the patients. Ichthyotic changes were reported in 66.7% and pruritus in 20.2%. Gastrointestinal symptoms occurred in 20 patients (about 4%); other effects such as discoloration of sweat, urine, and tears were minor.[2]

1. Moore VJ. A review of side-effects experienced by patients taking clofazimine. *Lepr Rev* 1983; **54:** 327–35.
2. Kumar B, *et al*. More about clofazimine—3 years experience and review of the literature. *Indian J Lepr* 1987; **59:** 63–74.

Effects on the eyes. Accumulation of clofazimine crystals in the eye can lead to pigmentation of the cornea and conjunctiva. Degeneration of the retinal pigment epithelium has also been attributed to clofazimine therapy in a patient.[1] Slight repigmentation was observed after withdrawal of clofazimine.

1. Forster DJ, *et al*. Bull's eye retinopathy and clofazimine. *Ann Intern Med* 1992; **116:** 876–7.

Effects on the gastrointestinal tract. Gastrointestinal effects are uncommon at doses of clofazimine less than 100 mg daily. However, there have been some reports of severe gastrointestinal adverse events, including fatalities, in patients taking clofazimine.[1-4] An 11-year-old child given clofazimine (150 mg daily) for graft-versus-host disease developed severe enteropathy 2 years after starting treatment.[1] Clofazimine was stopped and symptoms resolved after 5 weeks. Enteropathy has also been reported in a 20-year-old patient who had taken 200 mg of clofazimine daily for 4 years.[2] Clofazimine was stopped but his symptoms did not resolve; he developed peripheral oedema and hypoalbuminaemia and died 2 years later due to cerebral thrombosis. In another report,[4] partial intestinal obstruction developed in a patient after 12 months of treatment with clofazimine 100 mg daily for the treatment of multidrug-resistant tuberculosis. The patient recovered 3 weeks after stopping clofazimine. Splenic infarction has been reported after 11 months treatment with high-dose clofazimine for the management of pyoderma gangrenosum.[5] Chronic abdominal pain due to crystal-storing histiocytosis of mesenteric lymph nodes is well recognised, and may mimic the symptoms of gastrointestinal lymphoma or myeloma.[3]

1. Parizhskaya M, *et al*. Clofazimine enteropathy in a pediatric bone marrow transplant recipient. *J Pediatr* 2001; **138:** 574–6.
2. Hameed A, *et al*. A case of clofazimine enteropathy. *Int J Clin Pract* 1998; **52:** 439–40.
3. Sukpanichnant S, *et al*. Clofazimine-induced crystal-storing histiocytosis producing chronic abdominal pain in a leprosy patient. *Am J Surg Pathol* 2000; **24:** 129–35.
4. Üsküdar O, *et al*. Partial intestinal obstruction due to clofazimine in a patient with multidrug-resistant tuberculosis. *Int J Tuberc Lung Dis* 2005; **9:** 703–4.
5. McDougall AC, *et al*. Splenic infarction and tissue accumulation of crystals associated with the use of clofazimine (Lamprene; B663) in the treatment of pyoderma gangrenosum. *Br J Dermatol* 1980; **102:** 227–30.

Effects on the heart. Ventricular tachycardia, thought to be probably torsade de pointes, was reported to be associated with clofazimine.[1]

1. Choudhri SH, *et al*. Clofazimine induced cardiotoxicity—a case report. *Lepr Rev* 1995; **66:** 63–8.

Precautions

Clofazimine should be used with caution in patients with gastrointestinal symptoms such as abdominal pain and diarrhoea. If gastrointestinal symptoms develop during treatment, the dose should be reduced and, if necessary, the interval between doses increased, or the drug should be stopped. Daily doses of more than 100 mg should not be used for more than 3 months because of dose-related adverse effects on the gastrointestinal tract; patients receiving doses greater than 100 mg daily should be under medical supervision.

Patients should be warned that clofazimine may cause a reddish-brown discoloration of breast milk, hair, skin, conjunctiva, tears, sputum, sweat, urine, and faeces. Nails may be discoloured at higher doses.

