Valganciclovir

Essential medicine status

Section: 6. Anti-infective medicines > 6.4. Antiviral medicines > 6.4.3. Other antivirals

EMLc | ATC codes: J05AB14

Indication	Cytomegaloviral retinitis ICD11 code: 9B72.00
INN	Valganciclovir
Medicine type	Chemical agent
List type	Core (EML) Complementary (EMLc)
Formulations	Oral > Liquid: 50 mg per mL powder for oral solution (EMLc) Oral > Solid > tablet: 450 mg
EML status history	First added in 2015 (TRS 994)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Valganciclovir
DrugBank	Valganciclovir

Summary of evidence and Expert Committee recommendations

An application was submitted by Dr Nathan Ford, WHO Department of HIV/AIDS, for the addition of valganciclovir to the Model List for the treatment of cytomegalovirus retinitis (CMVr), a preventable late-stage opportunistic infection in people living with HIV/AIDS. Comments in support of the application were received from Myriam Henkens, International Medical Coordinator, Medecins Sans Frontieres. CMVr is part of a systemic infection, although in HIV/AIDS patients in low- and middle-income countries, the eye is the only end-organ where the presence of clinical infection is easy to establish. Evidence from both before and after the introduction of highly active anti-retroviral therapy (HAART) in resource-rich and resource-poor settings has shown that CMV viraemia predicts mortality and, in most reports, is the most powerful predictor of mortality (1-4). Left untreated, CMVr can lead to permanent loss of vision as a result of damage to the optic nerve or macula, of retinal detachment (which can present years after CMVr has been treated) or of the development of immune recovery uveitis. Early diagnosis and treatment are crucial to preventing both vision loss and transmission of CMVr to the contralateral eye, which occurs within six months of infection in 50–61% of untreated CMVr cases (5). Estimates of the incidence and prevalence of CMVr in resource-limited settings vary. CMVr incidence ranges from 0 to 19.6% in sub-Saharan Africa (6), while estimated prevalence ranges from less than 5% in southern Africa to more than 30% in south-east Asia (7). Although the introduction and scaleup of HAART in developed countries has dramatically reduced the prevalence of CMVr in these settings, high ART accessibility does not correlate completely with reduced CMVr. Clinical guidelines first recommend that HIV/AIDS patients at risk for or recently diagnosed with CMVr have access to HAART, which slows progression of the condition (6). Treatment options for CMVr include intravenous ganciclovir, foscarnet, or cidofovir; ganciclovir implant; intravitreal injections of ganciclovir, foscarnet, cidofovir or fomivirsen; and oral valganciclovir or ganciclovir (8). Intravenous ganciclovir has been the gold standard for treatment of CMVr; however, this requires daily infusions and indwelling catheters, with attendant risks of secondary sepsis (6), and this treatment is not always feasible in resource-limited settings. Valganciclovir is an oral medication that has been shown to be therapeutically equivalent to intravenous ganciclovir in adults (9) and is recommended because of its lower cost, lower risk of adverse reactions, high efficacy and easy administration, and the fact

that it can be used for both induction and maintenance therapy (6). Oral valganciclovir is the standard of care in developed countries and has shown to reduce CMVr-related mortality even in patients failing HAART (10, 11). Induction treatment (900 mg twice a day for 21 days) is followed by maintenance treatment (900 mg once daily) until the following criteria are met: the retinitis has become inactive on retinal examination; the patient has been receiving ART for at least 3 months; and the CD4 count is above 100 cells/mm3. Valganciclovir is well tolerated; the most common adverse reactions reported included diarrhoea, nausea, fever, neutropenia and oral candidiasis (12). The Expert Committee acknowledged that CMV infection is an increasing concern in paediatric patients, with a high incidence of congenital CMV infections and a growing number of immunocompromised patients (13). The Committee considered that a clinical need exists for antiviral therapy to be available for paediatric patients with CMV infection. Data on the clinical efficacy of valganciclovir in the paediatric population are limited; however, several studies have shown that, in various paediatric dosing algorithms, combined with therapeutic drug monitoring to ensure exposure within the therapeutic window, valganciclovir might be used in anti-CMV treatment for neonates, infants and children (13-15). Following an agreement between Roche and the Medicines Patent Pool (August 2013), the price of valganciclovir for 138 developing countries was reduced to approximately US$ 275 for 60 tablets (15). Based on this, courses of 12 weeks (3 weeks induction, 9 weeks maintenance therapy) and 27 weeks (3 weeks induction, 24 weeks maintenance) will cost approximately US$ 907.20 and US$ 1814.40 respectively. With generic formulations available, prices are expected to decline further. The Expert Committee recommended addition of valganciclovir to the core list of the EML for treatment of cytomegalovirus retinitis. The Committee accepted that oral valganciclovir provides systemic effects equivalent to those of IV ganciclovir in both induction and maintenance treatment of CMVr. The Committee considered that valganciclovir, being an oral preparation, offered advantages over IV ganciclovir, particularly in resource-limited settings, in terms of price and ease of administration. In view of the clinical need for effective antiviral treatments for children, the Expert Committee also recommended that valganciclovir be added to the complementary list of the EMLc for the treatment of paediatric patients with CMVr. Inclusion on the complementary list was considered appropriate because of the need for therapeutic drug monitoring. References: 1. Wohl DA, Zeng D, Stewart P, Glomb N, Alcorn T, Jones S, et al. 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