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.

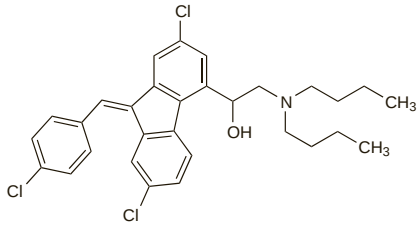
Lumefantrine *(BAN, rINN)*

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)

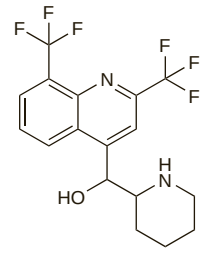
Hidrocloruro de mefloquina; Meflochin-hydrochlorid; Meflokiini-hydrokloridi; Meflokin-hidroklorid; Meflokinhydroklorid; Meflokvino hidrochloridas; Méfloquine, chlorhydrate de; Mefloquini hydrochloridum; Ro-21-5998 (mefloquine); Ro-21-5998/001 (mefloquine hydrochloride); WR-142490 (mefloquine). (*RS*)-[2,8-Bis(trifluoromethyl)-4-quinolyl]-(*SR*)-(2-piperidyl)meth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