

**Toxoplasmosis.** Pyrimethamine is given, usually with sulfadiazine or another appropriate sulphonamide, in the treatment of toxoplasmosis (p.826). Folic acid is also given to counteract the megaloblastic anaemia associated with these drugs.

Oral doses suggested by WHO<sup>1</sup> are:

- in *pregnancy* (second and third trimesters), pyrimethamine 25 mg daily for 3 to 4 weeks with sulfadiazine 3 g daily in 4 divided doses
- in *neonates*, pyrimethamine 1 mg/kg daily, with sulfadiazine 85 mg/kg daily in 2 divided doses; treatment should be given for 6 months if there is overt neonatal disease, or for 4 weeks to those without overt disease but whose mother was infected during pregnancy
- in *immunodeficiency*, pyrimethamine 200 mg in divided doses on the first day, then 75 to 100 mg daily for at least 6 weeks, followed by a suppressive dose of 25 to 50 mg daily; sulfadiazine is also given in a dose of 4 to 6 g daily in 4 divided doses for at least 6 weeks, followed by a suppressive dose of 2 to 4 g daily
- in *chorioretinitis*, pyrimethamine 75 mg daily for 3 days, then 25 mg daily for 4 weeks, followed in unresponsive patients by 50 mg daily for a further 4 weeks; sulfadiazine is also given in a dose of 2 g daily in 4 divided doses

Pyrimethamine with clindamycin is an alternative in patients unable to tolerate a sulfonamide.

Other drugs that have been tried with pyrimethamine include azithromycin,<sup>2</sup> clarithromycin,<sup>3</sup> and doxycycline.<sup>4,5</sup>

Alternative regimens tried for long-term maintenance therapy in patients with AIDS have included pyrimethamine plus sulfadiazine given twice weekly<sup>6,7</sup> or pyrimethamine alone in doses of 25 mg or 50 mg daily or 50 mg three times weekly.<sup>8-10</sup> However, results from a study involving 396 patients suggested that the mortality rate was higher in those receiving pyrimethamine 25 mg three times weekly for primary prophylaxis than in those receiving placebo.<sup>11</sup> Pyrimethamine with dapsone given once a week can provide effective prophylaxis but was not well tolerated.<sup>12</sup> Pyrimethamine with sulfadoxine, also given once weekly, was of benefit in bone-marrow transplant recipients.<sup>13</sup>

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5. Hagberg L, et al. Doxycycline and pyrimethamine for toxoplastic encephalitis. *Scand J Infect Dis* 1993; **25**: 157-60.
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8. Murphy K, et al. Pyrimethamine alone as long-term suppressive therapy in cerebral toxoplasmosis. *Am J Med* 1994; **96**: 95-6.
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## Preparations

**BP 2008:** Pyrimethamine Tablets; Sulfadoxine and Pyrimethamine Tablets.  
**USP 31:** Pyrimethamine Tablets; Sulfadoxine and Pyrimethamine Tablets.

**Proprietary Preparations** (details are given in Part 3)

**Arg.:** Daraprim; **Austral.:** Daraprim; **Austria:** Daraprim; **Belg.:** Daraprim; **Braz.:** Daraprim; **Canad.:** Daraprim; **Chile:** Daraprim; **Fr.:** Malocide; **Ger.:** Daraprim; **Irl.:** Daraprim; **Israel:** Daraprim; **Malaysia:** Fansidar; **Mex.:** Daraprim; **Neth.:** Daraprim; **Pol.:** Daraprim; **S.Afr.:** Daraprim; **Spain:** Daraprim; **Switz.:** Daraprim; **Thai.:** Daraprim; **UK:** Daraprim; **USA:** Daraprim.

