Amoebiasis. For a discussion of the treatment of amoebiasis with mention of chloroquine for hepatic amoebiasis, see p.822.

Inflammatory disorders. Chloroquine and hydroxychloroquine possess anti-inflammatory properties and they have been tried or used with some benefit in a range of inflammatory conditions which often have an immunological basis, although they rarely constitute first-line therapy in these disorders. Such conditions include rheumatoid arthritis and SLE (see under Hydroxychloroquine, p.604), ulcerative colitis,[1] infantile interstitial pneumonitis,[2,3] asthma,[4] giant cell arteritis,[5] and various skin disorders (see below). The mode of action in these conditions is unclear. Results of studies have been conflicting but it does appear that chloroquine and hydroxychloroquine might have some immunosuppressive effects.[6,7]

1. Mayer L, Sachar DB. Efficacy of chloroquine in the treatment of inflammatory bowel disease. *Gastroenterology* 1988; **94:** A293.
2. Springer C, *et al.* Chloroquine treatment in desquamative interstitial pneumonia. *Arch Dis Child* 1987; **62:** 76–7.
3. Kerem E, *et al.* Sequential pulmonary function measurements during treatment of infantile chronic interstitial pneumonitis. *J Pediatr* 1990; **116:** 61–7.
4. Charous BL. Open study of hydroxychloroquine in the treatment of severe symptomatic or corticosteroid-dependent asthma. *Ann Allergy* 1990; **65:** 53–8.
5. Le Guennec P, *et al.* Management of giant cell arteritis: value of synthetic antimalarial agents: a retrospective study of thirty six patients. *Rev Rhum* 1994; **61:** 423–8.
6. Bygbjerg IC, Flachs H. Effect of chloroquine on human lymphocyte proliferation. *Trans R Soc Trop Med Hyg* 1986; **80:** 231–5.
7. Prasad RN, *et al.* Immunopharmacology of chloroquine. *Trans R Soc Trop Med Hyg* 1987; **81:** 168–9.

Malaria. The overall treatment and prophylaxis of malaria and the place of chloroquine in current recommendations are discussed on p.594.

TREATMENT. In the treatment of patients with chloroquine-sensitive falciparum malaria studies have found chloroquine to be at least as effective as quinine in both uncomplicated and severe infections. However, very few areas exist where *Plasmodium falciparum* remains sensitive to chloroquine. There are also reports of resistance to chloroquine in *P. vivax*.[1]

Treatment with chloroquine is usually by mouth, adults and children being given the equivalent of 25 mg of chloroquine base per kg body-weight over 3 days. Any chloroquine lost through vomiting needs to be replaced by additional doses.[2]

Intravenous therapy has been used if the infection is severe or oral dosage is not possible. There should be close monitoring for hypotension and other signs of cardiovascular toxicity. The intramuscular or subcutaneous routes have been used if intravenous dosage is not possible. Patients should be transferred to oral therapy as soon as possible and treatment continued until a total dose equivalent to 25 mg of the base per kg has been given.

If injections cannot be given a chloroquine suspension or syrup appears to be well absorbed when given by nasogastric tube even in comatose patients. Rectal use in young children has also produced beneficial responses.[3,4]

PROPHYLAXIS. The widespread prevalence of strains of *P. falciparum* resistant to chloroquine has considerably diminished the value of chloroquine for malaria chemoprophylaxis and has made recommendations increasingly complex (see p.594). If chloroquine is used for prophylaxis it is usually given with proguanil. For **adults** a dose equivalent to 300 mg of chloroquine base is given by mouth once each week, beginning about one week before exposure and continuing throughout, and for at least 4 weeks after, exposure. Some countries advise the use of 100 mg daily for 6 days a week. For **children**, a weekly dose of chloroquine base 5 mg/kg has been recommended, although UK malaria experts[5] have suggested the following prophylactic doses for children based on fractions of the adult dose of 300 mg weekly:

- under 6.0 kg (0 to 12 weeks of age), one-eighth the adult dose
- 6.0 to 9.9 kg (3 to 11 months), one-quarter the adult dose
- 10.0 to 15.9 kg (1 year to 3 years 11 months), three-eighths the adult dose
- 16.0 to 24.9 kg (4 years to 7 years 11 months), half the adult dose
- 25.0 to 44.9 kg (8 years to 12 years 11 months), three-quarters the adult dose
- over 45 kg (13 years and over), the adult dose

They noted that body-weight was a better guide to dosage than age for children over 6 months.

