3. D'Alessandro AM, *et al.* Successful treatment of severe cytomegalovirus infections with ganciclovir and CMV hyperimmune globulin in liver transplant recipients. *Transplant Proc* 1989; **21:** 3560–1.
4. Salmela K, *et al.* Ganciclovir in the treatment of severe cytomegalovirus disease in liver transplant patients. *Transplant Proc* 1990; **22:** 238–40.
5. Emanuel D, *et al.* Cytomegalovirus pneumonia after bone marrow transplantation successfully treated with the combination of ganciclovir and high-dose intravenous immune globulin. *Ann Intern Med* 1988; **109:** 777–82.
6. Studies of Ocular Complications of AIDS Research Group, in Collaboration with the AIDS Clinical Trials Group. Combination foscarnet and ganciclovir therapy vs monotherapy for the treatment of relapsed cytomegalovirus retinitis in patients with AIDS: the Cytomegalovirus Retreatment Trial. *Arch Ophthalmol* 1996; **114:** 23–33.
7. Mylonakis E, *et al.* Combination antiviral therapy for ganciclovir-resistant cytomegalovirus infection in solid-organ transplant recipients. *Clin Infect Dis* 2002; **34:** 1337–41.
8. Anand R, *et al.* Control of cytomegalovirus retinitis using sustained release of intraocular gancyclovir. *Arch Ophthalmol* 1993; **111:** 223–7.
9. Martin DF, *et al.* Treatment of cytomegalovirus retinitis with an intraocular sustained-release ganciclovir implant: a randomized controlled clinical trial. *Arch Ophthalmol* 1994; **112:** 1531–9.
10. Musch DC, *et al.* Treatment of cytomegalovirus retinitis with a sustained-release ganciclovir implant. *N Engl J Med* 1997; **337:** 83–90.
11. Ausayakhun S, *et al.* Treatment of cytomegalovirus retinitis in AIDS patients with intravitreal ganciclovir. *J Med Assoc Thai* 2005; **88** (suppl 9): S15–S20.
12. Velez G, *et al.* High-dose intravitreal ganciclovir and foscarnet for cytomegalovirus retinitis. *Am J Ophthalmol* 2001; **131:** 396–7.
13. Martin DF, *et al.* Oral ganciclovir for patients with cytomegalovirus retinitis treated with a ganciclovir implant. *N Engl J Med* 1999; **340:** 1063–70.
14. Lalezari JP, *et al.* High dose oral ganciclovir treatment for cytomegalovirus retinitis. *J Clin Virol* 2002; **24:** 67–77.
15. Goodrich JM, *et al.* Ganciclovir prophylaxis to prevent cytomegalovirus disease after allogeneic marrow transplant. *Ann Intern Med* 1993; **118:** 173–8.
16. Winston DJ, *et al.* Ganciclovir prophylaxis of cytomegalovirus infection and disease in allogeneic bone marrow transplant recipients. *Ann Intern Med* 1993; **118:** 179–84.
17. Hibberd PL, *et al.* Preemptive ganciclovir therapy to prevent cytomegalovirus disease in cytomegalovirus antibody-positive renal transplant recipients: a randomized controlled trial. *Ann Intern Med* 1995; **123:** 18–26.
18. Winston DJ, *et al.* Randomised comparison of ganciclovir and high-dose acyclovir for long-term cytomegalovirus prophylaxis in liver-transplant recipients. *Lancet* 1995; **346:** 69–74.
19. Gane E, *et al.* Randomised trial of efficacy and safety of oral ganciclovir in the prevention of cytomegalovirus disease in liver-transplant recipients. *Lancet* 1997; **350:** 1729–33.
20. Singh N. Preemptive therapy versus universal prophylaxis with ganciclovir for cytomegalovirus in solid organ transplant recipients. *Clin Infect Dis* 2001; **32:** 742–51.
21. Paya CV, *et al.* Preemptive use of oral ganciclovir to prevent cytomegalovirus infection in liver transplant patients: a randomized, placebo-controlled trial. *J Infect Dis* 2002; **185:** 854–60.
22. Keven K, *et al.* Cytomegalovirus prophylaxis using oral ganciclovir or valganciclovir in kidney and pancreas-kidney transplantation under antibody preconditioning. *Transplant Proc* 2004; **36:** 3107–12.
23. Monforte V, *et al.* Preemptive therapy with intravenous ganciclovir for the prevention of cytomegalovirus disease in lung transplant recipients. *Transplant Proc* 2005; **37:** 4039–42.
24. McCarthy M. Oral ganciclovir fails to prevent CMV in HIV trial. *Lancet* 1995; **346:** 895.
25. Spector SA, *et al.* Oral ganciclovir for the prevention of cytomegalovirus disease in persons with AIDS. *N Engl J Med* 1996; **334:** 1491–7.
26. Michaels MG, *et al.* Treatment of children with congenital cytomegalovirus infection with ganciclovir. *Pediatr Infect Dis J* 2003; **22:** 504–8.
27. Kimberlin DW, *et al.* Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involving the central nervous system: a randomized, controlled trial. *J Pediatr* 2003; **143:** 16–25.

