

Essential Drugs

WHO Model Formulary

As described in the previous issue of this journal, work is now under way on the WHO Model Formulary, and draft texts will be published regularly to obtain comments on the material proposed for publication. Observations concerning the following section related to anthelmintics should be addressed to: Drug Selection and Information (DSI), Division of Drug Management & Policies, World Health Organization, 1211 Geneva 27, Switzerland.

Anti-infective drugs: anthelmintics

Drugs used for cestode (tapeworm) infections

Cestode infections include intestinal taeniasis and cysticercosis, hymenolepiasis, diphylobothriasis and echinococcosis.

Praziquantel is generally used for the treatment of cestode infections due to *Taenia solium*, *T. saginata*, *Hymenolepis nana* and *Diphyllobothrium latum* and *D. pacificum*. It is well tolerated and extensively absorbed and kills adult intestinal taenia worms in a single dose. Cestode infections occurring during pregnancy should always be treated immediately because of the risk of cysticercosis.

Praziquantel also kills *T. solium* cysticerci when taken for 14 days in high doses. It thus offers the prospect of a cure for neurocysticercosis, which was previously treatable only by surgery, anti-inflammatory corticosteroids and use of anti-convulsants. However, because dying and disintegrating cysts may induce localized cerebral oedema, treatment with praziquantel must always be undertaken in a hospital setting. Albendazole, which is an alternative to praziquantel, kills cysticerci, but only when administered at a daily dosage of 15 mg/kg for 30 days. The longer-established compound niclosamide acts only against the adult intestinal worms.

In hymenolepiasis, praziquantel is more effective than niclosamide, although resistance to prazi-

quantel has already been reported. Repeated treatment may be necessary to cure intense infections or to eliminate the parasite within a family group or institution.

In diphylobothriasis, niclosamide or praziquantel in a single dose is highly effective. Hydroxocobalamin injections and folic acid supplements may also be required.

In echinococcosis, although surgery is still the treatment of choice for operable cystic disease due to *Echinococcus granulosus*, chemotherapy with benzimidazoles, such as mebendazole and albendazole, may be of value as adjunctive therapy. Alveolar echinococcosis due to *E. multilocularis* requires both surgery and long-term treatment with either mebendazole or albendazole to inhibit metastatic spread

ALBENDAZOLE

Anthelmintic agent

Chewable tablet: 200 mg, 400 mg

Uses: *Echinococcus multilocularis* and *E. granulosus* infections prior to or when not amenable to surgery, and neurocysticercosis.

Dosage:

Cystic echinococcosis

Adults: Up to four 30-day courses of 10–15 mg/kg daily in two divided doses separated by treatment-free periods of 15 days. Patients with *E. multilocularis* infections may need further treatment cycles.

Neurocysticercosis

Adults: 15 mg/kg daily for 30 days. Recent data suggest that an 8-day course may be equally effective.

Contraindications: Known hypersensitivity; first-trimester pregnancy.

Precautions: Liver function tests and blood counts should be regularly monitored throughout treatment when high doses are used.

Adverse effects: Occasionally, transient gastrointestinal discomfort and headache occur and, rarely, rash and fever, alopecia, reversible leukopenia and reversible increases in serum levels of hepatic enzymes.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

MEBENDAZOLE

Anthelmintic agent

Chewable tablet: 100 mg, 500 mg

Uses: *Echinococcus multilocularis* and *E. granulosus* infections prior to surgery.

Dosage: Each dose should preferably be taken between meals. *Adults:* 4.5 g daily in three divided doses for 6 months.

Contraindications: Known hypersensitivity and pregnancy.

Adverse effects: Occasionally, transient gastrointestinal discomfort and headaches occur and, rarely, hypersensitivity reactions and liver abnormalities.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

NICLOSAMIDE

Anthelmintic agent

Chewable tablet: 500 mg

Uses: Infections due to *Taenia saginata*, *T. solium*, *Hymenolepis nana* and *Diphyllobothrium latum*.

Dosage: The tablets should be chewed thoroughly before swallowing and washed down with 250 ml water.

Hymenolepis nana infections

Adults: 2 g on day 1, followed by 1 g daily for 6 days.

For all other indications

Adults: 2 g as a single dose.

Children <10 kg: 0.5 g as a single dose.