1. Whitby M. Drug resistant Plasmodium vivax malaria. *J Antimicrob Chemother* 1997; **40:** 749–52.
2. WHO. *WHO model formulary*. Geneva: WHO, 2004.
3. Westman L, *et al.* Rectal administration of chloroquine for treatment of children with malaria. *Trans R Soc Trop Med Hyg* 1994; **88:** 446.
4. Antia-Obong OE, *et al.* Chloroquine phosphate suppositories in the treatment of childhood malaria in Calabar, Nigeria. *Curr Ther Res* 1995; **56:** 928–35.
5. Chiodini P, *et al.* HPA Advisory Committee on Malaria Prevention in UK Travellers. Guidelines for malaria prevention in travellers from the United Kingdom (issued 01/07). Available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1203496943523 (accessed 17/06/08)

Porphyria cutanea tarda. Chloroquine and hydroxychloroquine have been used with some benefit in the treatment of porphyria cutanea tarda (p.1448) and low doses (such as chloroquine phosphate 125 mg or hydroxychloroquine sulfate 200 mg given twice weekly) have been considered by some to be useful in patients unsuitable for phlebotomy.[1-4] However, the acute increase in urinary porphyrins and fall in hepatic porphyrin content produced by these drugs have been associated with a variable degree of hepatotoxicity[5,6] and others prefer to use desferrioxamine.[7]

1. Grossman ME, *et al.* Porphyria cutanea tarda. *Am J Med* 1979; **67:** 277–86.
2. Cainelli T, *et al.* Hydroxychloroquine versus phlebotomy in the treatment of porphyria cutanea tarda. *Br J Dermatol* 1983; **108:** 593–600.
3. Ashton RE, *et al.* Low-dose oral chloroquine in the treatment of porphyria cutanea tarda. *Br J Dermatol* 1984; **111:** 609–13.
4. Stölzel U, *et al.* Hemochromatosis (HFE) gene mutations and response to chloroquine in porphyria cutanea tarda. *Arch Dermatol* 2003; **139:** 309–13.
5. Scholnick PL, *et al.* The molecular basis of the action of chloroquine in porphyria cutanea tarda. *J Invest Dermatol* 1973; **61:** 226–32.
6. Rossmann-Ringdahl I, Olsson R. Porphyria cutanea tarda: effects and risk factors for hepatotoxicity from high-dose chloroquine treatment. *Acta Derm Venereol* 2007; **87:** 401–5.
7. Rocchi E. Treatment of porphyria cutanea tarda. *Br J Dermatol* 1987; **116:** 139–40.

Rheumatoid arthritis. For reference to the use of chloroquine in the treatment of rheumatoid arthritis, see under Hydroxychloroquine, p.604.

Sarcoidosis. Chloroquine and hydroxychloroquine have been tried in the management of sarcoidosis (p.1512) as alternatives or adjuncts to corticosteroid therapy.

References.

1. O'Leary TJ, *et al.* The effects of chloroquine on serum 1,25-dihydroxyvitamin D and calcium metabolism in sarcoidosis. *N Engl J Med* 1986; **315:** 727–30.
2. Adams JS, *et al.* Effective reduction in the serum 1,25-dihydroxyvitamin D and calcium concentration in sarcoidosis-associated hypercalcemia with short-course chloroquine therapy. *Ann Intern Med* 1989; **111:** 437–8.
3. DeSimone DP, *et al.* Granulomatous infiltration of the talus and abnormal vitamin D and calcium metabolism in a patient with sarcoidosis: successful treatment with hydroxychloroquine. *Am J Med* 1989; **87:** 694–6.
4. Jones E, Callen JP. Hydroxychloroquine is effective therapy for control of cutaneous sarcoidal granulomas. *J Am Acad Dermatol* 1990; **23:** 487–9.
5. Zic JA, *et al.* Treatment of cutaneous sarcoidosis with chloroquine: review of the literature. *Arch Dermatol* 1991; **127:** 1034–40.
6. Baltzan M, *et al.* Randomized trial of prolonged chloroquine therapy in advanced pulmonary sarcoidosis. *Am J Respir Crit Care Med* 1999; **160:** 192–7.