Epstein-Barr virus infections. There have been anecdotal reports[1-4] of some improvement in patients with Epstein-Barr virus (EBV) infection given ganciclovir, although no antiviral therapy is entirely satisfactory (p.854).

1. Pirsch JD, *et al.* Treatment of severe Epstein-Barr virus-induced lymphoproliferative syndrome with ganciclovir: two cases after solid organ transplantation. *Am J Med* 1989; **86:** 241–4.
2. Ishida Y, *et al.* Ganciclovir for chronic active Epstein-Barr virus infection. *Lancet* 1993; **341:** 560–1.
3. MacGinley R, *et al.* Epstein-Barr virus encephalitis in a renal allograft recipient diagnosed by polymerase chain reaction on cerebrospinal fluid and successfully treated with ganciclovir. *Nephrol Dial Transplant* 2001; **16:** 197–8.
4. Adams LA, *et al.* Ganciclovir and the treatment of Epstein-Barr virus hepatitis. *J Gastroenterol Hepatol* 2006; **21:** 1758–60.

Herpesvirus infections. Ganciclovir 0.15% gel is licensed in a number of countries for the treatment of superficial ocular infections with herpes simplex. In patients with herpes simplex keratitis it has been reported to be as effective as aciclovir 3% ointment,[1] the drug most commonly used in this infection (see Ocular Herpes Simplex Infections, p.854).

1. Hoh HB, *et al.* Randomised trial of ganciclovir and acyclovir in the treatment of herpes simplex dendritic keratitis: a multicentre study. *Br J Ophthalmol* 1996; **80:** 140–3.

Preparations

USP 31: Ganciclovir for Injection; Ganciclovir Oral Suspension.

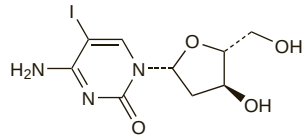
Proprietary Preparations (details are given in Part 3)
Arg.: Cigan clor; Cymevene; Cytovene†; Gasmilen; Grinevel; Virgan; ***Austral.:*** Cymevene; Vitrasert†; ***Austria:*** Cymevene; ***Belg.:*** Cymevene; Virgan; ***Braz.:*** Cymevene; Gancivir†; Ganvirax; ***Canad.:*** Cytovene; ***Chile:*** Cymevene; ***Cz.:*** Cymevene; Virgan; ***Denm.:*** Cymevene; ***Fin.:*** Cymevene; ***Fr.:*** Cymevan; Virgan; ***Ger.:*** Cymeven; ***Gr.:*** Cymevene; ***Hong Kong:*** Cymevene; ***Hung.:*** Cymevene; ***Indon.:*** Cymevene; ***Irl.:*** Cymevene; ***Israel:*** Cymevene; ***Ital.:*** Citovirax; Cymevene; ***Mex.:*** Cymevene; ***Neth.:*** Cymevene; ***Norw.:*** Cymevene; ***NZ:*** Cymevene; ***Philipp.:*** Cymevene; Virgan; ***Pol.:*** Cymevene; Virgan; ***Port.:*** Cymevene; Virgan; ***S.Afr.:*** Cymevene; ***Singapore:*** Cymevene; ***Spain:*** Cymevene; Vitrasert†; ***Swed.:*** Cymevene; ***Switz.:*** Cymevene; ***Thai.:*** Cymevene; ***Turk.:*** Cymevene; ***UK:*** Cymevene; Virgan†; ***USA:*** Cytovene; Vitrasert; ***Venez.:*** Cymevene.

