



NDA 21304/S-011
NDA 22257/S-005

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
REQUIREMENTS**

Roche Palo Alto LLC
c/o Genentech, Incorporated
Attention: Diane deBruin
Regulatory Agent on behalf of Roche, OptumInsight
1DNA Way
South San Francisco, CA 94080-4990

Dear Ms. deBruin:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received March 31, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for VALCYTE® (valganciclovir hydrochloride) 450 mg tablets and 50 mg per mL oral solution.

We acknowledge receipt of your amendments dated June 4, 2014, June 6, 2014, June 19, 2014, June 27, 2014, July 23, 2014, August 14, 2014, October 9, 2014, November 4, 2014, November 14, 2014 (2), January 23, 2015, January 30, 2015, February 13, 2015, February 20, 2015, March 23, 2015, March 25, 2015, April 1, 2015, April 9, 2015, April 17, 2015 (2) and April 21, 2015.

These “Prior Approval” sNDAs were submitted to expand the Indications and Usage to include heart transplant patients from 1 month to 4 months of age and to extend the duration of dosing regimen from 100 days to 200 days post-transplantation for the prevention of CMV disease in pediatric kidney transplant patients 4 months to 16 years of age.

We have completed our review of these sNDAs, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

**WAIVER OF PREGNANCY, LABOR AND DELIVERY, AND NURSING MOTHERS
SUBSECTIONS**

We are waiving the current requirements of 21 CFR 201.56(d)(1) and 201.57(c)(9)(i) through (iii), regarding the content and format of labeling for subsections 8.1 Pregnancy, 8.2 Labor and Delivery, and 8.3 Nursing Mothers of prescribing information. Your approved labeling for subsections 8.1, 8.2, and 8.3 reflects the content and format requirements of the Pregnancy and Lactation Labeling Rule (79 FR 72063, December 4, 2014) which implements on June 30, 2015.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for pediatric heart transplant patients less than 1 month of age because such a study would be impossible given that heart transplantation is extremely uncommon in this age group.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

These Prior Approval Supplements were also submitted to fulfill the following PREA postmarketing requirements:

- 1670-1 Tolerability study of up to 200 days of valganciclovir for oral solution or tablets in pediatric kidney transplant recipients.
- 1533-2 Perform a pharmacokinetic and safety study in pediatric heart transplant recipients <4 months of age in order to determine appropriate dosing in this age group and submit dosing recommendations for inclusion in the package insert.

The approval of these supplemental new drug applications fulfills these postmarketing requirements.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Victoria Tyson, Regulatory Project Manager, at (301) 796-0827.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DEBRA B BIRNKRANT
04/23/2015