

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

Ph. Eur. 6.2 (Oxacillin Sodium Monohydrate). A white or almost white powder. Freely soluble in water; practically insoluble in dichloromethane; soluble in methyl alcohol. A 3.0% solution in water has a pH of 4.5 to 7.5.

USP 31 (Oxacillin Sodium). A fine white crystalline powder, odourless or having a slight odour. Freely soluble in water, in dimethyl sulfoxide, and in methyl alcohol; slightly soluble in dehydrated alcohol, in chloroform, in methyl acetate, and in pyridine; insoluble in ether, in ethyl acetate, in ethylene chloride, and in benzene. pH of a 3% solution in water is between 4.5 and 7.5. Store in airtight containers at a mean temperature not exceeding 25°.

Incompatibility. Oxacillin sodium has been reported to be incompatible with aminoglycosides and tetracyclines.

Adverse Effects and Precautions

As for Flucloxacillin, p.277.

Effects on the liver. References.

1. Onorato IM, Axelrod JL. Hepatitis from intravenous high-dose oxacillin therapy: findings in an adult inpatient population. *Ann Intern Med* 1978; **89**: 497–500.
2. Saliba B, Herbert PN. Oxacillin hepatotoxicity in HIV-infected patients. *Ann Intern Med* 1994; **120**: 1048.
3. Maraga NF, et al. Higher occurrence of hepatotoxicity and rash in patients treated with oxacillin, compared with those treated with nafcillin and other commonly used antimicrobials. *Clin Infect Dis* 2002; **34**: 50–4.

Sodium content. Each g of oxacillin sodium contains about 2.3 mmol of sodium.

Interactions

As for Benzylpenicillin, p.214.

Antimicrobial Action

As for Flucloxacillin, p.277.

Resistance. The isolation of pneumococci resistant to oxacillin but sensitive to benzylpenicillin has been reported.^{1,2} The resistance was due to acquisition of a low-affinity penicillin-binding protein and conferred cross-resistance to methicillin and cloxacillin, and, to a lesser degree, to cefotaxime.

1. Johnson AP, et al. Oxacillin-resistant pneumococci sensitive to penicillin. *Lancet* 1993; **341**: 1222.
2. Dowson CG, et al. Genetics of oxacillin resistance in clinical isolates of *Streptococcus pneumoniae* that are oxacillin resistant and penicillin susceptible. *Antimicrob Agents Chemother* 1994; **38**: 49–53.

Pharmacokinetics

Oxacillin is incompletely absorbed from the gastrointestinal tract. Absorption is reduced by the presence of food in the stomach and is less than with cloxacillin. Peak plasma concentrations of 3 to 6 micrograms/mL have been achieved 1 hour after an oral dose of 500 mg given to fasting subjects. After intramuscular injection of 500 mg, peak plasma concentrations of up to 15 micrograms/mL have been achieved by 30 minutes. Doubling the dose can double the plasma concentration. About 93% of the oxacillin in the circulation is bound to plasma proteins. Oxacillin has been reported to have a plasma half-life of about 0.5 hours. The half-life is prolonged in neonates.

The distribution of oxacillin into body tissues and fluids is similar to that of cloxacillin (p.256).

Oxacillin undergoes some metabolism, and the unchanged drug and metabolites are excreted in the urine by glomerular filtration and renal tubular secretion.

About 20 to 30% of an oral dose, and more than 40% of an intramuscular dose, is rapidly excreted in the urine. Oxacillin is also excreted in the bile.

Plasma concentrations are enhanced by probenecid.

Uses and Administration

Oxacillin is an isoxazolyl penicillin used similarly to flucloxacillin (p.277) in the treatment of infections due to staphylococci resistant to benzylpenicillin.

Oxacillin is given orally or by injection as the sodium salt. Doses are expressed in terms of the equivalent amount of oxacillin; 1.1 g of oxacillin sodium is equivalent to about 1 g of oxacillin. Oral doses should preferably be given at least 1 hour before, or 2 hours after, meals. The usual adult oral dose is 1 g of oxacillin twice daily. Oxacillin may be given by intramuscular injection, by slow intravenous injection over about 10

minutes, or by intravenous infusion. Usual parenteral doses for adults are 250 to 500 mg every 4 to 6 hours; doses may be increased to 1 g every 4 to 6 hours for severe infections.