Ibacitabine *(rINN)*

Ibacitabina; Ibacitabinum; Iododesoxycytidine. 2′-Deoxy-5-iodocytidine.

Ибацитабин

$C_9H_{12}IN_3O_4$ = 353.1.
CAS — 611-53-0.
ATC — D06BB08.
ATC Vet — QD06BB08.



Profile

Ibacitabine is an antiviral used topically as a 1% gel in the treatment of herpes labialis (p.854).

Preparations

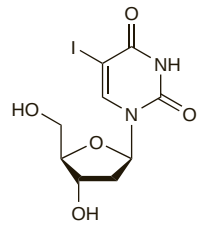
Proprietary Preparations (details are given in Part 3)
Fr.: Cuterpes.

Idoxuridine *(BAN, USAN, rINN)*

Allergan 211; GF-115; Idoksuridiini; Idoksuridinas; Idoxuridin; Idoxuridina; Idoxuridinum; IDU; 5-IDUR; 5-IUDR; NSC-39661; SKF-14287. 2′-Deoxy-5-iodouridine.

Идоксуридин

$C_9H_{11}IN_2O_5$ = 354.1.
CAS — 54-42-2.
ATC — D06BB01; J05AB02; S01AD01.
ATC Vet — QD06BB01; QJ05AB02; QS01AD01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Idoxuridine). A white or almost white crystalline powder. M.p. about 180°, with decomposition. Slightly soluble in water and in alcohol; dissolves in dilute solutions of alkali hydroxides. A 0.1% solution in water has a pH of 5.5 to 6.5. Protect from light.
USP 31 (Idoxuridine). A white, practically odourless, crystalline powder. Slightly soluble in water and in alcohol; practically insoluble in chloroform and in ether. Store in airtight containers. Protect from light.

Stability. Iodine vapour is liberated on heating idoxuridine. It has been reported that some decomposition products such as iodouracil are more toxic than idoxuridine and reduce its antiviral activity.

Adverse Effects

Hypersensitivity reactions such as irritation, pain, and pruritus may occur occasionally when idoxuridine is applied to the eyes. Other adverse effects include stinging, conjunctivitis, oedema and inflammation of the eye or eyelids, photophobia, pruritus, and rarely, occlusion of the lachrymal duct. Prolonged or excessive use may damage the cornea.

Idoxuridine applied to the skin may produce irritation, stinging, and hypersensitivity reactions. Taste disturbance may also occur. Excessive application of topical idoxuridine to the skin may cause skin maceration.

Idoxuridine is a potential carcinogen and teratogen.

Carcinogenicity. Squamous carcinoma has been reported in association with topical idoxuridine treatment.[1]

1. Koppang HS, Aas E. Squamous carcinoma induced by topical idoxuridine therapy? *Br J Dermatol* 1983; **108:** 501–3.

Precautions

Idoxuridine should be used with caution in conditions where there is deep ulceration involving the stromal layers of the cornea, as delayed healing has resulted in corneal perforation. Prolonged topical use should be avoided.

The potential teratogenicity of idoxuridine should be taken into account when treating pregnant patients or patients likely to become pregnant. Corticosteroids should be applied with caution in patients also receiving idoxuridine as they may accelerate the spread of viral infection.

Interactions

Preparations containing boric acid should not be applied to the eye in patients also receiving ocular preparations of idoxuridine as irritation ensues.