Children 10–35 kg: 1 g as a single dose.

Precautions: Chronically constipated patients should receive a purgative before treatment.

Adverse effects: Mild gastrointestinal disturbances.

PRAZICQUANTEL

Anthelmintic agent

Tablet: 150 mg, 600 mg

Uses: Infections due to *Taenia saginata*, *T. solium*, *Hymenolepis nana* and *Diphyllobothrium latum*.

Dosage:**Intestinal taeniasis**

Adults and children over 4 years: a single dose of 5–10 mg/kg.

Hymenolepiasis

Adults and children over 4 years: a single dose of 15–25 mg/kg.

Diphyllobothriasis

Adults and children over 4 years: a single dose of 10–25 mg/kg.

Cysticercosis

Adults and children over 4 years: a total of 50 mg/kg daily in three divided doses for 14 days. A corticosteroid such as prednisolone should be administered for 2–3 days beforehand and then throughout the period of treatment.

Because of the risk of pericystic oedema, patients with neurocysticercosis should always be treated in a hospital setting.

Dermal cysticercosis

Adults and children over 4 years: a total of 60 mg/kg in three divided doses for 6 days.

Contraindications: Ocular cysticercosis.

Adverse effects: Occasionally, abdominal discomfort, nausea, headache, dizziness and drowsiness. Rarely, pyrexia, urticaria and rectal bleeding.

Drugs used for intestinal nematode infections

Intestinal nematode infections include ascariasis, hookworm infection, strongyloidiasis, enterobiasis, trichuriasis, trichostrongyliasis and capillariasis.

Ideally, all cases of hookworm infection should be treated. However, when this is impracticable, priority should be given to women in second- and third-trimester pregnancy, children and debilitated patients. In hookworm, broad-spectrum anthelmintics should be preferred wherever other nematode infections are endemic. Both mebendazole and albendazole are effective.

Levamisole is effective in the treatment of mixed ascaris and hookworm infections and pyrantel has been highly effective in some community-based control programmes, although several doses are often needed to eliminate *Necator americanus* infection. Anaemic patients require supplementary iron salts and should receive ferrous sulfate (200 mg for adults daily) for at least 3 months after the haemoglobin concentration has regained the threshold of 12 g/100 ml.

In strongyloidiasis, all infected patients should be treated. Albendazole, 400 mg administered for 3 consecutive days, is well tolerated by both adults and children over 2 years of age and reports suggest it may eradicate up to 80% of infections.

Mebendazole has also been used but to be effective it must be administered for longer periods as it has a limited effect on larvae and hence upon the cycle of autoinfection. Ivermectin is also effective against strongyloidiasis.

In enterobiasis, all household members should be treated concurrently with a single dose of mebendazole, albendazole or pyrantel. Since reinfection readily occurs, at least one further dose is required 2–4 weeks later. Piperazine is also effective, but must be taken regularly for at least 7 consecutive days.

In trichuriasis, chemotherapy is required whenever symptoms develop or when faecal samples are found to be heavily contaminated (over 10 000 eggs per gram). A single dose of albendazole (400 mg) or mebendazole (500 mg) is effective in mild to moderate infections, but heavy infections require a 3-day course.

In symptomatic trichostrongyliasis, a single dose of pyrantel or albendazole (400 mg) is effective.

In capillariasis, prolonged treatment with mebendazole or albendazole offers the only prospect of cure.

ALBENDAZOLE

Anthelmintic agent

Chewable tablet: 200 mg, 400 mg

Uses: Ascariasis, hookworm infections, strongyloidiasis, enterobiasis, trichuriasis, trichostrongyliasis and capillariasis.

Dosage: *Adults and children over 2 years:* a single dose of 400 mg is sufficient to eliminate most cases of ascariasis, hookworm infection, enterobiasis, trichostrongyliasis, and moderate trichuriasis infections. Strongyloidiasis and heavy trichuriasis infections require a 3-day course of treatment. The dose should be continued for at least 10 days in capillariasis.

Contraindications: Known hypersensitivity; first-trimester pregnancy.

Adverse effects: Occasionally, transient gastrointestinal discomfort and headache.

LEVAMISOLE

Anthelmintic agent

Tablet: 40 mg, 50 mg (as hydrochloride)

Uses: Ascariasis and mixed ascariasis/hookworm infections.