Skin disorders. In addition to their use in lupus erythematosus hydroxychloroquine and chloroquine have been tried in a number of other skin disorders including polymorphic light eruptions[1] (see Photosensitivity Disorders, p.1581), lichen planus[2,3] (p.1580), cutaneous symptoms of dermatomyositis (p.1510), erythema nodosum,[4,5] and recurrent erythema multiforme (p.1580). It has also been tried in mild type 2 lepra reactions (erythema nodosum leprosum, see p.176).

1. Murphy GM, *et al.* Hydroxychloroquine in polymorphic light eruption: a controlled trial with drug and visual sensitivity monitoring. *Br J Dermatol* 1987; **116:** 379–86.
2. Mostafa WZ. Lichen planus of the nail: treatment with antimalarials. *J Am Acad Dermatol* 1989; **20:** 289–90.
3. De Argila D, *et al.* Isolated lichen planus of the lip successfully treated with chloroquine phosphate. *Dermatology* 1997; **195:** 284–5.
4. Alloway JA, Franks LK. Hydroxychloroquine in the treatment of chronic erythema nodosum. *Br J Dermatol* 1995; **132:** 661–2.
5. Jarrett P, Goodfield MJD. Hydroxychloroquine and chronic erythema nodosum. *Br J Dermatol* 1996; **134:** 373.

Systemic lupus erythematosus. For reference to the use of chloroquine in cutaneous and systemic lupus erythematosus, see Hydroxychloroquine, p.605.

Preparations

BP 2008: Chloroquine Phosphate Tablets; Chloroquine Sulphate Injection; Chloroquine Sulphate Tablets;
USP 31: Chloroquine Hydrochloride Injection; Chloroquine Phosphate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Nivaquine; ***Austral.:*** Chlorquin; ***Austria:*** Resochin; ***Belg.:*** Nivaquine; ***Braz.:*** Clopirim†; Diclokin; Quinacris; ***Canad.:*** Aralen†; ***Cz.:*** Delagil; ***Denm.:*** Malarex; ***Fin.:*** Heliopar; ***Fr.:*** Nivaquine; ***Ger.:*** Resochin; Weimerquin; ***Hong Kong:*** Syncoquin; ***Hung.:*** Delagil; ***India:*** Clo-Kit; Emquin; Lariago; Maliago; Melubrin; Nivaquine-P; Resochin; ***Indon.:*** Avloclor; Malarex; Mexaquin; Resochin; Riboquin; ***Irl.:*** Avloclor; ***Israel:*** Avloclor; ***Mex.:*** Aralen; Maclorex; Paluken†; ***Neth.:*** Nivaquine; ***NZ:*** Chlorquin; Nivaquine; ***Philipp.:*** Aralen; Chlorofoz; ***Pol.:*** Arechin; ***Port.:*** Resochina; ***Rus.:*** Delagil (Делагил); ***S.Afr.:*** Daramal; Mirquin; Nivaquine; Plasmoquine; ***Spain:*** Resochin; ***Switz.:*** Chlorochin; Nivaquine; ***Thai.:*** Diroquine; Genocin; Maliaquine; P-Roquine†; ***UK:*** Avloclor; Malarivon; Malaviron; Nivaquine; ***USA:*** Aralen.

Multi-ingredient: ***Arg.:*** Tri-Emcortina†; ***Fr.:*** Savarine; ***S.Afr.:*** Daramal-Paludrine†.

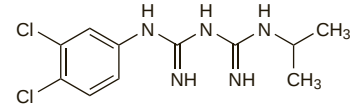
Chlorproguanil Hydrochloride *(BANM, rINNM)*

Chlorproguanil, Chlorhydrate de; Chlorproguanili Hydrochloridum; Hidrocloruro de clorproguanil; M-5943. 1-(3,4-Dichlorophenyl)-5-isopropylbiguanide hydrochloride.

Хлорпрогуанила Гидрохлорид

$C_{11}H_{15}Cl_2N_5,HCl$ = 324.6.

CAS — 537-21-3 (chlorproguanil); 15537-76-5 (chlorproguanil hydrochloride).



