

Accupro; **Denm.**: Accupro; **Fin.**: Accupro; **Fr.**: Acufilet; Korec; **Ger.**: Accupro; Quinalich; **Gr.**: Accupron; **Hong Kong**: Accupril; **Hung.**: Accupro; Acermed; **Indon.**: Accupril; **Irl.**: Accupro; Quinapro; **Ital.**: Accuprin; Acerquin; Quinazil; **Jpn.**: Conan; **Malaysia**: Accupril; **Mex.**: Accupril; **Neth.**: Accupril; **NZ**: Accupril; **Philipp.**: Accupril; **Pol.**: Accupro; Acurenal; AprilGen; **Port.**: Accupril; **Vasocor**; **Rus.**: Accupro (Акуприл); **S.Afr.**: Accupril; Quinaspen; **Singapore**: Accupril; **Spain**: Accuprel; Acuretic; Ectrem; Lidaltrin; **Swed.**: Accupro; **Switz.**: Accupro; **Thal.**: Accupril; **Turk.**: Accutel; **UK**: Accupro; Quinil; **USA**: Accupril; **Venez.**: Accupril; Quinilar; Solpres.

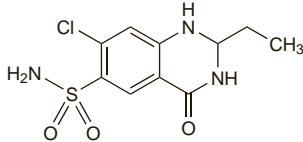
**Multi-ingredient:** **Arg.**: Acuretic; **Austral.**: Acuretic; **Austria**: Accuzide; **Belg.**: Accuzide; Co-Quinapril; **Canad.**: Accuretic; **Chile**: Accuretic; **Cz.**: Accuzide; Stadapress; **Fin.**: Accupro Comp; **Fr.**: Acufilet; Koretic; **Ger.**: Accuzide; Quinalich comp; Quinapril; Quinapril comp; **Gr.**: Accuretic; Quimea; **Hung.**: Accuzide; **Irl.**: Accuretic; **Ital.**: Accuprin; Acequide; Quinazide; **Neth.**: Accuzide; **NZ**: Accuretic; **Philipp.**: Accuzide; **Pol.**: Accuzide; **Port.**: Accuretic; **S.Afr.**: Accuretic; **Spain**: Bicetil; Lidaltrin Diu; **Swed.**: Accupro Comp; **Switz.**: Accuprel; **Turk.**: Accuzide; **UK**: Accuretic; **USA**: Accuretic; Quinaretic; **Venez.**: Accuretic; Quinaretic.

### Quinethazone (BAN, rINN) $\otimes$

Chinethazonum; Kinetatsoni; Kinetazon; Quinetazone; Quinéthazone; Chinethazonum. 7-Chloro-2-ethyl-1,2,3,4-tetrahydro-4-oxoquinazoline-6-sulphonamide.

Хинетазон

$C_{10}H_{12}ClN_3O_3S = 289.7$ .  
CAS — 73-49-4.  
ATC — C03BA02.  
ATC Vet — QC03BA02.



### Profile

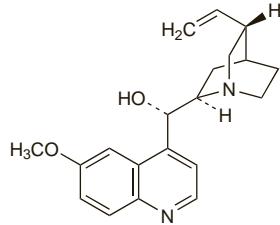
Quinethazone is a diuretic that is related chemically to metolazone and has properties similar to those of the thiazide diuretics (see Hydrochlorothiazide, p.1307). It has been used for oedema, including that associated with heart failure, and for hypertension.

### Quinidine (BAN)

Chinidinum; Chinidyna; Kinidiini; Kinidin; Kinin; Quinidina. (8R,9S)-6'-Methoxycinchonan-9-ol; (+)-(αS)-α-(6-Methoxy-4-quinolyl)-α-[{(2R,4S,5R)-(5-vinylquinuclidin-2-yl)}]methanol.

Хинидин

$C_{20}H_{24}N_2O_2 = 324.4$ .  
CAS — 56-54-2 (anhydrous quinidine); 63717-04-4 (quinidine hydrate); 72402-50-7 ( $\pm$  quinidine).  
ATC — C01BA01.  
ATC Vet — QC01BA01.



**Description.** Quinidine is an isomer of quinine, obtained from the bark of species of *Cinchona* and their hybrids; it may also be obtained from *Remijia pedunculata*, or prepared from quinine.

### Quinidine Bisulfate

Quinidina, bisulfato de; Quinidine Bisulphate (BANM).

Хинидина Бисульфат

$C_{20}H_{24}N_2O_2 \cdot H_2SO_4 = 422.5$ .  
CAS — 747-45-5 (anhydrous quinidine bisulfate); 6151-39-9 (quinidine bisulfate tetrahydrate).  
ATC — C01BA01.  
ATC Vet — QC01BA01.

### Pharmacopoeias. In Br.

**BP 2008** (Quinidine Bisulphate). Colourless, odourless or almost odourless, crystals. It contains not more than 15% of hydroquinidine.

The symbol  $\dagger$  denotes a preparation no longer actively marketed

dine bisulfate. Freely soluble in water and in alcohol; practically insoluble in ether. A 1% solution in water has a pH of 2.6 to 3.6. Protect from light.