Dosage: *Adults and children:* a single dose of 2.5 mg/kg is used widely for both individual treatment and community-based campaigns. In cases of severe hookworm infection, a second dose may be given 7 days after the first.

Adverse effects Occasionally abdominal pain, nausea, vomiting, dizziness and headache occur.

MEBENDAZOLE

Anthelmintic agent

Chewable tablet: 100 mg, 500 mg

Uses: Hookworm infections, enterobiasis, ascariasis, trichuriasis and capillariasis. Mass treatment control programmes.

Dosage: Each dose should preferably be taken between meals. All doses are suitable for adults and children over 2 years.

Ascariasis

A single dose of 500 mg.

Hookworm infections and trichuriasis

A dose of 100 mg twice daily for 3 consecutive days. A second course may be given after 3 to 4 weeks if eggs persist in the faeces. Recently, a single dose of 500 mg has been effective in mass treatment control programmes, and this will improve compliance.

Enterobiasis

A single dose of 100 mg repeated at least once after an interval of 2 to 4 weeks. All members of the household should be treated at the same time.

Capillariasis

A dose of 200 mg daily for 20–30 days.

For mass treatment control programmes: A single dose of 500 mg four times a year.

Contraindications: Known hypersensitivity; first-trimester pregnancy.

Adverse effects: Occasionally, transient gastrointestinal discomfort and headache.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

PYRANTEL

Anthelmintic agent

Chewable tablet: 250 mg (as embonate)

Oral suspension: 50 mg (as embonate)/ml

Uses: Hookworm infections, ascariasis, enterobiasis and trichostrongyliasis.

Dosage: *Adults and children:* A single dose of 10 mg/kg is sufficient to eliminate many cases of hookworm infection, ascariasis, enterobiasis and trichostrongyliasis. Patients with enterobiasis, however, should receive a second dose after 2–4 weeks. Heavy hookworm infections are relatively resistant and three further doses should be given on consecutive days.

Mass treatment control programmes: A single dose of 2.5 mg/kg 3 or 4 times a year.

Contraindications: Known hypersensitivity.

Precautions: Lower doses should be administered to patients with hepatic function impairment.

Adverse effects: Occasionally, mild gastrointestinal disturbance, headache, dizziness, drowsiness, insomnia and rash have been reported.

Drug interactions: Pyrantel, piperazine and older anthelmintics have antagonistic effects; they should not be administered together.

Drugs used for tissue nematode infections

Tissue nematode infections include dracunculiasis, trichinellosis, cutaneous larva migrans, visceral larva migrans, anisakiasis and angiostrongyliasis. In dracunculiasis, metronidazole (25 mg/kg daily for 10 days, with a daily maximum of 750 mg for children) provides rapid symptomatic relief. It also weakens the anchorage of the worms in the subcutaneous tissues, and they can then be removed by traction. However, since it has no effect on pre-emergent worms, it does not immediately prevent transmission.

Each case of confirmed or even suspected trichinellosis infection should be treated in order to prevent the continued production of larvae. In both adults and children, mebendazole (200 mg for 5 days), albendazole (400 mg for 3 days), and pyrantel (10 mg/kg daily for 5 days) are each effective. Prednisolone, 40–60 mg daily, may be needed to alleviate allergic and inflammatory responses.

In cutaneous larva migrans, albendazole in a single dose of 400 mg is effective. Calamine lotion provides symptomatic relief.

In visceral larva migrans caused by *Toxocara canis* and, less frequently, *T. cati*, treatment should be reserved for symptomatic infections. A 3-week oral course of diethylcarbamazine kills the larvae and arrests the disease, but established lesions are irreversible. To reduce the intensity of allergic reactions induced by dying larvae, dosage is commonly commenced at 1 mg/kg twice daily and raised progressively to 3 mg/kg twice daily (adults and children).

In order to suppress allergic inflammatory responses in patients with ophthalmic lesions, prednisolone should be administered concurrently, either topically or systemically.

In anisakiasis, anthelmintic treatment is rarely necessary. Prevention is dependent upon informing communities of the hazards of eating raw or inadequately prepared salt-water fish, and the need for early evisceration of fish after capture, and freezing of seafood at -20°C for at least 60 hours before sale.