(chlorproguanil)

Profile

Chlorproguanil is a biguanide antimalarial used for malaria prophylaxis similarly to proguanil (p.609). It is sometimes given with dapsone. Combination with both dapsone and artesunate is also being investigated for malaria treatment.

◊ Reviews.

1. Bukirwa H, *et al.* Chlorproguanil-dapsone for treating uncomplicated malaria. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 17/05/05).

Halofantrine Hydrochloride *(BANM, USAN, rINNM)*

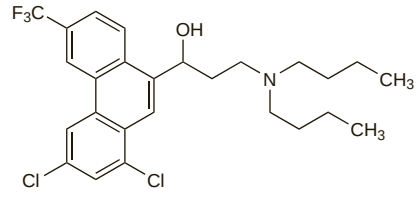
Halofantriinihydrokloridi; Halofantrin hydrochlorid; Halofantrine, Chlorhydrate d'; Halofantrine, chlorhydrate de; Halofantrin-hidroklorid; Halofantrinhydroklorid; Halofantrini hydrochloridum; Halofantrino hidrochloridas; Hidrocloruro de halofantrina; WR-171669. (*RS*)-3-Dibutylamino-1-(1,3-dichloro-6-trifluoromethyl-9-phenanthryl)propan-1-ol hydrochloride; 1,3-Dichloro-α-[2-(dibutylamino)ethyl]-6-trifluoromethyl-9-phenanthrene-methanol hydrochloride.

Галофантрина Гидрохлорид

$C_{26}H_{30}Cl_2F_3NO,HCl$ = 536.9.

CAS — 69756-53-2 (halofantrine); 36167-63-2 (halofantrine hydrochloride); 66051-63-6 (±-halofantrine).

ATC — P01BX01.



(halofantrine)

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Halofantrine Hydrochloride). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol; freely soluble in methyl alcohol. Protect from light.

Adverse Effects and Precautions

Adverse effects associated with halofantrine include diarrhoea, abdominal pain, nausea, vomiting, pruritus, and skin rash. Transient elevation of serum transaminases, intravascular haemolysis, and hypersensitivity reactions have also been reported.

Halofantrine can adversely affect the heart particularly by prolonging QT interval. Serious ventricular arrhythmias have been reported and fatalities have occurred. As a result it is contra-indicated in patients known to have a prolonged QT interval or those with cardiac disease or a family history of congenital QT prolongation, and also in those with unexplained syncopal attacks, thiamine deficiency, or electrolyte disturbances, or taking other arrhythmogenic drugs (see also Effects on the Heart, below, and Interactions, below).

Halofantrine is not recommended during pregnancy or breast feeding. It should not be taken on a full stomach since this increases its bioavailability and thus the risk of toxicity; after taking halofantrine, fatty food should be avoided for 24 hours.

Effects on the blood. Halofantrine has been associated with acute intravascular haemolysis.[1,2]

1. Vachon F, *et al.* Halofantrine and acute intravascular haemolysis. *Lancet* 1992; **340:** 909–10.
2. Mojon M, *et al.* Intravascular haemolysis following halofantrine intake. *Trans R Soc Trop Med Hyg* 1994; **88:** 91.

Effects on the heart. Prolonged PR[1,2] and QT[1-5] intervals have been reported in patients given halofantrine and there are individual reports of fatal cardiac arrest[1,5] and of torsade de pointes.[4] In 1994, the UK CSM[6] noted that QT interval prolongation occurred at recommended doses of halofantrine in the ma-

jority of patients and that worldwide there had been 14 reports of cardiac arrhythmias associated with halofantrine; 8 patients were known to have died. To reduce the risk of arrhythmias they stressed that halofantrine should *not* be taken with meals, with other drugs that may induce arrhythmias (e.g. quinine, chloroquine, and mefloquine; tricyclic antidepressants; antipsychotics; certain antiarrhythmics; and the antihistamines terfenadine and astemizole), or with drugs causing electrolyte disturbances. They also stated that it should *not* be given to patients known to have prolongation of the QT interval or with any form of cardiac disease associated with QT interval prolongation or ventricular arrhythmia (e.g. coronary heart disease, cardiomyopathy, or congenital heart disease). Some workers[2] have suggested ECG screening of all patients before starting treatment with halofantrine. Others[7] found pretreatment ECGs to be poorly predictive of QT lengthening during treatment. Children may experience serious cardiac effects at standard doses.[8]