The usual oral dose for children is 500 mg twice daily. The parenteral dose for children weighing less than 40 kg is 50 mg/kg daily in 4 to 6 divided doses; the dose may be increased to 100 mg/kg daily for severe infections.

Preparations

USP 31: Oxacillin for Injection; Oxacillin Injection; Oxacillin Sodium Capsules; Oxacillin Sodium for Oral Solution.

Proprietary Preparations (details are given in Part 3)

Belg.: Penstapho; **Braz.:** Oxacil; Oxanon; Oxapen; Prodoxacin; Roxacilin; Staficlin N; Teutoclin; **Cz.:** Prostaphlin; **Fr.:** Bristopen; **Ger.:** InfectoStaph; **Ital.:** Penstapho; **Philipp.:** Prostaphlin; Stafcil; Wydox; **Venez.:** Bioclin; Oxacilin; Oxipen; Pebenaf; Prostafina.

Multi-ingredient: **Ger.:** Optocilin; **Rus.:** Oxamp (Оксамп).

Oxolinic Acid (BAN, USAN, rINN)

Acide oxolinique; Ácido oxolinico; Acidum oxolinicum; Kyselina oxolinová; NSC-110364; Oksolinhappo; Oksolinik Asit; Oksolino rūgštis; Oxolinsav; Oxolinsyra; W-4565. 5-Ethyl-5,8-dihydro-8-oxo-1,3-dioxolo[4,5-g]quinoline-7-carboxylic acid.

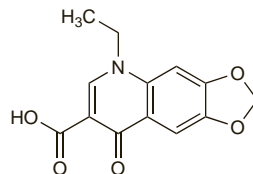
ОКСОЛИНОВАЯ КИСЛОТА

C₁₃H₁₁NO₅ = 261.2.

CAS = 14698-29-4.

ATC = J01MB05.

ATC Vet = QJ01MB05.



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

Ph. Eur. 6.2 (Oxolinic Acid). An almost white or pale yellow crystalline powder. Practically insoluble in water and in alcohol; very slightly soluble in dichloromethane; dissolves in dilute solutions of alkali hydroxides. Protect from light.

Profile

Oxolinic acid is a 4-quinolone antibacterial with properties similar to those of nalidixic acid (p.303), although adverse effects on the CNS may be more frequent. It has been given orally in the treatment of urinary-tract infections.

Preparations

Proprietary Preparations (details are given in Part 3)

Braz.: Unilin; **Cz.:** Desurof; **Port.:** Cistopax; **Spain:** Oxoinex.

Oxytetracycline (BAN, rINN)

Glomycin; Hydroxytetracycline; Oksitetrasiklinas; Oksitetrasiklin; Oksitetrasikliini; Oksytetracyclina; Oxitetraciclina; Oxitetraciklin; Oksitetrasiklin; Oksytetracycline; Oksytetracyclinum; Oksytetracyclin; Riomitsin; Terrafungine. 4S,4aR,5S,5aR,6S,12aS-4-Dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methylene-1,11-dioxonaphthacene-2-carboxamide; 5β-Hydroxytetracycline.

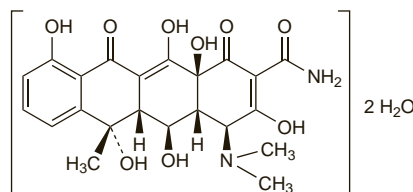
ОКСИТЕТРАЦИКЛИН

C₂₂H₂₄N₂O₉ = 460.4.

CAS = 79-57-2 (anhydrous oxytetracycline); 6153-64-6 (oxytetracycline dihydrate).

ATC = D06AA03; G01AA07; J01AA06; S01AA04.

ATC Vet = QD06AA03; QG01AA07; QG51AA01; QJ01AA06; QJ51AA06; QS01AA04.



(oxytetracycline dihydrate)

Pharmacopoeias. In *Eur.* (see p.vii) and *Int.*, which specify the dihydrate (C₂₂H₂₄N₂O₉·2H₂O = 496.5); *US* allows the anhydrous substance or the dihydrate.

Ph. Eur. 6.2 (Oxytetracycline Dihydrate). A substance produced by the growth of certain strains of *Streptomyces rimosus* or obtained by any other means. A yellow, crystalline powder. Very slightly soluble in water; dissolves in dilute acid and alkaline solutions. A 1% suspension in water has a pH of 4.5 to 7.5. Store in airtight containers. Protect from light.