In angiostrongyliasis, symptomatic treatment pending spontaneous recovery is often all that is required.

Antifilarials

Infections caused by filaria include (1) loiasis, (2) lymphatic filariasis and (3) onchocerciasis.

1. Loiasis

Diethylcarbamazine (DEC) is effective against both the adult worms and larvae of all forms of the parasite and a single weekly dose is normally effective as prophylaxis. During individual treatment, particularly of persons with heavy microfilaraemia ($>50\,000$ microfilariae/ml blood), a condition simulating meningoencephalitis can occasionally occur. This probably results from sludging of moribund microfilariae within the cerebral capillaries. The frequency of meningoencephalitis associated with DEC therapy of loiasis is reported as 1.25%, with a mortality rate of about 50% in affected patients. Permanent cerebral damage is common among patients who survive and this possibility should be considered when treatment is decided upon. Treatment of heavily infected patients should thus begin at low dosage and corticosteroid and antihistamine cover should be provided for the first 2–3 days.

DIETHYLCARBAMAZINE

Antifilarial agent

Tablet: 50 mg (dihydrogen citrate)

Uses: Treatment of loiasis and prophylaxis against loiasis in temporary residents of endemic areas.

Dosage:

Treatment

Adults: 1 mg/kg as a single dose initially, doubled on 2 successive days and then adjusted to 2–3 mg/kg three times daily for a further 18 days.

Prophylaxis

Adults: 300 mg weekly for as long as exposure continues.

The recommended dosage regimen should be strictly followed to minimize allergic reactions to dying parasites.

Contraindications: During pregnancy, treatment should be delayed until after delivery. Dosage should be reduced in patients with renal impairment. Patients who are severely ill with other acute diseases should not receive diethylcarbamazine until after recovery.

Adverse effects: Immunological disturbances (similar to the Mazzotti reaction in onchocerciasis) are induced by disintegrating microfilariae. Fever, headache, dizziness, anorexia, malaise, urticaria, vomiting and asthmatic attacks may occur within a few hours of the first dose and usually subside by the fifth day of treatment. When microfilaraemia is heavy, there is a risk of meningoencephalitis and the advantages of treatment must be weighed against the possibility of life-threatening encephalitis. Reversible proteinuria may occur.

2. Lymphatic filariasis

Diethylcarbamazine has both microfilaricidal and macrofilaricidal activity, but some adult worms may survive even after repeated courses of therapy. Total cumulative dosages of 72 mg/kg are generally recommended for *Wuchereria bancrofti* infections, with half this dose for *Brugia malayi* and *B. timori* infections. In all cases where microfilaraemia is heavy, treatment is best initiated with smaller doses for 2–3 days in order to avoid the danger of immunological reactions.

It has recently been shown that ivermectin, administered in a single dose of 400 $\mu\text{g}/\text{kg}$ is as effective as a single dose of 6 mg/kg diethylcarbamazine.

Mass treatment control programmes: A single yearly dose of 6 mg/kg diethylcarbamazine can be used. The addition of DEC to table salt at a concentration of 0.1–0.3% is also effective.

DIETHYLCARBAMAZINE

Antifilarial agent

Tablet: 50 mg (dihydrogen citrate)

Uses: Individual and community treatment of systemic lymphatic filariasis and occult filariasis (tropical pulmonary eosinophilia).

Dosage: The following dosage schedules are intended only as a guide since many countries have developed their own specific treatment regimens. The doses given are suitable for both adults and children aged over 10 years. Children under 10 years of age should be given half the total adult dose.

***W. bancrofti* infections**

6 mg/kg daily for 12 days administered orally, preferably in divided doses after meals.

Mass treatment control programmes: 6 mg/kg weekly, monthly or as a single annual dose.

***B. malayi* and *B. timori* infections**

3–6 mg/kg daily for 6–12 days administered orally, preferably in divided doses after meals.

Mass treatment control programmes: 3–6 mg/kg, 6 times either weekly or monthly.

In China and India several trials have shown that when used consistently over a period of at least 6 months, table salt fortified with diethyl-carbamazine at a concentration of 0.1% can eliminate *W. bancrofti* lymphatic filariasis. A concentration of 0.3% for 3–4 months may be necessary where *B. malayi* is endemic.

