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)*

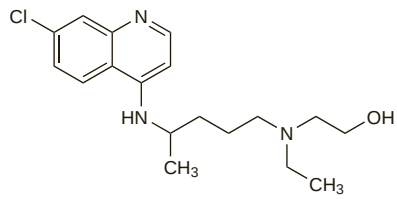
Hydroxychloroquine, Sulfate d'; Hydroxychloroquine Sulphate *(BANM)*; Hydroxychloroquini Sulfas; Oxichlorochin Sulphate; Sulfato de hidroxicloroquina; Win-1258-2. 2-{*N*-[4-(7-Chloro-4-quinolylamino)pentyl]-*N*-ethylamino}ethanol sulphate.

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]

Chloroquine and hydroxychloroquine have also been reported to be of use in **palindromic rheumatism**.[9-11]

1. Suarez-Almazor ME, *et al.* Antimalarials for treating rheumatoid arthritis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2000 (accessed 17/05/05).
2. HERA Study Group. A randomized trial of hydroxychloroquine in early rheumatoid arthritis: the HERA study. *Am J Med* 1995; **98:** 156–68.
3. Clegg DO, *et al.* Safety and efficacy of hydroxychloroquine as maintenance therapy for rheumatoid arthritis after combination therapy with methotrexate and hydroxychloroquine. *J Rheumatol* 1997; **24:** 1896–1902.
4. O'Dell JR. Triple therapy with methotrexate, sulfasalazine, and hydroxychloroquine in patients with rheumatoid arthritis. *Rheum Dis Clin North Am* 1998; **24:** 465–77.
5. O'Dell JR, *et al.* Treatment of rheumatoid arthritis with methotrexate and hydroxychloroquine, methotrexate and sulfasalazine, or a combination of the three medications: results of a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2002; **46:** 1164–70.
6. Pavelka K, *et al.* Hydroxychloroquine sulphate in the treatment of rheumatoid arthritis: a double blind comparison of two dose regimens. *Ann Rheum Dis* 1989; **48:** 542–6.
7. Brewer EJ, *et al.* Penicillamine and hydroxychloroquine in the treatment of severe juvenile rheumatoid arthritis. *N Engl J Med* 1986; **314:** 1269–76.
8. Grondin C, *et al.* Slow-acting antirheumatic drugs in chronic arthritis of childhood. *Semin Arthritis Rheum* 1988; **18:** 38–47.
9. Richardson MR, Zalin AM. Treatment of palindromic rheumatism with chloroquine. *BMJ* 1987; **294:** 741.
10. Hanonen P, *et al.* Treatment of palindromic rheumatism with chloroquine. *BMJ* 1987; **294:** 1289.
11. Youssef W, *et al.* Palindromic rheumatism: a response to chloroquine. *J Rheumatol* 1991; **18:** 35–7.

Sarcoidosis. Chloroquine and hydroxychloroquine have been tried in the management of sarcoidosis (p.1512) as alternatives or adjuncts to corticosteroid therapy. For references to the use of hydroxychloroquine, see under Chloroquine, p.603.

Skin disorders. For reference to the use of hydroxychloroquine in a variety of skin disorders, see under Chloroquine, p.603.

Systemic lupus erythematosus. Antimalarials have been widely used in the treatment of lupus erythematosus (p.1513), particularly its cutaneous manifestations, although much of the evidence is based on case series and reports.[1] Hydroxychloroquine is most widely used, as it is thought to have fewer adverse effects than chloroquine, although any benefit with chloroquine generally starts to become evident within several weeks of starting treatment, whereas it may take up to 2 months for any effect of hydroxychloroquine to be seen. For extracutaneous disease, antimalarials are often combined with other drugs; treatment may be continued for many years. For reference to precautions to reduce the risk of retinopathy see Effects on the Eyes, under Adverse Effects of Chloroquine, p.600.

1. Wozniacka A, McCauliffe DP. Optimal use of antimalarials in treating cutaneous lupus erythematosus. *Am J Clin Dermatol* 2005; **6:** 1–11.

Venous thromboembolism. Standard prophylaxis for surgical patients at high risk of venous thromboembolism (p.1189) is usually with an anticoagulant. Hydroxychloroquine has been described by some as an antiplatelet agent[1] and although its mechanism of action is uncertain the incidence of fatal pulmonary embolism has been reduced in patients given hydroxychloroquine prophylactically after total hip replacement;[2] the usual daily divided oral dose was about 800 mg from the day before surgery until discharge; larger doses had been used.

1. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy—III: reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients. *BMJ* 1994; **308:** 235–46.
2. Loudon JR. Hydroxychloroquine and postoperative thromboembolism after total hip replacement. *Am J Med* 1988; **85:** (suppl 4A): 57–61.