Antiviral Action

After intracellular phosphorylation to the triphosphate, idoxuridine is incorporated into viral DNA instead of thymidine so inhibiting replication of sensitive viral strains. Idoxuridine is also incorporated into mammalian DNA. Idoxuridine is active against herpes simplex and varicella zoster viruses. It has also been shown to inhibit vaccinia virus, CMV, and adenovirus.

Pharmacokinetics

Penetration of idoxuridine into the cornea and skin is reported to be poor. Idoxuridine is rapidly metabolised in the body to iodouracil, uracil, and iodide, which are excreted in the urine.

Uses and Administration

Idoxuridine is a pyrimidine nucleoside structurally related to thymidine. It is used topically in the treatment of herpes simplex keratitis and cutaneous infections with herpes simplex (p.854) and herpes zoster (see Varicella-zoster Infections, p.855), but has generally been superseded by other antivirals.

In the treatment of herpes simplex keratitis, idoxuridine is applied as a 0.1% ophthalmic solution or a 0.5% eye ointment.

Idoxuridine 5% in dimethyl sulfoxide (to aid absorption) may be painted onto the lesions of cutaneous herpes simplex and herpes zoster four times daily for 4 days.

Preparations

BP 2008: Idoxuridine Eye Drops;
USP 31: Idoxuridine Ophthalmic Ointment; Idoxuridine Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Idulea; ***Austral.:*** Herplex-D†; Stoxil; ***Belg.:*** Virexen†; ***Braz.:*** Herpesine; ***Canad.:*** Herplex; ***Ger.:*** Virunguent; Zostrum; ***Hung.:*** Oftan IDU†; ***India:*** Ridinox; ***Indon.:*** Isotic Ixodine; ***Irl.:*** Zostrum†; ***Israel:*** Virusan†; ***Ital.:*** Iducher; Idustatin; ***Malaysia:*** Virunguent†; ***Mex.:*** Idina†; ***Neth.:*** Virexen; ***NZ:*** Virasolve; ***Port.:*** Virexen†; Virunguent†; ***Rus.:*** Oftan IDU (Офтан ИДУ); ***Singapore:*** Virunguent; ***Spain:*** Virexen; ***Switz.:*** Iderpes†; Virunguent; ***UK:*** Herpid; ***Venez.:*** Herpidum†.

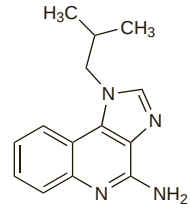
Multi-ingredient: ***Arg.:*** Itro†; ***Austral.:*** Virasolve; ***Ger.:*** Virunguent P†; ***Hong Kong:*** Virasolve†.

Imiquimod *(BAN, USAN, rINN)*

Imikimod; Imikimodi; Imiquimodum; R-837; S-26308. 4-Amino-1-isobutyl-1*H*-imidazo[4,5-*c*]quinoline.

Имихимод

$C_{14}H_{16}N_4$ = 240.3.
CAS — 99011-02-6.
ATC — D06BB10.
ATC Vet — QD06BB10.



Adverse Effects

Adverse effects after topical application of imiquimod include local skin erosion, erythema, excoriation, flaking, and oedema. There have been reports of localised hypopigmentation and hyperpigmentation. Skin reactions away from the site of application have been reported. Systemic effects after topical application include headache, flu-like symptoms, and myalgia.

Hypotension has occurred after repeated ingestion.

Hypersensitivity. Angioedema, initially of both the hands and feet and later the tongue, occurred in a 61-year-old man 3 weeks after starting treatment with a 5% imiquimod cream for squamous cell carcinoma *in situ* (Bowen's disease).[1]

1. Barton JC. Angioedema associated with imiquimod. *J Am Acad Dermatol* 2004; **51:** 477–8.

Uses and Administration

Imiquimod is an immune response modifier used topically in the treatment of external genital and perianal warts (p.1584), superficial basal cell carcinomas, and actinic keratoses (see below). For the treatment of genital and perianal **warts**, it is applied as a