

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

 **STROMEKTOL™**

ivermectin tablet, USP

3 mg

Antiparasitic Agent

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RECENT MAJOR LABEL CHANGES

Not applicable

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

STROMEKTOL™ (ivermectin) is indicated for the treatment of:

- intestinal strongyloidiasis;
- onchocerciasis;

1.1 Pediatrics

Pediatrics (less than 15 kg): Safety and effectiveness of STROMEKTOL™ in pediatric patients weighing less than 15 kg has not been established (See [6. WARNINGS and PRECAUTIONS](#)).

1.2 Geriatrics

Geriatrics (≥65 years of age): Evidence from clinical studies and experience in the geriatric population has not identified differences in responses between the elderly and younger patients. (See [6. WARNINGS and PRECAUTIONS](#)).

2 CONTRAINDICATIONS

STROMEKTOL™ is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 5. Dosage Forms, Strengths, Composition and Packaging.

3 DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

The dosage tables below show the number of 3-mg tablets recommended for various body weights for each indication.

3.2 Recommended Dose and Dosage Adjustment

Strongyloidiasis (See Table 1)

The recommended dosage of STROMEKTOL™ for the treatment of strongyloidiasis is a single oral dose designed to provide approximately 200 mcg of ivermectin per kg of body weight. (See TABLE 1 for dosage guidelines.) Patients should take tablets on an empty stomach with water. In general, additional doses are not necessary. However, follow-up stool examinations should be performed to verify eradication of infection. (See 13. CLINICAL TRIALS)

TABLE 1
 Dosage Guidelines for Strongyloidiasis
 Dosage by WEIGHT

BODY WEIGHT (kg)	DOSE (approx. 200 mcg/kg) (Number of 3-mg tablets)
15 to 24	one
25 to 35	two
36 to 50	three
51 to 65	four
66 to 79	five
≥80	approx. 200 mcg/kg

Onchocerciasis (See Table 2)

The recommended dosage of STROMECTOL™ for the treatment of onchocerciasis is a single oral dose designed to provide approximately 150 mcg/kg of body weight. Patients should take tablets on an empty stomach with water. In mass distribution campaigns for onchocerciasis, the most commonly used dose interval is 12 months. For the treatment of individual patients, retreatment may be considered at intervals as short as 3 months.

TABLE 2
 Dosage Guidelines for Onchocerciasis
 Dosage by WEIGHT

	For Onchocerciasis
BODY WEIGHT (kg)	DOSE when given once every 12 months (approx. 150 mcg/kg) Number of 3-mg Tablets
15 to 25	one
26 to 44	two
45 to 64	three
65 to 84	four
≥85	approx. 150 mcg/kg

3.3 Administration

STROMEKTOL™ is administered as a single oral dose given with water on an empty stomach.

3.4 Reconstitution

Not applicable

3.5 Missed Dose

The dosing of STROMEKTOL™ for Onchocerciasis or Strongyloidiasis is a single oral dose (see 3. DOSAGE AND ADMINISTRATION).

4 OVERDOSAGE

There are reports of accidental overdosage of ivermectin, but no fatalities have been attributable to ivermectin overdosing.

In accidental intoxication with or significant exposure to unknown quantities of veterinary formulations of ivermectin in humans, either by ingestion, inhalation, injection, or exposure to body surfaces, the following adverse effects have been reported most frequently: rash, contact dermatitis, edema, headache, dizziness, asthenia, nausea, vomiting, and diarrhea. Other adverse effects that have been reported include: seizure, ataxia, dyspnea, abdominal pain, paresthesia, and urticaria.

In case of accidental poisoning, supportive therapy, if indicated, should include parenteral fluids and electrolytes, respiratory support (oxygen and mechanical ventilation if necessary) and pressor agents if clinically significant hypotension is present. Induction of emesis and/or gastric lavage as soon as possible, followed by purgatives and other routine antipoison measures may be indicated if needed to prevent absorption of ingested material.

In a study in which healthy volunteers were orally administered up to 2000 mcg/kg ivermectin in a fasted state or up to 600 mcg/kg ivermectin following a high-fat (48.6 g of fat) meal, there were no indications of central nervous system toxicity observed at any dose irrespective of food intake. (See [8. DRUG INTERACTIONS](#))

For management of a suspected drug overdose, contact your regional poison control centre.