### Quinidine Gluconate (BANM)

Quinidina, gluconato de; Quinidinium Gluconate.

Хинидина Глюконат

$C_{20}H_{24}N_2O_2 \cdot C_6H_{12}O_7 = 520.6$ .  
CAS — 7054-25-3.  
ATC — C01BA01.

ATC Vet — QC01BA01.

### Pharmacopoeias. In US.

**USP 31** (Quinidine Gluconate). A white, odourless powder. It contains not more than 20% of hydroquinidine gluconate. Freely soluble in water; slightly soluble in alcohol. Store at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

**Adsorption.** More than 40% of a dose of quinidine gluconate was lost when the drug was given by intravenous infusion using a PVC infusion bag and tubing.<sup>1</sup>

1. Darbar D, et al. Loss of quinidine gluconate injection in a polyvinyl chloride infusion system. *Am J Health-Syst Pharm* 1996; **53**: 655-8.

### Quinidine Polygalacturonate

Quinidina, poligalacturonato de. Quinidine poly(D-galacturonate) hydrate.

Хинидина Полигалактуронат

$C_{20}H_{24}N_2O_2 \cdot (C_6H_{10}O_7)_x \cdot xH_2O$ .  
CAS — 27555-34-6 (anhydrous quinidine polygalacturonate); 65484-56-2 (quinidine polygalacturonate hydrate).  
ATC — C01BA01.

ATC Vet — QC01BA01.

### Quinidine Sulfate

Chinidin sulfát dihydrát; Chinidini sulfás; Chinidino sulfatas; Chindinsulfate; Chinidinum Sulfiricum; Chinidiny siarczan; Kinidinisulfatti; Kinidin Sulfát; Kinidinsulfat; Kinidin-sulfáz; Quinidina, sulfato de; Quinidine, sulfate de; Quinidine Sulphate (BANM); Quinidini Sulfas; Quinidini Sulfas Dihydricus.

Хинидина Сульфат

$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O = 782.9$ .  
CAS — 50-54-4 (anhydrous quinidine sulfate); 6591-63-5 (quinidine sulfate dihydrate).  
ATC — C01BA01.

ATC Vet — QC01BA01.

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

**Ph. Eur. 6.2** (Quinidine Sulphate). White or almost white, crystalline powder, or silky, colourless needles. It contains not more than 15% of hydroquinidine sulfate. Slightly soluble in water; soluble in boiling water and in alcohol; practically insoluble in acetone. A 1% solution in water has a pH of 6.0 to 6.8. Protect from light.

**USP 31** (Quinidine Sulfate). Fine, needle-like, white crystals, frequently cohering in masses, or a fine, white powder. It is odourless and darkens on exposure to light. It contains not more than 20% of hydroquinidine sulfate. Its solutions are neutral or alkaline to litmus. Soluble 1 in 100 of water, 1 in 10 of alcohol, and 1 in 15 of chloroform; insoluble in ether. Protect from light.

**Stability.** Quinidine sulfate was reported<sup>1</sup> to be stable for up to 60 days in several extemporaneously prepared oral liquid formulations.

1. Allen LV, Erickson MA. Stability of bethanechol chloride, pyrazinamide, quinidine sulfate, rifampin, and tetracycline hydrochloride in extemporaneously compounded oral liquids. *Am J Health-Syst Pharm* 1998; **55**: 1804-9.

### Adverse Effects and Treatment

Quinidine and its salts have both cardiac and non-cardiac adverse effects. Gastrointestinal irritation is common, with nausea, vomiting, and diarrhoea.

Hypersensitivity similar to that occurring with quinine may also occur and a test dose has been recommended (see Uses and Administration, below). Reactions include respiratory difficulties, urticaria, pruritus, skin rashes, purpura, thrombocytopenia and other blood dyscrasias, and, rarely, fever and anaphylaxis. Granulomatous hepatitis and a lupus-like syndrome have been reported.

Quinidine may give rise to cinchonism (see Quinine, p.612) with tinnitus, impaired hearing, visual disturbances, headache, confusion, vertigo, vomiting, and abdominal pain; it is usually associated with large doses, but may occur in idiosyncratic subjects given small doses.

Quinidine may induce hypotension, particularly in overdosage or if intravenous infusions are given too

rapidly. It prolongs the QT interval and may precipitate ventricular arrhythmias, including torsade de pointes.

In quinidine overdosage, the cardiac symptoms of intoxication predominate. Quinidine is cumulative in action and inappropriately high plasma concentrations may induce ECG changes, heart block, asystole, ventricular tachycardia, ventricular fibrillation, syncope, seizures, coma, and sometimes death. Treatment of adverse effects and overdosage is symptomatic and supportive. Activated charcoal may be considered if the patient presents within 1 hour of ingestion.

### ◊ Reviews.

1. Kim SY, Benowitz NL. Poisoning due to class IA antiarrhythmic drugs quinidine, procainamide and disopyramide. *Drug Safety* 1990; **5**: 393-420.