**Multi-ingredient:** **Austral.:** Fansidar; Maloprim; **Belg.:** Co-Arinate; Daf-  
rafin; Malastop; **Braz.:** Fansidar; **Canad.:** Fansidar; **Denm.:** Fansidar; **Fr.:** Fansidar; **India:** Artemal; Laridox; Pyralin; Pyramet; Rimodar; **Indon.:** Fansidar; Suldox; **Irl.:** Fansidar; Maloprim; **Israel:** Fansidar; **Ital.:** Metakelfin; **Malaysia:** Madomine; **Philipp.:** Fansidar; **S.Afr.:** Fansidar; Maloprim; **Singapore:** Madomine; Pyrisone; **Switz.:** Fansidar; Fansimef; **Thai.:** Vivaxine; **UK:** Fansidar; **USA:** Fansidar.

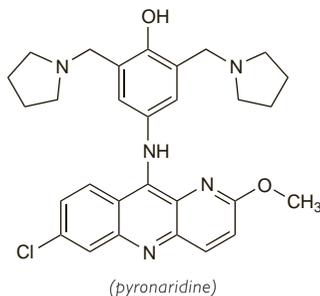
## Pyronaridine Phosphate (riNMM)

Fosfato de pironaridina; Malaridine Phosphate; Pyronaridine, Phosphate de; Pyronaridini Phosphas. 7-Chloro-2-methoxy-10-[3,5-bis(pyrrrolidinomethyl)-4-hydroxyanilino]benzo-[b]-1,5-naphthyridine phosphate.

Пиронаридина Фосфат

$C_{29}H_{32}ClN_5O_2 \cdot 4H_3PO_4 = 910.0$ .

CAS — 74847-35-1 (pyronaridine); 76748-86-2 (pyronaridine phosphate).



**Pharmacopoeias.** In *Chin.*

### Profile

Pyronaridine is a naphthyridine derivative used in China in the treatment of vivax malaria and chloroquine-resistant falciparum malaria. Its use has also been investigated in Africa and in Thailand. Combination of pyronaridine with artesunate is also being investigated. Pyronaridine has been given as the phosphate by mouth or by intramuscular or intravenous injection.

### References

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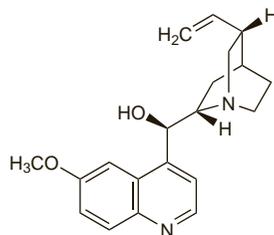
## Quinine (BAN)

Chinina; Chininum; Kiniini; Kinin; Quinina. (8S,9R)-6'-Methoxycinchonan-9-ol; ( $\alpha$ R)- $\alpha$ -(6-Methoxy-4-quinolyl)- $\alpha$ -[(2S,4S,5R)-(5-vinylquinuclidin-2-yl)methanol.

$C_{20}H_{24}N_2O_2 = 324.4$ .

CAS — 130-95-0 (anhydrous quinine).

ATC — P01BC01.



**Description.** Quinine is the chief alkaloid of various species of *Cinchona* (Rubiaceae). It is an optical isomer of quinidine.

### Quinine Bisulfate

Chininum Bisulfuricum; Neutral Quinine Sulphate; Quinina, bisulfato de; Quinine Acid Sulphate; Quinine Bisulfate (BANM); Quinini Bisulfas.

$C_{20}H_{24}N_2O_2 \cdot H_2SO_4 \cdot 7H_2O = 548.6$ .

CAS — 549-56-4 (anhydrous quinine bisulfate).

ATC — P01BC01.

**Pharmacopoeias.** In *Br., Int., and Viet.*

**BP 2008** (Quinine Bisulphate). Colourless crystals or a white crystalline powder. It effloresces in dry air. Freely soluble in water; sparingly soluble in alcohol. A 1% solution in water has a pH of 2.8 to 3.4. Protect from light.

### Quinine Dihydrochloride (BANM)

Chinini Dihydrochloridum; Neutral Quinine Hydrochloride; Quinina, dihydrochloruro de; Quinine Acid Hydrochloride; Quinini Dihydrochloridum.

$C_{20}H_{24}N_2O_2 \cdot 2HCl = 397.3$ .

CAS — 60-93-5.

ATC — P01BC01.

**Pharmacopoeias.** In *Br., Chin., and Int.*

*Viet.* includes the injection.

