DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 20-156/S-046
NDA 21-183/S-023

Bristol-Myers Squibb Company
Attention: Madhu Anant, Ph.D.
Director, Mature Products
Global Regulatory Sciences
Rte 206 & Provinceline Rd
Princeton NJ, 08543

Dear Dr. Anant:

Please refer to your supplemental new drug applications dated and received November 12, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following drug products:

- NDA 20-156 VIDEX (didanosine) Pediatric Powder for Oral Solution, 10 mg/mL
- NDA 21-183 VIDEX EC (didanosine) Delayed Release Capsules, 125 mg, 200 mg, 250 mg, and 400 mg

We acknowledge receipt of your submission dated January 8, 2010.

SAFETY LABELING CHANGES

Reference is also made to our letter dated October 14, 2009 notifying you, under section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for VIDEX (didanosine) Pediatric Powder for Oral Solution and VIDEX EC (didanosine) Delayed Release Capsules. This information pertains to the risk of non-cirrhotic portal hypertension.

This supplemental new drug application provides for revisions to the labeling for VIDEX (didanosine) Pediatric Powder for Oral Solution and VIDEX EC (didanosine) Delayed Release Capsules consistent with our October 14, 2009 Safety Labeling Change Notification letter.

We have completed our review of this supplemental application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the

package insert, Medication Guide). For administrative purposes, please designate this submission, "**SPL for approved NDA 20-156/S-046 and NDA 21-183/S-023"**.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 20-156/S-046 and NDA 21-183/S-023**." Approval of this submission by FDA is not required before the labeling is used.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, Medication Guide, carton and container).

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

Since VIDEX (didanosine) Pediatric Powder for Oral Solution was approved in 1991 and VIDEX EC (didanosine) Delayed Release Capsule was approved in 2000, we have become aware of well-documented published case reports and post-marketing Adverse Events Reporting System (AERS) reports of non-cirrhotic portal hypertension (NCPH), confirmed by liver biopsy, in patients receiving VIDEX (didanosine) and VIDEX EC (didanosine), that in some cases resulted in death or the need for liver transplant. We consider this information to be "new safety information" as defined in section 505-1(b) of FDCA.

Your proposed REMS, submitted on January 8, 2010, and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS.

The REMS assessment plan should include, but is not limited to, an evaluation of patients' understanding of the serious risks of VIDEX (didanosine) Pediatric Powder for Oral Solution and VIDEX EC (didanosine) Delayed Release Capsule.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), information on the status of any post approval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including

any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 20-156/NDA 21-183 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 20-156/NDA 21-183
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT FOR (NEW INDICATION FOR USE)
FOR NDA 20-156/NDA 21-183
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send five copies of REMS-related submissions.

If you have any questions, please contact Stacy Powers Newalu, M.P.H. at (301) 796-3978.

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

Enclosures
Content of Labeling
Carton and Container Labeling
REMS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21183	SUPPL-23	BRISTOL MYERS SQUIBB CO	VIDEX EC
NDA-20156	SUPPL-46	BRISTOL MYERS SQUIBB CO PHARMACEUTICAL RESEARCH INSTITUTE	VIDEX

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

/s/

KENDALL A MARCUS
01/25/2010