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 3 – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	tablet 3 mg	butylated hydroxyanisole, citric acid, magnesium stearate, microcrystalline cellulose and pregelatinized starch

STROMECTIONOL™ tablets, 3 mg, are white, round, flat, bevel-edged tablets engraved with MSD on one side and 32 on the other side. They are supplied in unit dose packages in cartons of 4 tablets.

6 WARNINGS AND PRECAUTIONS

General

Do not use STROMECTIONOL™ if there is a history of hypersensitivity reaction to this product

Rarely, patients who are also heavily infected with *Loa loa* may develop a serious or even fatal encephalopathy either spontaneously or following treatment with an effective microfilaricide. In these patients, the following adverse experiences have also been reported: pain (including neck and back pain), red eye, conjunctival hemorrhage, dyspnea, urinary and/or fecal incontinence, difficulty in standing/walking, mental status changes, confusion, lethargy, stupor, seizures, or coma. This syndrome has been seen very rarely following the use of STROMECTIONOL™. In individuals who warrant treatment with STROMECTIONOL™ for any reason and have had significant exposure to *Loa loa*-endemic areas of West or Central Africa, pretreatment assessment for loiasis and careful post-treatment follow-up should be implemented

After treatment with microfilaricidal drugs, patients with hyperreactive onchodermatitis (sowda) may be more likely than others to experience severe adverse reactions, especially edema and aggravation of onchodermatitis

Onchocerciasis

STROMECTIONOL™ has no activity against adult *Onchocerca volvulus* parasites. The adult parasites reside in subcutaneous nodules which are infrequently palpable. Surgical excision of these nodules (nodulectomy) may be considered in the management of patients with onchocerciasis, since this procedure will eliminate the microfilariae-producing adult parasites. Alternatively repeated follow-up and retreatment with STROMECTIONOL™ may be required.

Historical data have shown that microfilaricidal drugs, such as diethylcarbamazine citrate (DEC), might cause cutaneous and/or systemic reactions of varying severity (the Mazzotti reaction) and ophthalmological reactions in patients with onchocerciasis. These reactions are probably due to allergic and inflammatory responses to the death of microfilariae. Patients treated with STROMECTIONOL™ for onchocerciasis may experience these reactions in addition to clinical adverse reactions possibly, probably, or definitely related to the drug itself. (See [7. ADVERSE REACTIONS](#))

The treatment of severe Mazzotti reactions has not been subjected to controlled clinical trials. Oral hydration, recumbency, intravenous normal saline, and/or parenteral corticosteroids have been used to treat postural hypotension. Antihistamines and/or non-steroidal anti-inflammatory drugs such as aspirin/acetaminophen (paracetamol) have been used for most mild to moderate cases.

No data are available to support the use of STROMECTIONOL™ prophylactically against onchocerciasis.

Strongyloidiasis In Immunocompromised Hosts

In immunocompromised (including HIV-infected) patients being treated for intestinal strongyloidiasis, repeated courses of therapy have been required. Adequate and well-controlled clinical studies have not been conducted in such patients to determine the optimal dosing regimen. Several treatments, e.g., at 2 week intervals, may be required, and even then cure may not be achievable. Control of extra-intestinal strongyloidiasis in these patients is difficult, and suppressive therapy, i.e., once per month may be helpful.

The patient should be reminded of the need for repeated stool examinations to document clearance of infection with *Strongyloides stercoralis*.

6.1 Special Populations

6.1.1 Pregnant Women

Safety in pregnant women has not been established. Limited post marketing surveillance has not established a relationship between exposure to ivermectin during the first trimester and the occurrence of adverse pregnancy outcomes. The frequencies of congenital anomalies, spontaneous abortions, fetal deaths/stillbirths and infant mortalities in approximately 400 women inadvertently treated with ivermectin during the first trimester in mass treatment campaigns for onchocerciasis were similar to frequencies in women not treated with ivermectin during pregnancy. There are not sufficient data to assess the safety of a single dose of ivermectin administered during the second and third trimesters.

Ivermectin caused cleft palates in mice and rats at oral doses of 0.4 and 10 mg/kg/day respectively, and cleft palates and clubbed feet in rabbits dosed at 3 mg/kg/day..These developmental effects were found only at or near doses that were maternotoxic to the pregnant female.