1. Nosten F, *et al.* Cardiac effects of antimalarial treatment with halofantrine. *Lancet* 1993; **341:** 1054–6.
2. Monlun E, *et al.* Cardiac complications of halofantrine: a prospective study of 20 patients. *Trans R Soc Trop Med Hyg* 1995; **89:** 430–3.
3. Castot A, *et al.* Prolonged QT interval with halofantrine. *Lancet* 1993; **341:** 1541.
4. Monlun E, *et al.* Prolonged QT interval with halofantrine. *Lancet* 1993; **341:** 1541–2.
5. Anonymous. Halofantrine: revised data sheet. *WHO Drug Inf* 1993; **7:** 66–7.
6. Committee on Safety of Medicines/Medicines Control Agency. Cardiac arrhythmias with halofantrine (Halfan). *Current Problems* 1994; **20:** 6. Available at: http://www.mhra.gov.uk/Publications/Safetyguidance/CurrentProblemsinPharmacovigilance/CON2023215 (accessed 18/06/08)
7. Matson PA, *et al.* Cardiac effects of standard-dose halofantrine therapy. *Am J Trop Med Hyg* 1996; **54:** 229–31.
8. Sowunmi A, *et al.* Cardiac effects of halofantrine in children suffering from acute uncomplicated falciparum malaria. *Trans R Soc Trop Med Hyg* 1998; **92:** 446–8.

Effects on the skin. For a comparison of the incidence of pruritus associated with halofantrine and other antimalarials, see Effects on the Skin under Adverse Effects of Chloroquine, p.600.

Interactions

Halofantrine prolongs the QT interval and should not be used with other drugs that have the potential to induce cardiac arrhythmias, in particular the antimalarials mefloquine, chloroquine, and quinine, and also tricyclic antidepressants, phenothiazine antipsychotics, some antiarrhythmics (including amiodarone, disopyramide, flecainide, procainamide, quinidine, and the beta blocker sotalol), cisapride, and the antihistamines astemizole and terfenadine. Also, halofantrine should not be given with drugs that cause electrolyte disturbances (such as diuretics) or with HIV-protease inhibitors.

Grapefruit juice. In a study in 12 healthy patients, the bioavailability of halofantrine was reported to be increased when taken with grapefruit juice and this was found to accentuate halofantrine-associated QT prolongation.[1] It was suggested that grapefruit juice should be contra-indicated during use of halofantrine.

1. Charbit B, *et al.* Pharmacokinetic and pharmacodynamic interaction between grapefruit juice and halofantrine. *Clin Pharmacol Ther* 2002; **72:** 514–23.

Tetracycline. Plasma concentrations of halofantrine were increased in 8 healthy subjects who were also given tetracycline.[1]

1. Bassi PU, *et al.* Effects of tetracycline on the pharmacokinetics of halofantrine in healthy volunteers. *Br J Clin Pharmacol* 2004; **58:** 52–5.

Pharmacokinetics

Halofantrine is slowly and erratically absorbed after oral dosage, although it appears in the circulation within about 1 hour, peak concentrations occurring in 3 to 7 hours. Bioavailability of halofantrine is increased when given with or after food, particularly food high in fat content, and it must therefore be taken on an empty stomach because of the risk of cardiac toxicity. The elimination half-life of halofantrine varies considerably between individuals, but is generally about 1 to 2 days. Halofantrine is metabolised in the liver, its major metabolite being desbutylhalofantrine, which appears to be as active as the parent compound. Excretion of halofantrine is primarily via the faeces.

◊ References.

1. Karbwang J, Na Bangchang K. Clinical pharmacokinetics of halofantrine. *Clin Pharmacokinet* 1994; **27:** 104–19.
2. Watkins WM, *et al.* Halofantrine pharmacokinetics in Kenyan children with non-severe and severe malaria. *Br J Clin Pharmacol* 1995; **39:** 283–7.
3. Ohrt C, *et al.* Pharmacokinetics of an extended-dose halofantrine regimen in patients with malaria and in healthy volunteers. *Clin Pharmacol Ther* 1995; **57:** 525–32.