USP 31 (Oxytetracycline). A pale yellow to tan, odourless crystalline powder, that darkens on exposure to strong sunlight. Soluble 1 in 4150 of water, 1 in 66 of dehydrated alcohol, and 1 in 6250 of ether; sparingly soluble in alcohol; practically insoluble in chloroform; freely soluble in 3N hydrochloric acid and in alkaline solutions. pH of a 1% suspension in water is between 4.5 and 7.0. It loses potency in solutions of pH below 2 and is rapidly destroyed by alkali hydroxide solutions. Store in airtight containers. Protect from light.

Oxytetracycline Calcium (BANM, rINN)

Calcii Oxytetracyclinum; Oxitetraciclina cálcica; Oxytétracycline Calcique.

Кальций Окситетрациклин

C₄₄H₄₆CaN₂O₁₈ = 958.9.

CAS = 15251-48-6 (x·Ca).

ATC = D06AA03; G01AA07; J01AA06; S01AA04.

ATC Vet = QD06AA03; QG01AA07; QJ01AA06; QS01AA04.

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

BP 2008 (Oxytetracycline Calcium). A pale yellow to greenish-fawn, crystalline powder. Practically insoluble in water; soluble in dilute acids; dissolves slowly in dilute ammonia solution. A 2.5% suspension in water has a pH of 6.0 to 7.5. Store at a temperature of 2° to 8°. Protect from light.

USP 31 (Oxytetracycline Calcium). A yellow to light brown crystalline powder. Insoluble in water; soluble 1 in more than 1000 of alcohol, of chloroform, and of ether, and 1 in 15 of 0.1N sodium hydroxide. pH of a 2.5% suspension in water is between 6.0 and 8.0. Store in airtight containers at a temperature between 8° and 15°. Protect from light.

Oxytetracycline Hydrochloride (BANM, rINN)

Hidrocloruro de oxitetraciclina; Oksitetrasiklino hidrochloridas; Oksitetrasiklin Hidroklorür; Oksitetrasikliinihidrokloridi; Oksytetracyklini chlorowodorek; Oksitetrasiklin-hidroklorid; Oksytetracyklinhidroklorid; Oxytétracycline, chlorhydrate d'; Oxytetracyclini hydrochloridum; Oxytetracyclin-hydrochlorid.

Окситетрациклина Гидрохлорид

C₂₂H₂₄N₂O₉·HCl = 496.9.

CAS = 2058-46-0.

ATC = D06AA03; G01AA07; J01AA06; S01AA04.

ATC Vet = QD06AA03; QG01AA07; QJ01AA06; QS01AA04.

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

Ph. Eur. 6.2 (Oxytetracycline Hydrochloride). A yellow, hygroscopic, crystalline powder. Freely soluble in water; sparingly soluble in alcohol. Solutions in water become turbid on standing owing to the precipitation of oxytetracycline. A 1% solution in water has a pH of 2.3 to 2.9. Store in airtight containers. Protect from light.

USP 31 (Oxytetracycline Hydrochloride). A yellow, odourless, hygroscopic, crystalline powder. It decomposes at temperatures exceeding 180°, and exposure to strong sunlight or temperatures exceeding 90° in moist air causes it to darken. Its potency is diminished in solutions having a pH below 2, and it is rapidly destroyed by alkali hydroxide solutions. Freely soluble in water, but crystals of oxytetracycline separate as a result of partial hydrolysis of the hydrochloride; sparingly soluble in alcohol and in methyl alcohol, and even less soluble in dehydrated alcohol; insoluble in chloroform and in ether. pH of a 1% solution in water is between 2.0 and 3.0. Store in airtight containers. Protect from light.

Incompatibility. Oxytetracycline injections have an acid pH and incompatibility may reasonably be expected with alkaline preparations, or with drugs unstable at low pH. Tetracyclines can chelate metal cations to produce insoluble complexes, and incompatibility has been reported with solutions containing metallic salts.

Reports of incompatibility are not always consistent, and other factors, such as the strength and composition of the vehicles used, may play a role.

Adverse Effects and Precautions

As for Tetracycline, p.347.

Oxytetracycline may produce less tooth discoloration than some other tetracyclines but gastrointestinal symptoms tend to be more severe.

Porphyria. For the suggestion that oxytetracycline might be porphyrinogenic, see under Tetracycline, p.348.