Treatment of pregnant women with ivermectin should be limited to mass treatment campaigns in which the risk of complications from untreated onchocerciasis exceeds the potential risk to the fetus from treatment.

6.1.2 Breast-feeding

Less than 2% of the administered dose of ivermectin appeared in breast milk. Safety in newborn infants has not been established; therefore, the drug should be given to nursing mothers only if the benefit to the mother outweighs the potential risk to the breast-fed infant, and treatment of mothers who intend to breast feed their infants should be delayed until at least 1 week after birth of the child.

6.1.3 Pediatrics

Pediatrics (less than 15 kg): The safety and efficacy of STROMECTOL™ in pediatric patients weighing less than 15 kg has not been established

6.1.4 Geriatrics

Clinical studies of STROMECTIONOL™ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, treatment of an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

7 ADVERSE REACTIONS

7.1 Adverse Reaction Overview

STROMECTIONOL™ (ivermectin) has been demonstrated to be generally well tolerated. For the most part side effects have been mild and transient in nature.

7.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Strongyloidiasis

In four clinical studies involving a total of 109 patients given either one or two doses of 170 to 200 mcg/kg of ivermectin, the following adverse reactions were reported as possibly, probably, or definitely related to ivermectin:

Body as a whole: asthenia/fatigue (0.9%), abdominal pain (0.9%)

Gastrointestinal: anorexia (0.9%), constipation (0.9%), diarrhea (1.8%), nausea (1.8%), vomiting (0.9%)

Nervous System/Psychiatric: dizziness (2.8%), somnolence (0.9%), vertigo (0.9%), tremor (0.9%)

Skin: pruritus (2.8%), rash (0.9%), and urticaria (0.9%)

In comparative trials, patients treated with STROMECTIONOL™ experienced more abdominal distention and chest discomfort than patients treated with albendazole. However, STROMECTIONOL™ was better tolerated than thiabendazole in comparative studies involving 37 patients treated with thiabendazole.

The Mazzotti-type and ophthalmologic reactions associated with the treatment of onchocerciasis or the disease itself would not be expected to occur in strongyloidiasis patients treated with ivermectin.

Onchocerciasis

In clinical trials involving 963 adult patients treated with 100 to 200 mcg/kg ivermectin, worsening of the following signs and symptoms during the first 4 days post-treatment were reported: arthralgia/synovitis (9.3%), axillary lymph node enlargement and tenderness (11.0%)

and 4.4%, respectively), cervical lymph node enlargement and tenderness (5.3% and 1.2%, respectively), inguinal lymph node enlargement and tenderness (12.6% and 13.9%, respectively), other lymph node enlargement and tenderness (3.0% and 1.9%, respectively), pruritus (27.5%), skin involvement including edema, papular and pustular or frank urticarial rash (22.7%), and fever (22.6%). These signs and symptoms are considered part of the Mazzotti-type reactions. (See [6. WARNINGS and PRECAUTIONS](#)).

In clinical trials, ophthalmological conditions were examined in 963 adult patients before treatment, at day 3, and months 3 and 6 after treatment with 100 to 200 mcg/kg ivermectin. Changes observed were primarily deterioration from baseline 3 days post-treatment. Most changes either returned to baseline condition or improved over baseline severity at the month 3 and 6 visits. The percentages of patients with worsening of the following conditions at day 3, month 3 and 6, respectively, were: limbitis: 5.5%, 4.8%, and 3.5% and punctate opacity: 1.8%, 1.8%, and 1.4%. The corresponding percentages for patients treated with placebo were: limbitis: 6.2%, 9.9% and 9.4% and punctate opacity: 2.0%, 6.4% and 7.2%.

In clinical trials involving 963 adult patients who received 100 to 200 mcg/kg ivermectin, the following clinical adverse reactions were reported as possibly, probably, or definitely related to the drug in $\geq 1\%$ of the patients: facial edema (1.2%), peripheral edema (3.2%), orthostatic hypotension (1.1%), and tachycardia (3.5%). Drug-related headache and myalgia occurred in $< 1\%$ of patients (0.2%, and 0.4%, respectively). However, these were the most common adverse experiences reported overall during these trials regardless of causality (22.3% and 19.7%, respectively).

A similar safety profile was observed in an open study in pediatric patients ages 6 to 13.