Uses and Administration

Halofantrine is a 9-phenanthrenemethanol antimalarial that has been used in the *treatment* of uncomplicated chloroquine-resistant falciparum and of chloroquine-resistant vivax malaria. Halofantrine is a blood schizontocide but has no activity against exoerythrocytic forms. Its value is limited by its unpredictable bioavailability and by cardiotoxicity. It should *not* be used where mefloquine has been used for prophylaxis (for cardiac hazard, see Effects on the Heart, above). Halofantrine should also *not* be used for malaria prophylaxis and is no longer recommended for standby treatment.

In the treatment of malaria, halofantrine hydrochloride has been given orally as 3 doses of 500 mg at intervals of 6 hours, on an empty stomach. Dosage for children is based on 24 mg/kg divided into 3 doses. The following doses have been recommended: 23 to 31 kg body-weight, 3 doses of 250 mg at intervals of 6 hours; 32 to 37 kg, 3 doses of 375 mg at intervals of 6 hours; over 37 kg, adult dose. A second course should be given after a week to patients with little or no previous exposure to malaria.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Halfan†; ***Fr.:*** Halfan; ***Ger.:*** Halfan†; ***Port.:*** Halfan; ***S.Afr.:*** Halfan; ***Spain:*** Halfan; ***Switz.:*** Halfan†.

Hydroxychloroquine Sulfate *(rINNM)*

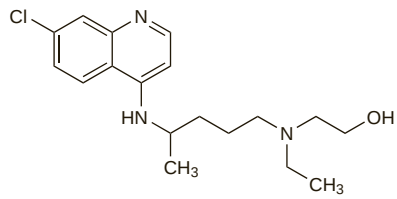
Hydroxychloroquine, Sulfate d'; Hydroxychloroquine Sulphate *(BANM)*; Hydroxychloroquini Sulfas; Oxichlorochin Sulphate; Sulfato de hidroxicloroquina; Win-1258-2. 2-{*N*-[4-(7-Chloro-4-quinolylamino)pentyl]-*N*-ethylamino}ethanol sulphate.

Гидроксихлорохина Сульфат

$C_{18}H_{26}ClN_3O,H_2SO_4$ = 434.0.

CAS — 118-42-3 (hydroxychloroquine); 747-36-4 (hydroxychloroquine sulfate).

ATC — P01BA02.



(hydroxychloroquine)

Pharmacopoeias. In *Br.* and *US.*

BP 2008 (Hydroxychloroquine Sulphate). A white or almost white, odourless or almost odourless, crystalline powder. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether. A 1% solution in water has a pH of 3.5 to 5.5. Protect from light.

USP 31 (Hydroxychloroquine Sulfate). A white or practically white, odourless, crystalline powder. It exists in two forms, the usual form melting at about 240° and the other form at about 198°. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether. Its solutions in water have a pH of about 4.5. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Chloroquine, p.599.

Breast feeding. Hydroxychloroquine has been detected in human breast milk[1,2] but no adverse effects have been seen in breast-fed infants and the American Academy of Pediatrics considers[3] that it is therefore usually compatible with breast feeding.

1. Nation RL, *et al.* Excretion of hydroxychloroquine in human milk. *Br J Clin Pharmacol* 1984; **17:** 368–9.
2. Østensen M, *et al.* Hydroxychloroquine in human breast milk. *Eur J Clin Pharmacol* 1985; **28:** 357.
3. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 19/04/04)

Effects on the eyes. The main adverse effects of chloroquine and hydroxychloroquine on the eye are keratopathy and retinopathy. With respect to retinopathy, precautions should be taken in patients undergoing long-term treatment, as described under Chloroquine on p.600.

Pregnancy. In a study[1] of 133 pregnancies in 90 women treated with hydroxychloroquine, no statistical difference in pregnancy outcome was found compared with a control group consisting of 70 pregnancies in 53 women. It was concluded that the findings supported preliminary evidence for the safety of hydroxychloroquine treatment in pregnancy, and that treatment should probably therefore be maintained during pregnancy in patients with SLE.

1. Costedoat-Chalumeau N, *et al.* Safety of hydroxychloroquine in pregnant patients with connective tissue diseases: a study of one hundred thirty-three cases compared with a control group. *Arthritis Rheum* 2003; **48:** 3207–11.

Interactions

As for Chloroquine, p.601.

Pharmacokinetics

The pharmacokinetics of hydroxychloroquine are similar to those of chloroquine (see p.602).

