Genentech
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080

IMPORTANT PRESCRIBING INFORMATION

June 2015

Subject: Important Changes to the VALCYTE® (valganciclovir) Prescribing Information: Dosing and Administration: Pediatric patients, Adverse Events: Pediatrics

Dear Health Care Provider:

The purpose of this letter is to inform you of important new prescribing information that has been added to the Dosage and Administration and Adverse Reactions sections of the VALCYTE prescribing information. VALCYTE is indicated in adult patients for treatment of CMV retinitis in patients with acquired immunodeficiency syndrome (AIDS) and for prevention of CMV disease in kidney, heart, or kidney-pancreas transplant patients at high risk. VALCYTE is also indicated in pediatric patients for prevention of CMV disease in kidney and in heart transplant at high risk.

These important new additions to the VALCYTE prescribing information are:

DOSAGE AND ADMINISTRATION

New and revised information in the **Recommended Dosage in Pediatric Patients** to include the extension of duration of use in pediatric kidney transplant patients from 100 to 200 days post-transplantation and lowering the age for use in pediatric heart transplant patients from 4 months to 1 month of age.

Prevention of CMV Disease in Pediatric Kidney Transplant Patients: For pediatric kidney transplant patients 4 months to 16 years of age, the recommended once daily mg dose (7x BSA x CrCL) should start within 10 days of post-transplantation until 200 days post-transplantation.

Prevention of CMV Disease in Pediatric Heart Transplant Patients: For pediatric heart transplant patients 1 month to 16 years of age, the recommended once daily mg dose (7x BSA x CrCL) should start within 10 days of transplantation until 100 days post transplantation.

The pediatric dosage is calculated using a modified Schwartz formula.

New information for calculation of pediatric VALCYTE dosage includes the following:

1) presentation of k values (used in the modified Schwartz formula) by age in Table 1;
2) inclusion of a k value (0.33) for pediatric heart transplant patients less than 1 year of age with low birth weight for gestational age; and
3) a statement that k values may need to be corrected when enzymatic methods of measuring serum creatinine are used.

It is also stated that serum creatinine levels should be monitored regularly in consideration of changes in height and body weight of pediatric patients and to adapt the dose as appropriate during treatment.

Table 1. k Values According to Pediatric Patient Age*

k value	Pediatric Patient Age
0.33	Infants less than 1 year of age with low birth weight for gestational age
0.45	Infants less than 1 year of age with birth weight appropriate for gestational age
0.45	Children aged 1 to less than 2 years of age
0.55	Boys aged 2 to less than 13 years Girls aged 2 to less than 16 years
0.7	Boys aged 13 to 16 years

*The k values provided are based on the Jaffe method of measuring serum creatinine, and may require correction when enzymatic methods are used.

ADVERSE EVENTS, identified during pediatric clinical trials with VALCYTE, and which are similar to the known safety profile observed in adults, are provided:

- the most frequently reported adverse events (greater than 10% of patients), regardless of seriousness and drug relationship in pediatric solid organ transplant patients taking VALCYTE until Day 100 post-transplant were diarrhea, pyrexia, upper respiratory tract infection, hypertension, vomiting, anemia, neutropenia, constipation, nausea and transplant rejection.
- the most frequently reported adverse event (greater than 10% of patients), in pediatric kidney transplant patients treated with valganciclovir until Day 200 post-transplant were upper respiratory tract infection, urinary tract infection, diarrhea, leukopenia, neutropenia, headache, abdominal pain, dysuria, tremor, pyrexia, hypertension, anemia, blood creatinine increase, vomiting, *E. coli* urinary tract infection and hematuria.

Prescriber Action

Please see enclosed VALCYTE detailed prescribing information and safety profile in children and adults.

Counsel patients about the risks and benefits of VALCYTE, including:

- The new dosing requirements in pediatric heart and kidney transplant patients to ensure appropriate dosing.

Reporting Adverse Events

Health care providers are encouraged to report adverse events in patients taking VALCYTE to Genentech/ Roche at 1-888-835-2555. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

You may also contact our Medical Communications Department at 1-800-821-8590 if you have any questions about the information contained in this letter or the safe and effective use of VALCYTE.

This letter is not intended as a complete description of the benefits and risks related to the use of VALCYTE. Please refer to the enclosed full prescribing information and approved patient information.

For additional information, please contact Genentech Medical Communications at 1-800-821-8590 or visit www.valcyte.com.

Yours sincerely,

Myriam Mendila, MD
Senior Vice President, Head of US Medical Affairs

Enclosure(s): Valcyte Full Prescribing Information and Patient Information