The following ophthalmological side effects do occur due to the disease itself but have also been reported after treatment with ivermectin: abnormal sensation in the eyes, eyelid edema, anterior uveitis, conjunctivitis, limbitis, keratitis, and chorioretinitis or choroiditis. These have rarely been severe or associated with loss of vision and have generally resolved without corticosteroid treatment.

7.3 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Strongyloidiasis

In clinical trials involving 109 patients given either one or two doses of 170 to 200 mcg/kg ivermectin, the laboratory adverse experiences, reported irrespective of drug relationship, were leukopenia/anemia in one patient and elevated ALT/alkaline phosphatase in one patient.

Onchocerciasis

In controlled clinical trials, the following laboratory adverse experiences were reported as possibly, probably, or definitely related to the drug in $\geq 1\%$ of the patients: eosinophilia (3%) and hemoglobin increase (1%).

7.4 Clinical Trial Adverse Reactions (Pediatrics)

Not applicable.

7.5 Post-Market Adverse Reactions

Onchocerciasis

Conjunctival Haemorrhage

All indications

Hypotension (mainly orthostatic hypotension), worsening of bronchial asthma, toxic epidermal necrolysis, Stevens-Johnson syndrome, seizures, hepatitis, elevation of liver enzymes, and elevation of bilirubin.

8 DRUG INTERACTIONS

8.1 Overview

Post-marketing reports of increased INR (International Normalized Ratio) have been reported when STROMEKTOL™ was co-administered with warfarin.

8.2 Drug-Drug Interactions

In vitro studies using human liver microsomes and recombinant CYP450 enzymes have shown that ivermectin is primarily metabolized by CYP3A4. Depending on the in vitro method used, CYP2D6 and CYP2E1 were also shown to be involved in the metabolism of ivermectin but to a significantly lower extent compared to CYP3A4. The findings of in vitro studies using human liver microsomes suggest that clinically relevant concentrations of ivermectin do not significantly inhibit the metabolizing activities of CYP3A4, CYP2D6, CYP2C9, CYP1A2, and CYP2E1.

8.3 Drug-Food Interactions

A multiple-dose clinical safety study has been conducted to assess the safety and pharmacokinetic properties of STROMEKTOL™ in healthy volunteers. Subjects received oral doses of 30 to 120 mg STROMEKTOL™ in a fasted state or 30 mg STROMEKTOL™ following a standard high-fat (48.6 g of fat) meal. Administration of 30 mg STROMEKTOL™ following a high-fat meal resulted in an approximate 2.5-fold increase in bioavailability relative to administration of 30 mg STROMEKTOL™ in the fasted state. However, there were no indications of central nervous system toxicity associated with either regimen. (See [4. OVERDOSAGE](#))

Drug-Herb Interactions

Interactions with herbal products has not been established

8.4 Drug-Laboratory Test Interactions

Interactions with laboratory test has not been established

8.5 Drug-Lifestyle Interactions

Interactions with drug-lifestyle has not been established

9 ACTION AND CLINICAL PHARMACOLOGY

9.1 Mechanism of Action

Ivermectin is a member of the avermectin class of broad-spectrum antiparasitic agents which have a unique mode of action. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve and muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite. Compounds of this class may also interact with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).

9.2 Pharmacodynamics

STROMECTOL™, an anthelmintic, is derived from the avermectins, a class of highly active broad-spectrum antiparasitic agents isolated from fermentation broths of *Streptomyces avermitilis*

9.3 Pharmacokinetics

Following oral administration of ivermectin, plasma concentrations are approximately proportional to the dose. In two studies, after single 12-mg doses of STROMECTOL™ in fasting healthy volunteers (representing a mean dose of 165 mcg/kg), the mean peak plasma concentrations of the major component (H2B1a) were 46.6 (\pm 21.9) (range: 16.4-101.1) and 30.6 (\pm 15.6) (range: 13.9-68.4) ng/mL, respectively, at approximately 4 hours after dosing. Ivermectin is metabolized in the liver, and ivermectin and/or its metabolites are excreted almost exclusively in the feces over an estimated 12 days, with less than 1% of the administered dose excreted in the urine. The plasma half-life of ivermectin in man is approximately 18 hours following oral administration.