Preparations

BP 2008: Hydroxychloroquine Tablets;
USP 31: Hydroxychloroquine Sulfate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Axokine; Evoquin; Metirel; Narbon; Plaquenil; Polirreumin; ***Austral.:*** Plaquenil; ***Austria:*** Plaquenil; ***Belg.:*** Plaquenil; ***Braz.:*** Plaquinol; Reuquinol; ***Canad.:*** Apo-Hydroxyquine; Plaquenil; ***Chile:*** Plaquinol; ***Cz.:*** Plaquenil; ***Denm.:*** Ercoquin; Plaquenil; ***Fin.:*** Oxiklorin; Plaquenil†; ***Fr.:*** Plaquenil; ***Ger.:*** Quensyl; ***Gr.:*** Plaquenil; ***Hong Kong:*** Plaquenil; ***India:*** HCQS; ***Irl.:*** Plaquenil; ***Israel:*** Plaquenil; ***Ital.:*** Plaquenil; ***Malaysia:*** Plaquenil; ***Mex.:*** Plaquenil; ***Neth.:*** Plaquenil; ***Norw.:*** Plaquenil; ***NZ:*** Plaquenil; ***Philipp.:*** Plaquenil; ***Port.:*** Plaquinol; ***Rus.:*** Plaquenil (Плаквенил); ***Singapore:*** Plaquenil; ***Spain:*** Dolquine; ***Swed.:*** Plaquenil; ***Switz.:*** Plaquenil; ***Thai.:*** Hydroquin; Plaquenil; ***UK:*** Plaquenil; ***USA:*** Plaquenil; ***Venez.:*** Plaquinol.

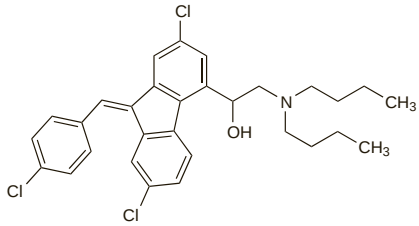
Lumefantrine *(BAN, rINN)*

Benflumelol; Benflumetol; Lumefantrina; Luméfantrine; Lumefantrinum. 2,7-Dichloro-9-[(4-chlorophenyl)methylene]-α-[(dibutylamino)methyl]-9*H*-fluorene-4-methanol.

Лумефантрин

$C_{30}H_{32}Cl_3NO$ = 528.9.

CAS — 82186-77-4.



Pharmacopoeias. In *Chin.*

Adverse Effects and Precautions

Adverse effects associated with lumefantrine in combination with artemether commonly include headache, dizziness, sleep disturbance, palpitations, gastrointestinal disturbances, anorexia, pruritus, rash, cough, arthralgia, myalgia, and fatigue. Lumefantrine-artemether should be given with caution in severe hepatic or renal impairment and ECG and blood potassium monitored.

Effects on the blood. Severe haemolytic anaemia necessitating corticosteroid treatment, blood transfusion, and haemodialysis occurred in a patient after taking 8 lumefantrine-artemether tablets after a malarial attack.[1] It was considered that, given its molecular similarity to other antimalarials known to cause haemolysis, the causative drug was probably lumefantrine.

1. Mérat S, *et al.* Case report: combination artemether-lumefantrine and haemolytic anaemia following a malarial attack. *Trans R Soc Trop Med Hyg* 2003; **97:** 433–4.

Pharmacokinetics

The bioavailability of lumefantrine after oral doses is variable; absorption begins after a lag-time of up to 2 hours and bioavailability is substantially increased when given with food, particularly meals high in fat. Peak plasma concentrations occur after about 6 to 8 hours. Lumefantrine is almost completely protein bound. It is considered to be metabolised mainly in the liver and is excreted in the faeces. The elimination half-life is reported to be between 4 to 6 days in patients with malaria.

◊ References.

1. White NJ, *et al.* Clinical pharmacokinetics and pharmacodynamics of artemether-lumefantrine. *Clin Pharmacokinet* 1999; **37:** 105–25.
2. Ezzet F, *et al.* Pharmacokinetics and pharmacodynamics of lumefantrine (benflumetol) in acute falciparum malaria. *Antimicrob Agents Chemother* 2000; **44:** 697–704.

Uses and Administration

Lumefantrine is a dichlorobenzylidine derivative given by mouth in combination with artemether (p.598) for the treatment of uncomplicated falciparum malaria. It is a blood schizontocide with a relatively slow onset of action but it has a longer duration of action than artemether.