**Effects on the blood.** Quinidine-induced thrombocytopenia is not uncommon and it is one of the best documented causes of drug-dependent thrombocytopenia.<sup>1</sup> It appears to be a hypersensitivity reaction, with quinidine inducing the production of autoantibodies that cause platelet destruction. Highly specific quinidine-dependent antibodies have been detected in patients with thrombocytopenia, and may have a role in diagnosis.<sup>2</sup> The exact mechanism of the reaction is unclear but it is generally thought that binding of quinidine to the platelet surface induces antibody production;<sup>1</sup> alternatively, an antibody-quinidine complex may be formed, which is then deposited on the platelets.<sup>1,3</sup> The antigenic constituent of the platelet membrane may be glycoprotein Ib although other surface glycoproteins have also been implicated.<sup>3,4</sup>

1. van den Bemt PMLA, et al. Drug-induced immune thrombocytopenia. *Drug Safety* 2004; **27**: 1243-52.
2. Reid DM, Shulman NR. Drug purpura due to surreptitious quinidine intake. *Ann Intern Med* 1988; **108**: 206-8.
3. Stricker RB, Shuman MA. Quinidine purpura: evidence that glycoprotein V is a target platelet antigen. *Blood* 1986; **67**: 1377-81.
4. Visentin GP, et al. Characteristics of quinine- and quinidine-induced antibodies specific for platelet glycoproteins IIb and IIIa. *Blood* 1991; **77**: 2668-76.

**Effects on the eyes.** Corneal deposits resembling those found in keratopathy developed in a patient who had been taking quinidine for 2 years.<sup>1</sup> Symptoms had improved and both corneas had cleared completely within 2 months of stopping the drug.

A small number of patients have also been identified<sup>2</sup> who developed uveitis during quinidine treatment.

1. Zaidman GW. Quinidine keratopathy. *Am J Ophthalmol* 1984; **97**: 247-9.

2. Fraunfelder FW, Rosenbaum JT. Drug-induced uveitis: incidence, prevention and treatment. *Drug Safety* 1997; **17**: 197-207.

**Effects on the joints.** Quinidine has been associated with a number of rheumatic disorders.<sup>1</sup> It is a recognised, though uncommon, cause of drug-induced lupus (see below), but there have also been reports<sup>2-4</sup> of reversible, symmetrical polyarthritides developing in patients with no evidence of antinuclear antibodies. Symptoms were generally milder than in drug-induced lupus, and onset was more rapid; recovery occurred within a week of stopping quinidine and in some patients symptoms recurred on rechallenge. Polymyalgia rheumatica-like symptoms have also been reported.<sup>1</sup>

1. Alloway JA, Salata MP. Quinidine-induced rheumatic syndromes. *Semin Arthritis Rheum* 1995; **24**: 315-22.

2. Kertes P, Hunt D. Polyarthritides complicating quinidine treatment. *BMJ* 1982; **284**: 1373-4.

3. Cohen MG, et al. Two distinct quinidine-induced rheumatic syndromes. *Ann Intern Med* 1988; **108**: 369-71.

4. Naschitz JE, Yeshurun D. Quinidine and rheumatic syndromes. *Ann Intern Med* 1988; **109**: 248-9.

**Effects on the liver.** Hypersensitivity reactions involving the liver have been reported in about 2% of patients receiving quinidine.<sup>1,2</sup> The main clinical symptom is fever<sup>1-3</sup> but skin rash,<sup>1-3</sup> purpura,<sup>2</sup> and hepatomegaly<sup>1</sup> may also occur. Liver enzyme values are raised<sup>1,4</sup> and the platelet count may be reduced.<sup>3</sup> The reaction is reversible on withdrawing quinidine with fever resolving in about 48 hours and liver enzymes values returning to normal within about 2 weeks. Liver biopsy often shows granulomatous hepatitis,<sup>1,3</sup> but other inflammatory changes<sup>2</sup> and cholestatic jaundice<sup>4</sup> have been found.

1. Geltner D, et al. Quinidine hypersensitivity and liver involvement: a survey of 32 patients. *Gastroenterology* 1976; **70**: 650-2.

2. Knobler H, et al. Quinidine-induced hepatitis. *Arch Intern Med* 1986; **146**: 526-8.

3. Bramlet DA, et al. Granulomatous hepatitis as a manifestation of quinidine hypersensitivity. *Arch Intern Med* 1980; **140**: 395-7.

4. Hogan DB, et al. Unusual hepatotoxic reaction to quinidine. *Can Med Assoc J* 1984; **130**: 973.

**Effects on mental state.** Gradually progressive cerebral dysfunction characterised by intermittent confusion, agitation, restlessness, personality change, and paranoid features occurred in a 62-year-old man who had taken quinidine for about 15 years.<sup>1</sup> Within 24 hours of stopping quinidine there was a marked improvement and after 5 days he had returned to normal with no

The symbol  $\otimes$  denotes a substance whose use may be restricted in certain sports (see p.vii)