The safety and pharmacokinetic properties of ivermectin were further assessed in a multiple-dose clinical pharmacokinetic study involving healthy volunteers. Subjects received oral doses of 30 to 120 mg (333 to 2000 mcg/kg) ivermectin in a fasted state or 30 mg (333 to 600 mcg/kg) ivermectin following a standard high-fat (48.6 g of fat) meal. Administration of 30 mg ivermectin following a high-fat meal resulted in an approximate 2.5-fold increase in bioavailability relative to administration of 30 mg ivermectin in the fasted state.

In vitro studies using human liver microsomes and recombinant CYP450 enzymes have shown that ivermectin is primarily metabolized by CYP3A4. Depending on the in vitro method used, CYP2D6 and CYP2E1 were also shown to be involved in the metabolism of ivermectin but to a significantly lower extent compared to CYP3A4. The findings of in vitro studies using human liver microsomes suggest that clinically relevant concentrations of ivermectin do not significantly inhibit the metabolizing activities of CYP3A4, CYP2D6, CYP2C9, CYP1A2, and CYP2E1.

Special Populations and Conditions

The pharmacokinetics of STROMECTOL™ has not been studied in patients with impaired

hepatic or renal function.

10 STORAGE, STABILITY AND DISPOSAL

Store at 15-30°C.

11 SPECIAL HANDLING INSTRUCTIONS

Not applicable

PART II: SCIENTIFIC INFORMATION

12 PHARMACEUTICAL INFORMATION

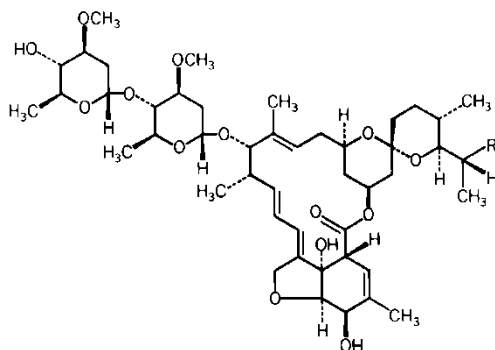
Drug Substance

Proper name: ivermectin

Chemical name: Ivermectin is a mixture which contains not less than 95.0 percent and not more than 102.0 percent for the sum of component 5-O-demethyl-22,23-dihydroavermectin A_{1a} (H₂B_{1a}) plus component 5-O-demethyl-25-de(1-methylpropyl)-25-(1-methylethyl)-22,23-dihydroavermectin A_{1a} (H₂B_{1b}), calculated on the anhydrous and alcohol- and formamide- free basis; and the ratio (calculated by area percentage) of component H₂B_a / H₂B_{1a} + H₂B_{1b}) is not less than 90.0 percent

Molecular formula and molecular mass: H₂B_{1a}: C₄₈H₇₄O₁₄; 875.1
H₂B_{1b}: C₄₇H₇₂O₁₄; 861.1

Structural formula:



Component B_{1a}, R = C₂H₅

Component B_{1b}, R = CH₃

Physicochemical properties: Ivermectin is a white to yellowish-white, crystalline powder which is practically insoluble in water, freely soluble in methanol and soluble in 95% ethanol and acetone.

13 CLINICAL TRIALS

Onchocerciasis

The evaluation of ivermectin in the treatment of onchocerciasis is based on the results of clinical studies involving 1278 patients. In a double-blind, placebo-controlled study involving adult patients with moderate to severe onchocercal infection, patients who received a single dose of 150 mcg/kg ivermectin experienced an 83.2% and 99.5% decrease in skin microfilariae count (geometric mean) 3 days and 3 months after the dose, respectively. A marked reduction of >90% was maintained for up to 12 months after the single dose. As with other microfilaricidal drugs, there was an increase in the microfilariae count in the anterior chamber of the eye at day

3 after treatment in some patients. However, at 3 and 6 months after the dose, a significantly greater percentage of patients treated with ivermectin had decreases in microfilariae count in the anterior chamber than patients treated with placebo.

In a separate open study involving pediatric patients ages 6 to 13 (n=103; weight range: 17 to 41 kg), similar decreases in skin microfilariae counts were observed for up to 12 months after dosing.

