References

1. Centers for Disease Control and Prevention. Apparent global interruption of wild poliovirus type 2 transmission. MMWR Morb Mortal Wkly Rep **2001**; 50:222.
2. Centers for Disease Control and Prevention. Public health dispatch: outbreak of poliomyelitis—Dominican Republic and Haiti, 2000. MMWR Morb Mortal Wkly Rep **2000**; 49: 1094.

VALGANCICLOVIR, A MORE POTENT ORAL THERAPY FOR CMV RETINITIS IN AIDS, APPROVED BY FDA

30 March (icanNEWS)—The US Food and Drug Administration (FDA) approved valganciclovir (Valcyte; Hoffman–La Roche [Roche]), a more potent oral therapy for the treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS), yesterday.

According to a press release, Roche expects valganciclovir will soon replace its currently used ganciclovir (Cytovene) for treatment of CMV retinitis in AIDS patients "because it offers comparable efficacy in a much more convenient dosing regimen for induction therapy."

The FDA notes in antiviral committee–briefing documents that the development of valganciclovir coincided with introduction of highly active antiretroviral therapy (HAART), which has decreased the prevalence of opportunistic infections like CMV. "However, based upon the public health need for a potent oral therapy for treatment of CMV disease," the FDA valganciclovir review team encouraged Roche to continue the development of valganciclovir, although both the FDA and the firm recognized that the study "would be significantly underpowered to demonstrate equivalence."

According to FDA briefing information, Roche submitted results from 2 clinical studies as well as several pharmacokinetic studies. One open-label trial enrolled 160 patients with newly diagnosed CMV retinitis (24% of patients in each treatment arm had zone 1 retinitis) who were randomly assigned to receive either induction therapy with iv ganciclovir or induction therapy with oral valganciclovir. After week 4, all patients in the study received valganciclovir maintenance therapy.

Seven patients in each treatment arm had progression of retinitis after 4 weeks, as determined by a masked ophthalmology reviewer. FDA briefing information points out that the mean time to progression of CMV retinitis was substantially longer in both treatment arms than the times observed in studies before the introduction of HAART.

In April 1998, Roche began a second study to evaluate valganciclovir for the maintenance treatment of CMV retinitis. According to FDA briefing information, the study provided primarily additional data to support the safety profile of valganciclovir in AIDS patients.

In clinical studies, adverse events included low blood-cell counts (granulocytopenia [27%], anemia [26%], and thrombocytopenia [6%]), diarrhea (41%), nausea (30%), vomiting (21%), abdominal pain (15%), fever (31%), headache (22%), insomnia (16%), peripheral neuropathy (9%), paresthesia (8%), and retinal detachment (15%). According to the FDA briefing information, valganciclovir's safety profile was similar to ganciclovir's, with the exception of a higher incidence of anemia among patients receiving valganciclovir than among patients receiving iv ganciclovir for induction therapy.

Valganciclovir was approved for both induction and maintenance therapy. For patients with active CMV retinitis, the recommended induction dose is two 450-mg tablets twice a day for 21 days, according to a Roche press release. After induction treatment, or for patients with inactive CMV retinitis who require maintenance therapy, the recommended dose is two 450-mg tablets once a day. The product is expected to be available in pharmacies in late spring 2001.

Valganciclovir is a prodrug of ganciclovir, with 10-fold increased bioavailability compared with the oral formulation of ganciclovir. According to a Roche press release, "two 450mg Valcyte tablets one or two times daily achieved systemic exposure of ganciclovir comparable to that achieved with the recommended doses of intravenous Cytovene of 5mg/kg once or twice daily, respectively."