Occult filariasis

A dose of 8 mg/kg daily for 14 days repeated, as necessary, if symptoms return.

Contraindications: During pregnancy, treatment should be delayed until after delivery. Dosage should be reduced in patients with renal impairment. Patients who are severely ill with other acute diseases should not receive diethylcarbamazine until after recovery.

Adverse effects: Immunological disturbances (similar to the Mazzotti reaction in onchocerciasis) are induced by disintegrating microfilariae. Fever, headache, dizziness, anorexia, malaise, urticaria, vomiting and asthmatic attacks may occur within a few hours of the first dose and usually subside by the fifth day of treatment. When microfilaraemia is heavy, there is a risk of meningoencephalitis and the advantages of treatment must be weighed against the possibility of life-threatening encephalitis. Reversible proteinuria may occur. Recently-killed adult worms often form nodules which are palpable subcutaneously and along the spermatic cord; their death may result in transient lymphangitis and an exacerbation of lymphoedema.

3. Onchocerciasis

Ivermectin has transformed the treatment of onchocerciasis and it is now used extensively in control programmes in many countries. Its microfilaricidal action is more persistent and less liable to provoke adverse reactions than that of diethylcarbamazine. A single oral dose reduces the microfilarial count to low levels for up to a year. It appears to kill both microfilariae and to inhibit their expulsion from the uterus of female worms. Available data suggest that a single annual dose will suppress microfilaraemia to a degree that prevents development of clinical disease. Although the drug is generally well tolerated, it is advisable to have medical support available during treatment programmes. Patients with a heavy microfilarial load occasionally react adversely and, rarely, transient severe postural hypotension has occurred within 12–24 hours of treatment.

Treatment of pregnant women with ivermectin should be limited to those situations where the risk of complications from untreated onchocerciasis exceeds the potential risk to the fetus from treatment. Diethylcarbamazine is now largely superseded as a microfilaricide in onchocerciasis because of the frequency with which it induces severe host (Mazzotti) reactions characterized by itching, skin rash, oedema, pain and swelling of the lymph nodes, fever and severe eye lesions.

Suramin is the only macrofilaricide that is currently available for use against *Onchocerca volvulus*. Administered intravenously over a period of several weeks, suramin also kills microfilariae. It is, however, one of the most toxic substances used in clinical medicine and should always be given under medical supervision in a hospital. A careful assessment must always be made of the patient's capacity to withstand the effects of suramin treatment both before and during administration.

IVERMECTIN

Antifilarial agent

Scored tablet: 6 mg

Uses: As a microfilaricide in the suppressive treatment of onchocerciasis. Although it may not be effective against immature larval stages of *O. volvulus*, it seems to impair the fecundity of the adult worm.

Dosage: Effective suppression of microfilariae is obtained by annual administration of a single oral

dose of 150 µg/kg (adults and children over 5 years of age).

Contraindications: Known hypersensitivity.

Precautions: Breast-feeding mothers should not be treated until the infant is at least 1 week old, by which time the blood-brain barrier should be fully developed.

Adverse effects: Mild ocular irritation may occur. Somnolence has been reported as well as Mazzotti reactions. Transient symptoms that may occur within 3 days of treatment include headache, pruritus, rash, arthralgia, myalgia, lymphadenopathy, lymphadenitis, oedema, fever, weakness, tachycardia, nausea, conjunctivitis, diarrhoea and vomiting, including reactions resulting from a heavy microfilarial load.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

SURAMIN SODIUM

Antifilarial agent

Powder for injection: 1 g in vial

Uses: As a macrofilaricide in the curative treatment of onchocerciasis.

Dosage: Suramin is administered by slow intravenous injection of a 10% solution in water for injection.

Adults: a total of 66.0 mg/kg should be administered in six incremental weekly doses apportioned as follows.

Week	1	2	3	4	5	6
Dose(mg/kg)	3.3	6.7	10.0	13.3	16.7	16.0

Because loss of consciousness has occasionally occurred, the first injection (0.2 g in 2 ml of water for injection for a 60 kg adult) should be administered with particular caution. Wait at least one minute after injecting the first few microlitres, inject the next 0.5 ml over 30 seconds and wait one more minute. Inject the remainder over several minutes.