Strongyloidiasis

Efficacy and safety for the use of ivermectin in the treatment of strongyloidiasis have been studied in two controlled clinical studies using albendazole as the comparative agent, and three controlled studies using thiabendazole as the comparative agent. Efficacy, as measured by cure rate, was defined as the absence of larvae in follow-up stool examinations. Based on this criterion, efficacy was significantly greater for ivermectin (a single dose of 170 to 200 mcg/kg) than for albendazole (200 mg b.i.d. for 3 days). Ivermectin administered as a single dose of 200 mcg/kg for 1 day was as efficacious as thiabendazole administered at 25 mg/kg b.i.d. for 3 days.

Table 4: Summary of Cure Rates for Ivermectin Versus Comparative Agents in the Treatment of Strongyloidiasis

	Cure Rate Number and (%) of evaluable patients	
	Ivermectin 170 to 200 mcg/kg	Comparative Agent
Albendazole* Comparative International Study	22/28 (79)	10/23 (43)
WHO Study	126/152 (83)	67/149 (45)
Thiabendazole** Comparative International Study	10/15 (67)	13/15 (87)
US Studies	14/14 (100)	16/17 (94)

* 200 mg b.i.d. for 3 days

** 25 mg/kg b.i.d. for 3 days

In one study conducted in France, a non-endemic area where there was no possibility of reinfection, several patients were observed to have recrudescence of *Strongyloides* larvae in their stool as long as 106 days following ivermectin therapy. Therefore, at least three stool examinations should be conducted over the three months following treatment to ensure eradication. If recrudescence of larvae is observed, retreatment with ivermectin is indicated. Concentration techniques (such as using a Baermann apparatus) should be employed when performing these stool examinations, as the number of *Strongyloides* larvae per gram of feces may be very low.

14 MICROBIOLOGY

Ivermectin is a member of the avermectin class of broad-spectrum antiparasitic agents which have a unique mode of action. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve and muscle cells. This

leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite. Compounds of this class may also interact with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).

The selective activity of compounds of this class is attributable to the facts that some mammals do not have glutamate-gated chloride channels and that the avermectins have a low affinity for mammalian ligand-gated chloride channels. In addition, ivermectin does not readily cross the blood-brain barrier in humans.

Ivermectin is active against various life-cycle stages of many but not all nematodes. It is active against the tissue microfilariae of *Onchocerca volvulus* but not against the adult form. Its activity against *Strongyloides stercoralis* is limited to the intestinal stages.

15 NON-CLINICAL TOXICOLOGY

Acute oral studies with ivermectin in mice, rats, and monkeys have shown clear species and strain differences in sensitivity, with rodents being relatively sensitive to the CNS toxicity produced by the compound. Doses of 200 mcg/kg in mice and slightly higher doses in rats have produced tremors and ataxia, while a 200 mcg/kg dose was generally well tolerated in studies in a variety of species. Acute oral studies in rhesus monkeys demonstrated that the minimum toxic dose was 2,000 mcg/kg or approximately 10-fold the clinical dose. Doses up to 24 mg/kg in this species (120-fold the clinical dose) produced only slight increases in the observed toxic effects including emesis, mydriasis, and sedation. A repeated dose study of 2 weeks' duration in rhesus monkeys produced no adverse effects at doses up to 1,200 mcg/kg/day. Fourteen-week studies in rats and dogs indicated no adverse effects at doses of 400 and 500 mcg/kg/day, respectively.

Breeding performance in various species has not been adversely affected by ivermectin.

Ivermectin caused cleft palates in mice and rats at oral doses of 0.4 and 10 mg/kg/day respectively, and cleft palates and clubbed feet in rabbits dosed at 3 mg/kg/day. These development effects were found only at or near doses that were maternotoxic to the pregnant female.

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

Ivermectin is negative in the Ames microbiological mutation and the mouse lymphoma mutation assays; it did not induce unscheduled DNA synthesis in human fibroblast cell culture.

Significant lethality was observed in mice and rats after single oral doses of 25 to 50 mg/kg and 40 to 50 mg/kg, respectively. No significant lethality was observed in dogs after single oral doses of up to 10 mg/kg. At these doses, the treatment related signs that were observed in these animals include ataxia, bradypnea, tremors, ptosis, decreased activity, emesis, and mydriasis.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

 **STROMECTIONOL™**
ivermectin tablets, USP

Read this carefully before you start taking **STROMECTIONOL™** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **STROMECTIONOL™**.

