(1) Does the application adequately address the issue of the public health need for the medicine?
   Yes X

There remains a significant burden of HIV-related cytomegalovirus retinitis in adults living in middle and low-income countries. CMV retinitis is by far the most common intraocular infection in patients whose immune system has been suppressed due to AIDS.

Untreated CMV retinitis inexorably progresses to visual loss and blindness. The goal of treatment is to stabilize or restore vision and prevent blindness. Long-term treatment is often needed. Medications may be given by orally, intravenously, or by intravitreal injection. A number of different antiviral medications are available for the treatment of CMV retinitis. Since routes of delivery and adverse effect profiles vary significantly, treatment programs should be tailored to individual patients and their response to treatment.

(2) Have all important studies that you are aware of been included in the application?
   Yes X

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?
   Yes X

Valganciclovir is a prodrug of ganciclovir. It possesses excellent oral bioavailability and antiviral activity. It has been shown to be effective in both the induction phase \[1\] and the maintenance phase \[2\] of CMV retinitis treatment. It is available in convenient once daily or twice daily dosing. It achieves levels comparable to those obtained with IV ganciclovir.

Valganciclovir has largely replaced other treatments since it avoids the need for frequent intravenous infusions and long-term intravenous access ports.
(4) Is there evidence of efficacy in diverse settings and/or populations?

No  X

Oral valganciclovir will provide a form of treatment that will be far more effective at reaching all patients in need.

(5) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?

Yes  X

There is a risk of cytopenias and thus valganciclovir should not be administered if absolute neutrophil count is < 500 cells/μl, platelet count is < 25,000/μl, or hemoglobin is < 8 g/dl. Filgrastim (granulocyte colony stimulating factor) can be used in conjunction with valganciclovir in patients experiencing neutropenia. It is Pregnancy Category C and women of childbearing age should use contraception while using valganciclovir. Valganciclovir is contraindicated in patients with hypersensitivity to ganciclovir. It has less renal toxicity than foscarnet and cidofovir which have become second-line treatments.

ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?

No  X

It is an oral administration of valganciclovir tablets so it does not require the training and specialization needed for other therapy regimens (e.g., intravitreal injections, etc.). This is a benefit given that resource-limited settings often lack access to trained ophthalmic providers.

At this time, primary treatment generally consists of induction with valganciclovir (900 mg orally twice a day for 2-3 wk) followed by maintenance with valganciclovir (900 mg orally once a day) until the CD4 count is above 100 cells/ml.

(7) Are there any issues regarding the registration of the medicine by regulatory authorities? (e.g., recent registration, new indications, off-label use)

Yes  X

Two new generics, both from India, were approved on November 4th 2014 by the US FDA since the original Valganciclovir HCl 450 mg tablet (Valcyte® by Hoffmann-la Roche) was approved on March 29th 2001, NDA # 021304. Valganciclovir HCl, 450 mg tablet, by Dr Reddys, ANDA # 200790 and Valganciclovir HCl, 450 mg tablet, by Endo Pharmaceuticals, ANDA # 203511
(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?

No  X

Not yet

(9) Please comment briefly on issues regarding cost and affordability of this medicine.

With the introduction of several generics into the market as is happening now, the cost of valganciclovir is expected to drop significantly.

(10) Any additional comments?

Highly active antiretroviral therapy has altered the long-term management of CMV retinitis. Because the antiviral medications used to treat CMV are virustatic, patients needed to continue their use for the rest of their lives. The advent of HAART, with consequent recovery of immune function (2 consecutive CD4+ T-cell counts of ≥ 100 cells/μl at least 6 mo apart) allows individuals to discontinue their CMV therapy if the retinitis has resolved adequately with antiviral treatment. As long as the CD4 count remains elevated, little risk exists of disease recurrence. Careful monitoring of both immune status and ophthalmic findings are necessary to prevent retinal damage from an asymptomatic recurrence.

(11) Please summarise the action you propose the Expert Committee takes.

I will recommend the addition of VALGANCICLOVIR HCl oral administration (450mg tablet) to the EML for the treatment of HIV related cytomegalovirus retinitis.