**BP 2008** (Quinine Dihydrochloride). A white or almost white powder. Very soluble in water; soluble in alcohol. A 3% solution in water has a pH of 2.0 to 3.0. Protect from light.

### Quinine Etanolate

Euquinina; Euquinine; Quinina, etilcarbonato de; Quinine Ethyl Carbonate.

$C_{23}H_{28}N_2O_4 = 396.5$ .

CAS — 83-75-0.

ATC — P01BC01.

**Pharmacopoeias.** In *Jpn.*

### Quinine Hydrobromide (BANM)

Basic Quinine Hydrobromide; Chinini Bromidum; Quinina, hidrobromuro de; Quinine Monohydrobromide.

$C_{20}H_{24}N_2O_2 \cdot HBr \cdot H_2O = 423.3$ .

CAS — 549-49-5 (anhydrous quinine hydrobromide).

ATC — P01BC01.

**Pharmacopoeias.** In *Fr.*

### Quinine Hydrochloride (BANM)

Basic Quinine Hydrochloride; Chinin hydrochlorid dihydrát; Chinini hydrochloridum; Chininii Chloridum; Chininium Chloratum; Chinino hydrochloridas; Chininum Hydrochloricum; Chininy chlorowodorek; Kiniinihydroklorid; Kinin-hydroklorid; Kিনিnhydroklorid; Quinina, hydrochloruro de; Quinine, chlorhydrate de; Quinine Monohydrochloride; Quinini Hydrochloridum; Quinini Hydrochloridum Dihydratum.

$C_{20}H_{24}N_2O_2 \cdot HCl \cdot 2H_2O = 396.9$ .

CAS — 130-89-2 (anhydrous quinine hydrochloride);

6119-47-7 (quinine hydrochloride dihydrate).

ATC — P01BC01.

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

**Ph. Eur. 6.2** (Quinine Hydrochloride). White or almost white, or colourless, fine, silky needles, often grouped in clusters. Soluble in water; freely soluble in alcohol. A 1% solution in water has a pH of 6.0 to 6.8. Protect from light.

### Quinine Sulfate

Basic Quinine Sulphate; Chinin sulfát dihydrát; Chinini sulfas; Chinino sulfatas; Chininum Sulfuricum; Chininy siarczan; Kiniini-sulfaatti; Kininsulfat; Kinin-sulfát; Quinina, sulfato de; Quinine, sulfato de; Quinine Sulphate (BANM); Quinini Sulfas; Quinini Sulfas Dihydricus.

$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O = 782.9$ .

CAS — 804-63-7 (anhydrous quinine sulfate); 6119-70-6

(quinine sulfate dihydrate).

ATC — P01BC01.

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

**Ph. Eur. 6.2** (Quinine Sulphate). A white or almost white, crystalline powder or fine, colourless needles. Slightly soluble in water; sparingly soluble in boiling water and in alcohol. A 1% suspension in water has a pH of 5.7 to 6.6. Protect from light.

**USP 31** (Quinine Sulfate). It is the sulfate of an alkaloid obtained from the bark of species of *Cinchona*. White, odourless, fine needle-like crystals, usually lusterless, making a light and readily compressible mass. It darkens on exposure to light. Soluble 1 in 500 of water and 1 in 120 of alcohol; sparingly soluble in water at 100°; slightly soluble in chloroform; freely soluble in alcohol at 80° and in a mixture of 2 parts of chloroform and one part of dehydrated alcohol; very slightly soluble in ether; Its saturated solution in water is neutral or alkaline to litmus. Protect from light.

**Sorption.** For reference to loss of quinine sulfate from solutions during membrane filtration, see Chloroquine, p.599.

### Adverse Effects

Quinine or its salts given in usual therapeutic doses may give rise to a train of symptoms known as cinchonism, characterised in its mild form by tinnitus, impaired hearing, headache, nausea, and disturbed vision, with, in its more severe manifestations, vomiting, abdominal pain, diarrhoea, and vertigo.