As clofazimine crosses the placental barrier, neonates of women receiving clofazimine may have skin discoloration at birth.

Breast feeding. The American Academy of Pediatrics[1] considers that the use of clofazimine by mothers during breast feeding may be of concern, since there is the possibility of transfer of a high percentage of the maternal dose and a possible increase in skin pigmentation in the infant. A small study in 8 women calculated that up to 30% of a maternal dose may be ingested by a breast-fed infant.[2]

1. 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 03/10/07)
2. Venkatesan K, *et al*. Excretion of clofazimine in human milk in leprosy patients. *Lepr Rev* 1997; **68:** 242–6.

Pregnancy. Two successful pregnancies in women who received clofazimine throughout pregnancy have been reported[1] but a literature review revealed 3 neonatal deaths in 13 pregnancies, although the deaths could not be directly attributed to clofazimine. However, WHO[2] states that its recommended multiple drug therapy regimens for leprosy, which may include clofazimine, are safe during pregnancy.

1. Farb H, *et al*. Clofazimine in pregnancy complicated by leprosy. *Obstet Gynecol* 1982; **59:** 122–3.
2. WHO. *Guide to eliminate leprosy as a public health problem*. 1st ed. Geneva: WHO, 2000. Also available at: http://www.who.int/lep/resources/Guide_Int_E.pdf (accessed 28/07/08)

Interactions

Some preliminary data have suggested that the anti-inflammatory action of clofazimine in Type 2 lepra reactions may be reduced by dapsone, although US licensed product information (*Lamprene; Novartis, USA*) states that these findings have not been confirmed; the antimycobacterial effect was not affected.

Elevated plasma and urine concentrations of clofazimine have been detected in patients receiving high doses of clofazimine with isoniazid, although skin concentrations were found to be lower.

For a report of the effect of clofazimine on rifampicin absorption, see p.327.

Antimicrobial Action

Clofazimine is bacteriostatic and weakly bactericidal against *Mycobacterium leprae*. Tissue antimicrobial activity in humans cannot be found until after about 50 days of therapy. Clofazimine is active *in vitro* against various other species of *Mycobacterium*. Resistance has been reported rarely and no cross-resistance occurs with rifampicin or dapsone.

Pharmacokinetics

Clofazimine is absorbed from the gastrointestinal tract in amounts varying from 45 to 70%. Absorption is greatest when clofazimine is given in microcrystalline formulations and when it is taken immediately after food. The time to steady-state plasma concentrations has not been determined but exceeds 42 days.

Average plasma concentrations in leprosy patients receiving 100 or 300 mg daily are reported as 0.7 micrograms/mL and 1.0 microgram/mL, respectively.

Because of its lipophilic nature, clofazimine is mainly distributed to fatty tissue and reticuloendothelial cells, including macrophages. Clofazimine is distributed to most organs and tissues and into breast milk; it crosses the placenta but not the blood-brain barrier.

The tissue half-life after a single dose has been reported to be about 10 days; that after multiple oral doses has been variously estimated to be between 25 and 90 days. Clofazimine accumulates in the body and is largely excreted unchanged in the faeces, both as unabsorbed drug and via biliary excretion. About 1% of the dose is excreted in 24 hours in the urine as unchanged clofazimine and metabolites. A small amount of clofazimine is also excreted through sebaceous and sweat glands, and in sputum.

◊ References.

1. Holdiness MR. Clinical pharmacokinetics of clofazimine: a review. *Clin Pharmacokinet* 1989; **16:** 74–85.

Uses and Administration

Clofazimine is an antimycobacterial and is used as part of multidrug regimens for the treatment of multibacillary leprosy (p.176). It has anti-inflammatory properties and has been given in chronic Type 2 lepra reactions (erythema nodosum leprosum) and in a variety of skin disorders.

Clofazimine is given orally with, or immediately after, food or milk for optimum absorption.

