death of microfilariae in skin
Incidence rare

During treatment of onchocerciasisPostural hypotension 25 (lightheadedness when getting up from a lying or sitting position)
During treatment of strongyloidiasis

Anorexia 34 (loss of appetite); somnolence 34 (sleepiness); tremor 34 (shaking or trembling)

Overdose

For more information on the management of overdose or unintentional ingestion, contact a Poison Control Center (see Poison Control Center Listing).

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:

Note: Accidental ingestion of or exposures to the veterinary formulation of ivermectin (via ingestion, inhalation, injection, or topical exposure) has occurred in humans.Asthenia; dizziness; edema; headache; rash; seizures

Treatment of overdose

To decrease absorption¾Induction of emesis and/or gastric lavage as soon as possible, followed by administration of purgatives and other routine overdose measures. 34

Supportive care¾If indicated, should include parenteral fluids and electrolytes, respiratory support, and pressor agents if clinically significant hypotension is present. 34

Side/adverse effects

During treatment of onchocerciasis¾signs of potential side effects, especially ophthalmologic effects including limbitis, punctate opacity, conjuctivitis, and eyelid edema

General Dosing Information

Ivermectin should be administered as a single dose with a full glass (240 mL) of water on an empty stomach (1 hour before breakfast). 8, 9, 34

Single doses as low as 50 mcg per kg of body weight have shown significant microfilaricidal activity. 4, 6, 7, 12 In addition, a single oral dose (approximately 150 mcg per kg of body weight) usually reduces the dermal microfilarial count to very low levels and maintains them for up to 12 months. 1, 7

Systemic corticosteroids, although rarely required, may be helpful when administered concurrently to suppress the inflammatory response to the death of microfilariae caused by ivermectin in patients with advanced disease and high microfilariae counts in the eye. 1, 3, 8, 14

For onchocerciasis¾

Ivermectin does not kill the adult Onchocerca parasite; treatment may need to be repeated for killing the new batch of larvae. 34