



## **Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children**

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## Valganciclovir Dosing in Children

The U.S. Food and Drug Administration (FDA) is notifying healthcare professionals of new pediatric dosing recommendations for Valcyte (valganciclovir hydrochloride) oral tablets and oral solution. This change is being made to prevent potential valganciclovir overdosing in children with low body weight, low body surface area, and below normal serum creatinine. The revised dosing recommendations are being updated to include an upper limit on the calculated creatinine clearance using the modified Schwartz formula, which is used to calculate the pediatric dose of Valcyte. The FDA has determined that adding an upper limit of 150 mL/min/1.73 m<sup>2</sup> to the creatinine clearance calculated using the Schwartz formula for the determination of pediatric doses can help prevent the potential for Valcyte overdosing. If the calculated pediatric dose of Valcyte exceeds 900 mg, a dose of 900 mg should be given to the child.

The FDA notice is available on <http://www.fda.gov/Drugs/DrugSafety/ucm225727.htm#ds> and is provided below:

## FDA Drug Safety Communication: New dosing recommendations to prevent potential Valcyte (valganciclovir) overdose in pediatric transplant patients

### Safety Announcement

**[09-15-2010]** The U.S. Food and Drug Administration (FDA) is notifying healthcare professionals of new pediatric dosing recommendations for Valcyte (valganciclovir hydrochloride) oral tablets and oral solution. This change is being made to prevent potential valganciclovir overdosing in children with low body weight, low body surface area, and below normal serum creatinine.

The revised dosing recommendations are being updated to include an upper limit on the calculated creatinine clearance using the modified Schwartz formula, which is used to calculate the pediatric dose of Valcyte.

Valganciclovir is an antiviral medication that can be effective for the prevention of cytomegalovirus (CMV) disease in children 4 months to 16 years of age who have undergone a kidney or heart transplant. Cytomegalovirus is a member of a group of herpes-type viruses that can cause disease in different parts of the body.<sup>1</sup> Patients with weakened immune systems, such as organ transplant patients, are particularly susceptible to CMV infection and must take medications such as Valcyte to prevent the disease.

See the [Data Summary](#) for the new dosing recommendations for Valcyte.

### Additional Information for Patients

- Talk to your healthcare professional about any concerns with your Valcyte dose.
- The side effects from Valcyte overdosing include abdominal pain, vomiting, diarrhea, tremor or seizure.
- Report any side effects you experience to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

### Additional Information for Healthcare Professionals

- The dosing recommendations for Valcyte in children have changed. The dosing calculation can be found in the [Data Summary](#) and in the [drug label](#).
- Be aware of possible valganciclovir overdose in pediatric patients with low body weight, low body surface area, or below normal serum creatinine.
- When calculating the pediatric dose of Valcyte with the modified Schwartz formula, a maximum value of 150 mL/min/1.73 m<sup>2</sup> should be used in the formula.
- When the calculated pediatric dose of Valcyte exceeds 900 mg, a dose of 900 mg should be administered to the child.
- Advise patients to contact a healthcare professional immediately if they experience signs and symptoms of valganciclovir overdose while taking Valcyte.
- Report adverse events involving Valcyte to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

## Data Summary

Healthcare professionals should follow the updated pediatric dosing algorithm in the [Valcyte label](#).<sup>2</sup> The pediatric dose of Valcyte is based on body surface area (BSA) and creatinine clearance (CrCl) derived from a modified Schwartz formula. Under the previous dosing recommendations, pediatric patients with low body weight, low body surface area, and below normal serum creatinine could have a high calculated Schwartz creatinine clearance, resulting in a pediatric dose that approached the adult dose of 900 mg. This type of patient was not routinely observed in the clinical trials used to derive and confirm the pediatric dose, and may have been overdosed according to the previous dosing algorithm. As a result, FDA has updated the dosing algorithm so that when calculating the pediatric dose, a maximum value of 150 mL/min/1.73 m<sup>2</sup> should be used in the formula, even if the calculated Schwartz creatinine clearance exceeds 150 mL/min/1.73 m<sup>2</sup>. Furthermore, if the calculated Valcyte dose exceeds 900 mg, a dose of 900 mg should be given to the child.

The revised language in Section 2.3 of the label, *Pediatric Patients*, is as follows (new language underlined)<sup>2</sup>:

Prevention of CMV Disease: For pediatric patients 4 months to 16 years of age who have received a kidney or heart transplant, the recommended once daily dose of Valcyte starting within 10 days of transplantation until 100 days post-transplantation is based on body surface area (BSA) and creatinine clearance (CrCl) derived from a modified Schwartz formula, and is calculated using the equation below:

Pediatric Dose (mg) = 7 x BSA x CrCl (calculated using a modified Schwartz formula). If the calculated Schwartz creatinine clearance exceeds 150 mL/min/1.73 m<sup>2</sup>, then a maximum value of 150 mL/min/1.73m<sup>2</sup> should be used in the equation.

Mosteller BSA (m<sup>2</sup>) = Square root of Height (cm) x Weight (kg)

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Schwartz Creatinine Clearance (mL/min/1.73 m<sup>2</sup>) =  $\frac{k \times \text{Height (cm)}}{\text{Serum Creatinine (mg/dL)}}$

Where k =

0.45 for patients aged 4 months to < 1 year,

0.45 for patients aged 1 to < 2 years (note k value is 0.45 instead of the typical value of 0.55),

0.55 for boys aged 2 to < 13 years and girls aged 2 to 16 years, and

0.7 for boys aged 13 to 16 years.

In summary, the FDA has determined that adding an upper limit of 150 mL/min/1.73 m<sup>2</sup> to the creatinine clearance calculated using the Schwartz formula for the determination of pediatric doses can help prevent the potential for Valcyte overdosing. If the calculated pediatric dose of Valcyte exceeds 900 mg, a dose of 900 mg should be given to the child.

## References

1. MedLinePlus health topics page. U.S. National Library of Medicine Web site. <http://www.nlm.nih.gov/medlineplus/ency/article/000663.htm>. Accessed August 25, 2010.
2. [Updated Valcyte label](#)

## Related Information

- [Valcyte Label - 8/05/2010](#)
- [FDA issues new dosing guide for children using Valcyte](#)  
9/15/2010 - FDA Note To Correspondents
- [Valganciclovir \(marketed as Valcyte\) Information](#)

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- 1-800-FDA-0178 Fax

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