For multibacillary leprosy the most common regimen is that recommended by WHO, in which rifampicin 600 mg and clofazimine 300 mg are both given *once a month*, together with *daily* doses of clofazimine 50 mg and dapsone 100 mg; this treatment continues for 12 months.

For details of doses in children, see below.

Clofazimine 50 mg daily is given with ofloxacin and minocycline in patients unable to take rifampicin. Clofazimine is not usually given in paucibacillary leprosy. However, it may be used with rifampicin instead of dapsone when the latter has caused severe toxicity.

Clofazimine has been used in the treatment of chronic Type 2 lepra reactions, although the effect may not be evident for 4 to 6 weeks. A dose of up to 300 mg daily has been suggested but it should not be given for longer than 3 months. Corticosteroids may be given with clofazimine, and standard antileprosy treatment should be continued. Clofazimine is not used in Type 1 lepra reactions.

Administration in children. For the treatment of multibacillary leprosy in children WHO recommends that children aged 10 to 14 years may be given oral clofazimine 150 mg plus rifampicin 450 mg and dapsone 50 mg *once a month*, together with dapsone 50 mg *daily* and clofazimine 50 mg on *alternate days*. For children less than 10 years of age the dose should be adjusted according to body weight. As for adults, treatment is given for 12 months.

Preparations

BP 2008: Clofazimine Capsules;
USP 31: Clofazimine Capsules.

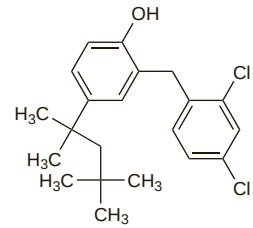
Proprietary Preparations (details are given in Part 3)
Austral.: Lamprene; ***Braz.:*** Neozimina; ***Cz.:*** Lamprene; ***Fr.:*** Lamprene; ***Gr.:*** Lamprene; ***Hong Kong:*** Lamprene†; ***India:*** Clofozine; Hansepran; ***Jpn:*** Lampren; ***Malaysia:*** Lamprene†; ***Neth.:*** Lampren; ***NZ:*** Lamprene; ***S.Afr.:*** Lamprene†; ***Spain:*** Lampren; ***Switz.:*** Lamprene†; ***Thai.:*** Lamcoin; ***UK:*** Lamprene†; ***USA:*** Lamprene.

Clofoctol *(rINN)*

Clofoctolum. 2-(2,4-Dichlorobenzyl)-4-(1,1,3,3-tetramethylbutyl)phenol.

Клофоктол

$C_{21}H_{26}Cl_2O$ = 365.3.
CAS — 37693-01-9.
ATC — J01XX03.
ATC Vet — QJ01XX03.



Profile

Clofoctol has bacteriostatic or bactericidal activity against Gram-positive organisms such as staphylococci and streptococci. It is given in doses of 750 mg twice daily rectally in the treatment of respiratory-tract infections.

Preparations

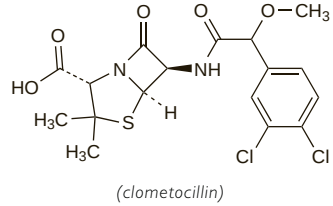
Proprietary Preparations (details are given in Part 3)
Fr.: Octofene†; ***Ital.:*** Gramplus; Octofene†; ***Port.:*** Octofene†.

Clometocillin Potassium *(rINNM)*

Clometocilina potásica; Clométocilline Potassique; 3,4-Dichloro-α-methoxybenzylpenicillin Potassium; Kalii Clometocillinum; Penicillin 356 (clometocillin). Potassium (6*R*)-6-[2-(3,4-dichlorophenyl)-2-methoxyacetamido]penicillanate.

Калия Клометоциллин

$C_{17}H_{17}Cl_2KN_2O_5S$ = 471.4.
CAS — 1926-49-4 (clometocillin); 15433-28-0 (clometocillin potassium).
ATC — J01CE07.
ATC Vet — QJ01CE07.



(clometocillin)

Profile

Clometocillin is a penicillin given orally as the potassium salt in the treatment of susceptible bacterial infections. Doses are ex-