IV Acyclovir Shortage Frequently Asked Questions

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When will the shortage be resolved?

There is currently no estimate for a shortage resolution date; the ASHP drug shortages page has updated shortage and resolution information: https://www.ashp.org/Drug-Shortages/Current-Shortages/Drug-Shortage-Deta... [1]

Do we have any supply of IV acyclovir? Can we get any more?

Pharmaceutical services has a small supply of IV acyclovir, reserved for patients in whom alternatives are not appropriate. The manufacturers are only releasing limited supplies for patients in specific need, and it is not known how long this supply will last.

Is IV ganciclovir an appropriate alternative to IV acyclovir?

Ganciclovir has excellent *in vitro* activity against the viruses (HSV, VZV) that acyclovir is commonly used to treat. It is more potent (lower IC50) than acyclovir against HSV-1 and -2 and has similar potency against VZV. Ganciclovir obtains good levels in the eye and cerebrospinal fluid and has been effective for viral infections of the eye, brain, and meninges.

Ganciclovir’s use is limited by its toxicity, primarily neutropenia and thrombocytopenia. In clinical trials, 10-50% of patients experience these effects to some degree. HSCT and oncology patients appear to be at highest risk, followed by AIDS patients,
with solid organ transplant patients at lower risk. Hematologic effects have been reversible on drug discontinuation. These effects appear to relate to cumulative exposure, with most cases occurring during the second week of therapy, so short courses of ganciclovir for empiric therapy would likely pose little risk of substantial toxicity. In some instances administration of G-CSF has enabled continuation of therapy for patients experiencing neutropenia. Appropriate dosage reduction of ganciclovir for patients with renal dysfunction can also reduce the risk of hematologic toxicity.

Because of ganciclovir’s greater toxicity than acyclovir, there are few clinical studies of its use as a substitute for acyclovir for HSV or VZV disease. However, ganciclovir has shown to be effective across a wide variety of manifestations of CMV disease.

**How should I dose and administer IV ganciclovir?**

Dosing recommendations are provided in the UCSF Adult and Pediatric Dosing guidelines. Note that the doses recommended are induction doses to treat CMV disease. These doses probably are reasonable for patients requiring high-dose (10mg/kg q8h) IV acyclovir. For patients who would normally receive standard-dose IV acyclovir (5mg/kg q8h), lower doses (e.g. 5mg/kg daily instead of q12h) are probably reasonable.

**Is oral acyclovir an appropriate alternative to IV acyclovir?**

Oral acyclovir displays low absorption (only approximately 25% of the orally administered dose is absorbed). Thus, it is difficult to provide similar drug exposure to typical doses of IV acyclovir used for treatment of serious infections using oral acyclovir. For example, an 80-kg patient receiving 5mg/kg of IV acyclovir q8h would need about 800mg given every four hours of oral acyclovir. However, for less severe infections (cutaneous HSV infections in immunocompetent patients) oral acyclovir has shown to be very effective.
Oral acyclovir is frequently used for prophylaxis against viral infections in transplant recipients. For patients experiencing difficulty taking oral medications, administration of oral acyclovir in a liquid formulation may be more tolerable. If a patient absolutely cannot tolerate oral acyclovir and requires IV acyclovir, the dose of IV acyclovir should be appropriately reduced (about 25% of the total daily dose of PO acyclovir).

Is oral valacyclovir an appropriate alternative to IV acyclovir?

Valacyclovir is an orally administered prodrug of acyclovir with about twice the bioavailability (about 50% of the administered dose makes it into the blood as acyclovir). Therefore, similar exposures to standard-dose IV acyclovir regimens may be able to be achieved using valacyclovir, depending on patient characteristics. For example, an 80-kg patient receiving standard-dose (e.g. 5mg/kg) of IV acyclovir q8h would achieve similar exposures with a valacyclovir regimen of 1000mg PO TID. Thus, for patients with adequate GI absorption in whom standard doses of IV acyclovir would be used (e.g. not CNS or disseminated disease), valacyclovir may be a good alternative.

For patients requiring high-dose IV acyclovir (e.g. 10mg/kg IV q8h), some data suggests that similar levels can be achieved using doses of valacyclovir up to 2g PO QID. However, clinical data is limited for this dosing. For patients who require high-dose IV acyclovir and who rapidly respond to treatment, transition to high-dose PO valacyclovir may be appropriate, but consultation with ID or ID pharmacy is recommended.

Are foscarnet and cidofovir appropriate alternatives to IV acyclovir?

These drugs have substantial toxicity (nephrotoxicity and electrolyte disturbances) and are generally reserved for patients who are known or suspected to have resistance to acyclovir or ganciclovir. Consultation with ID or ID pharmacy is recommended if considering these agents.