The following doses are recommended by WHO; 6 doses in total are given, starting at diagnosis and repeated after 8, 24, 36, 48, and 60 hours. Each dose is:

- adults and children weighing over 34 kg, lumefantrine 480 mg with artemether 80 mg
- children 5 to 14 kg, lumefantrine 120 mg with artemether 20 mg
- children 15 to 24 kg, lumefantrine 240 mg with artemether 40 mg
- children 25 to 34 kg, lumefantrine 360 mg with artemether 60 mg

◊ References.

1. Omari AAA, *et al.* Artemether-lumefantrine (six-dose regimen) for treating uncomplicated falciparum malaria. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 19/07/06).
2. Omari AAA, *et al.* Artemether-lumefantrine (four-dose regimen) for treating uncomplicated falciparum malaria. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 19/07/06).
3. Kokwaro G, *et al.* Artemether/lumefantrine in the treatment of uncomplicated falciparum malaria. *Expert Opin Pharmacother* 2007; **8:** 75–94.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Riamet; ***Austria:*** Riamet; ***Belg.:*** Co-Artesiane; ***Cz.:*** Riamet; ***Fr.:*** Riamet; ***Ger.:*** Riamet; ***Gr.:*** Riamet; ***Hong Kong:*** Riamet†; ***Neth.:*** Riamet; ***Norw.:*** Riamet†; ***Port.:*** Riamet; ***S.Afr.:*** Coartem; ***Swed.:*** Riamet; ***Switz.:*** Riamet; ***Thai.:*** Coartem; ***UK:*** Riamet.

Mefloquine Hydrochloride

(BANM, USAN, rINNM)

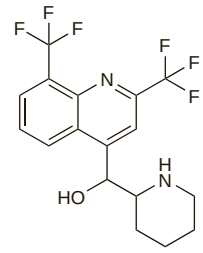
Hidrocloruro de mefloquina; Meflochin-hydrochlorid; Meflokiini-hydrokloridi; Meflokin-hidroklorid; Meflokinhydroklorid; Meflokvino hidrochloridas; Méfloquine, chlorhydrate de; Mefloquini hydrochloridum; Ro-21-5998 (mefloquine); Ro-21-5998/001 (mefloquine hydrochloride); WR-142490 (mefloquine). (*RS*)-[2,8-Bis(trifluoromethyl)-4-quinolyl]-(*SR*)-(2-piperidyl)methanol hydrochloride.

Мефлохина Гидрохлорид

$C_{17}H_{16}F_6N_2O,HCl$ = 414.8.

CAS — 53230-10-7 (mefloquine); 51773-92-3 (mefloquine hydrochloride).

ATC — P01BC02.



(mefloquine)

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.

Ph. Eur. 6.2 (Mefloquine Hydrochloride). A white or slightly yellow, crystalline powder. It shows polymorphism. Very slightly soluble in water; soluble in alcohol; freely soluble in methyl alcohol. Protect from light.

USP 31 (Mefloquine Hydrochloride). A white or slightly yellow, crystalline powder. It exhibits polymorphism. Very slightly soluble in water; soluble in alcohol; freely soluble in methyl alcohol. Store in airtight containers at a temperature between 15° and 30°. Protect from light.

Sorption. For reference to loss of mefloquine hydrochloride from solutions during membrane filtration, see Chloroquine, p.599.

Stability. A report of the photolytic degradation of mefloquine hydrochloride in water.[1]

1. Tønnesen HH, Grislingaas A-L. Photochemical stability of biologically active compounds II: photochemical decomposition of mefloquine in water. *Int J Pharmaceutics* 1990; **60:** 157–62.

Adverse Effects

Since mefloquine has a long elimination half-life, adverse effects may occur or persist up to several weeks after the last dose.

The most frequent adverse effects of mefloquine are nausea, diarrhoea, vomiting, abdominal pain, anorexia, headache, dizziness, loss of balance, somnolence, and sleep disorders, notably insomnia and abnormal dreams.

Neurological or psychiatric disturbances have also been reported with mefloquine and include sensory and motor neuropathies, tremor, ataxia, visual disturbances, tinnitus and hearing impairment, convulsions, anxiety, depression, confusion, hallucinations, panic attacks, emotional instability, aggression and agitation, and acute psychosis. There have been rare reports of suicidal ideation.

Other adverse effects include skin rashes, pruritus and urticaria, hair loss, muscle weakness, myalgia, liver function disturbances, and very rarely thrombocytopenia and leucopenia. There have been rare occurrences of erythema multiforme and Stevens-Johnson syndrome. Anaphylaxis has occurred rarely. Cardiovascular effects have included hypotension, hypertension,