What is STROMECTIONOL™ used for?

STROMECTIONOL™ is used to treat infections caused by some parasites (worms).

How does STROMECTIONOL™ work?

STROMECTIONOL™ works by killing the developing worms.

What are the ingredients in STROMECTIONOL™?

Medicinal ingredient: ivermectin

Non-medicinal ingredients: microcrystalline cellulose, pregelatinized starch, butylhydroxyanisole, citric acid and magnesium stearate.

STROMECTIONOL™ comes in the following dosage forms:

Tablets, 3 mg

Do not use STROMECTIONOL™ if:

- you are allergic (hypersensitive) to ivermectin or any of the other ingredients of STROMECTIONOL™.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take STROMECTIONOL™. Talk about any health conditions or problems you may have, including if you:

- Live or have spent time in parts of Africa. Certain infections from this area, such as “Loa Loa” or “eye-worm”, may cause side effects while taking STROMECTIONOL™. See “What are possible side effects from using STROMECTIONOL™?”, below.
- Have a weak immune system. In this case, your doctor may order tests and request stool samples to monitor your infection.
- Are pregnant or might become pregnant
- Are breast-feeding or intend to breast-feed, STROMECTIONOL™ is passed into breast milk.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with STROMECTIONOL™:

- warfarin

How to take STROMECTIONOL™:

Always take STROMECTIONOL™ exactly as your doctor has told you.

Take the tablets by mouth with water on an empty stomach.

Usual dose:

The dose depends on your illness and your weight.

For Strongyloidiasis: One dose of 0.2 mg per kg of body weight.

For Onchocerciasis: 0.15 mg per kg of body weight every 3 – 12 months.

Overdose:

If you think you have taken too much STROMECTIONTM, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

STROMECTIONTM is a single dose treatment. If you did not take your dose at the prescribed time, take it as soon as possible with water on an empty stomach.

What are possible side effects from using STROMECTIONTM?

These are not all the possible side effects you may feel when taking STROMECTIONTM. If you experience any side effects not listed here, contact your healthcare professional.

Side effects:

- Changes in some laboratory tests (increase of liver enzymes, increase of bilirubin in blood, increase of eosinophils)
- Low blood pressure (hypotension). You may feel dizzy or light-headed when standing up
- Worsening of asthma.

The side effects below depend on what you are taking STROMECTIONTM for. They also depend on whether you have any other infections.

People with intestinal strongyloidiasis (anguillulosis) may have the following side effects:

- feeling unusually weak
- loss of appetite, stomach pain, constipation or diarrhoea
- feeling dizzy
- shaking or tremors.

People with a heavy infection of the worm “Loa loa” may have the following side effects:

- abnormal brain function
- neck and back pain
- bleeding in the whites of your eyes
- loss of control of your bladder or your bowels
- difficulty standing or walking
- mental status changes
- not responding to other people or going into a coma.
- seizure

People infected with the worm “Onchocerca volvulus” which causes river blindness may have the following side effects:

- joint or muscle pains
- swelling of lymph nodes
- swelling, especially of the face, hands, ankles or feet
- fast heart rate
- changes to your vision and other eye problems such as infection, redness or unusual feelings
- bleeding in the whites of your eyes or swelling of your eye lids
- headache

Serious Side Effects			
Symptoms / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Allergic Reaction with symptoms of: <ul style="list-style-type: none"> • Sudden fever • Skin reactions (such as rash or itching) or other serious skin reactions • difficulty breathing 		X	
Stevens-Johnson syndrome with symptoms of: <ul style="list-style-type: none"> • flu like symptoms • peeling skin • blisters and sores around your mouth 		X	
Liver problems (hepatitis) with symptoms of: <ul style="list-style-type: none"> • Yellowing of the skin • Stomach pain • Nausea or vomiting • Feeling confused • Feeling tired or sleepy 		X	

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at 15-30°C.

Keep out of reach and sight of children.

If you want more information about STROMEKTOL™:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<http://hc-sc.gc.ca/index-eng.php>); or the Merck Canada website www.merck.ca or by calling Merck Canada at 1-800-567-2594.

To report an adverse event related to STROMEKTOL™, please contact 1-800-567-2594.

This leaflet was prepared by Merck Canada Inc.

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