Contraindications: Previous anaphylactic reactions or sensitivity to suramin; pregnancy; children less than 10 years old; elderly or infirm

patients with impaired liver or renal function; total blindness — unless required for relief from intensely itchy lesions.

Precautions: Suramin is extremely toxic and should always be given under medical supervision in a hospital. A satisfactory food and fluid intake should be maintained throughout treatment. Urine samples should be taken before and during treatment to detect the presence of albumin. Moderate albuminuria indicates that the dose should be reduced but heavy albuminuria with the passage of casts indicates the need for immediate discontinuation of treatment.

Adverse effects: Direct toxic effects require immediate withdrawal. Rarely, potentially fatal loss of consciousness may occur during the first injection. Heavy albuminuria, stomal ulceration, exfoliative dermatitis, severe diarrhoea, prolonged high fever and prostration may occur. Lesser, but common, symptoms include tiredness, anorexia, malaise, polyuria, increased thirst and tenderness of the palms of the hands and soles of the feet. Indirect reactions due to the death of the parasites including urticaria, swelling, tenderness and abscess formation around adult worms, painful immobilization of the hip, intensely itchy urticopapular rash, inflammatory and subsequent degenerative changes in the optic nerve and retina, and swollen, painful joints particularly of the hands and feet.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

Antischistosomal

Schistosomiasis, a waterborne parasitic infection, is caused by several species of trematode worms (blood flukes). Its socioeconomic impact as a parasitic disease is outstripped only by that of malaria. Intestinal schistosomiasis is caused principally by *Schistosoma mansoni*, as well as *S. japonicum*, *S. mekongi*, and *S. intercalatum*. Urinary schistosomiasis is caused by *S. haematobium*. The latter is an important predisposing cause of squamous-cell cancer of the bladder.

Praziquantel has transformed the treatment of schistosomiasis and is often effective in a single dose against all species of the parasite. It can be of particular value in patients with mixed infections and those who do not respond adequately to other

drugs. It is also extremely well tolerated and well suited for mass treatment control programmes. Extensive use over several years has provided no evidence of serious adverse effects or long-term toxicity, nor has mutagenic or carcinogenic activity been shown in animals. Despite lack of teratogenicity and embryotoxicity, however, it is preferable to delay treatment during pregnancy until after delivery, unless absolutely essential.

Other drugs still widely used for schistosomiasis include metrifonate, which is active against *S. haematobium*, and oxamniquine, which is effective against *S. mansoni*.

Strains resistant to oxamniquine, which have been reported in South America, have been treated effectively with praziquantel. Although neither metrifonate nor oxamniquine has been shown to be teratogenic or embryotoxic, it is preferable to delay treatment during pregnancy until after delivery unless immediate intervention is essential. There is no information on whether metrifonate or oxamniquine is excreted in breast milk, and it is therefore preferable not to administer these drugs to nursing mothers.

PRAZIQUANTEL

Anthelmintic agent

Tablet: 600 mg

Uses: Intestinal schistosomiasis due to *S. japonicum*, *S. intercalatum* or *S. mekongi* which is not responsive to oxamniquine. *S. mansoni*

infections unresponsive to oxamniquine, co-infections of *S. haematobium* and *S. mansoni* otherwise requiring treatment with both metrifonate and oxamniquine.

Dosage: The dosage for both adults and children is given in the table below.

Adverse effects: In patients with heavy worm loads, these include abdominal discomfort, nausea, headache, dizziness, drowsiness and rarely, pyrexia, urticaria and rectal bleeding.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

METRIFONATE

Anthelmintic agent

Tablet: 100 mg

Uses: Urinary schistosomiasis.

Dosage: *Adults and children:* A dose of 7.5–10 mg/kg on three occasions at intervals of 2 weeks will cure 40–80% of cases.

Precautions: Mass chemotherapy should not be undertaken in communities recently exposed to insecticides or other agricultural chemicals with anticholinesterase action. Treated patients should not receive depolarizing neuromuscular blocking agents such as suxamethonium until at least 48 hours after administration of metrifonate.