◊ References.

1. Tett SE, *et al.* Bioavailability of hydroxychloroquine tablets in healthy volunteers. *Br J Clin Pharmacol* 1989; **27:** 771–9.
2. Miller DR, *et al.* Steady-state pharmacokinetics of hydroxychloroquine in rheumatoid arthritis. *DICP Ann Pharmacother* 1991; **25:** 1302–5.
3. Ducharme J, *et al.* Enantioselective disposition of hydroxychloroquine after a single oral dose of the racemate to healthy subjects. *Br J Clin Pharmacol* 1995; **40:** 127–33.

Uses and Administration

Hydroxychloroquine sulfate is a 4-aminoquinoline antimalarial with actions similar to those of chloroquine (p.602), but is mainly used in the treatment of systemic and discoid lupus erythematosus and rheumatoid arthritis. It is also used in the treatment of light-sensitive skin eruptions.

Hydroxychloroquine sulfate is given orally.

In **lupus erythematosus** and **rheumatoid arthritis**, response to treatment may not be apparent for up to 6 months but if there is no improvement by then, treatment should be stopped. In the UK, treatment is usually started with 400 mg daily in divided doses with meals. In the USA, recommended initial doses are 400 to 600 mg daily for rheumatoid arthritis and 400 mg once or twice daily for lupus erythematosus. Doses are reduced to the minimum effective dose for maintenance; this is usually 200 to 400 mg daily but should not exceed 6.5 mg/kg daily (or 400 mg daily whichever is the smaller). To avoid excessive dosage in obese patients, special care is needed to calculate the dosage on the basis of lean body-weight. For further details, see under Effects on the Eyes in Chloroquine, p.600. In children, the minimum effective dose should be used up to a maximum of 6.5 mg/kg daily (or 400 mg daily whichever is the smaller).

Hydroxychloroquine sulfate is also used in similar doses for the treatment of **light-sensitive skin eruptions**, but treatment should only be given during periods of maximum exposure to light.

Hydroxychloroquine sulfate may be used in **malaria** both for treatment and prophylaxis, when chloroquine is not available, with the same limitations as for chloroquine. In the USA, a licensed dose for *prophylaxis* of malaria is 400 mg every 7 days; children may be given a weekly prophylactic dose of 6.5 mg/kg (up to a maximum of 400 mg). In *treating* an acute malarial attack, a dose of 800 mg has been used, followed after 6 to 8 hours by 400 mg and a further 400 mg on each of the 2 following days; alternatively, a single dose of 800 mg has been given. In children, an initial dose of 13 mg/kg may be given, followed by 6.5 mg/kg after 6 hours and again on the second and third days.

Inflammatory disorders. For the use of hydroxychloroquine and chloroquine in a range of inflammatory conditions, see under Chloroquine, p.603 and under Rheumatoid Arthritis, below.

Malaria. The role of chloroquine and potentially therefore of hydroxychloroquine in the treatment and prophylaxis of malaria is discussed on p.594.

Porphyria cutanea tarda. For reference to the use of hydroxychloroquine in the treatment of porphyria cutanea tarda, see under the Uses and Administration of Chloroquine, p.603.

Rheumatoid arthritis. Hydroxychloroquine and chloroquine are used orally as disease-modifying antirheumatic drugs (DMARDs) in the management of **rheumatoid arthritis** (p.11) in an attempt to suppress the rate of cartilage erosion or alter the course of the disease.[1] They are considered to be less effective than the other DMARDs but they are usually better tolerated and so may be preferred in patients with milder forms of the disease.[2] Additional benefit has been obtained using antimalarials with other DMARDs especially methotrexate and sulfasalazine,[3-5] although adverse effects may be more common. For reference to precautions to reduce the incidence of retinopathy, see under Effects on the Eyes in Adverse Effects of Chloroquine, p.600.

Generally the lowest effective dose should be used for maintenance to minimise toxicity; for hydroxychloroquine sulfate this should not exceed 6.5 mg/kg lean body-weight daily. Daily doses of 200 or 400 mg are commonly used but one study indicates that there is little advantage in using the higher dose.[6]

Experience with antimalarials to treat **juvenile idiopathic arthritis** (p.10) is limited and the results have been variable.[7,8]