Dosage of praziquantel in schistosomiasis

Parasite species	Single dose (mg/kg) adults & children	Initial cure rate (%) ^a	Reduction in egg count after 1 year (%) ^b
<i>S. haematobium</i>	40	80–95	90–95
<i>S. mansoni</i>	40 ^c	60–90	95
Mixed <i>S. haematobium</i> / <i>S. mansoni</i>	40 ^c	60–75	<i>S. haematobium</i> > <i>S. mansoni</i>
<i>S. intercalatum</i>	40	60–80	95
<i>S. japonicum</i>	40 ^c	60–80	95
<i>S. mekongi</i>	40 ^c	60–80	95

^a A "cure" is considered to be a complete absence of eggs from the urine or faeces 6 months after completion of treatment.

^b In patients who have not been cured.

^c In some areas dosage may be increased to 60 mg/kg.

Adverse effects: Abdominal pain, nausea, vomiting, diarrhoea, headache and vertigo are common. Cholinergic symptoms very rarely occur with currently recommended dosages.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

OXAMNIQUINE

Anthelmintic agent

Capsule: 250 mg

Syrup: 250 mg/5 ml

Uses: Intestinal schistosomiasis (*S. mansoni*) both in the acute stage and in patients with hepato-splenic involvement.

Dosage: The effective dose varies. The following regimens provide general guidance but definitive recommendations should be based on local experience.

West Africa, South America and the Caribbean

Adults: A single dose of 15 mg/kg.

Children (less than 30 kg): 20 mg/kg in two divided doses.

East and central Africa and the Arabian peninsula

Adults and children: 30 mg/kg in two divided doses

Egypt and southern Africa

Adults and children: 60 mg/kg administered over 2–3 days. The maximum single dose should not exceed 20 mg/kg.

Precautions: Epileptic patients should remain under observation for several hours following treatment since seizures may be precipitated. Patients should be advised not to drive or operate machinery for at least 24 hours, since drowsiness may occur.

Adverse effects: Mild and transient dizziness and drowsiness occur in about one-third of patients. Headache, vomiting and diarrhoea may also be troublesome and intense orange-red discoloration of the urine may occur. Rarely, hallucinations, excitation and epileptiform convulsions are reported; transient but inconsequential increases in levels of serum transaminases are sometimes detected.

In Egypt and some other countries of the Eastern Mediterranean region many patients develop

transient fever, peripheral blood eosinophilia and scattered pulmonary infiltrates (Loeffler's syndrome) following a 3-day course of treatment.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.

Drugs used in fluke infections

The intestinal flukes include *Fasciolopsis buski*, *Metagonimus yokogawai*, *Heterophytes heterophytes*, *Echinostoma* spp and *Gastrodiscoides hominis*. The liver flukes include *Clonorchis sinensis*, *Opisthorchis viverrini*, *O. felinus* and *Fasciola hepatica*. In some areas *Clonorchis sinensis* and *Opisthorchis* spp. infections are strongly associated with cholangiocarcinoma (cancer of the bile duct). Lung flukes belong to the genus *Paragonimus*.

Praziquantel has transformed the therapy of most fluke infections. Parasitological cure has been obtained in virtually all cases (with the exception of fasciola infections) without significant adverse effects, but the drug should be taken for several days for treatment of paragonimus infections.

Evidence suggests that a single dose of triclabendazole is effective and well tolerated in a high proportion of cases of both fasciola and paragonimus infections.

PRAZICUANTEL

Anthelmintic agent

Tablet: 150mg, 600 mg

Uses: Intestinal, liver and lung fluke infections including those due to *Fasciolopsis buski*, *Metagonimus yokogawai*, *Heterophytes heterophytes*, *Echinostoma* spp., *Clonorchis sinensis*, *Opisthorchis viverrini*, *O. felinus* and various species of paragonimus.

Dosage:

Intestinal fluke infections

Adults and children over 4 years: a single dose of 25 mg/kg is recommended.

Liver and lung fluke infections

Adults and children over 4 years: a dose of 25 mg/kg three times a day for 2 consecutive days produces virtually 100% cure rates in the majority of liver and lung fluke infections. A single dose of 40 mg/kg has also been shown to be effective.

Precautions: Patients with paragonimus infections should always be treated in a hospital since flukes can invade the central nervous system.

Adverse effects: Occasionally, abdominal discomfort, nausea, headache, dizziness and

drowsiness. Rarely, pyrexia, urticaria and rectal bleeding.

Drug interactions: These will appear in tabulated form in the appendix of the published edition of the WHO Model Formulary.