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APPLICATION NUMBER:

761029Orig1s000

OFFICE DIRECTOR MEMO

Deputy Office Director Decisional Memo

Date	(electronic stamp)
From	Robert Temple, MD
Subject	Deputy Office Director Decisional Memo
BLA #	761029
Applicant Name	Biogen Idec
Date of Submission	February 27, 2015
PDUFA Goal Date	May 27, 2016
Proprietary Name / Established (USAN) Name	Zinbryta (daclizumab)
Dosage Forms / Strength	150mg/mL injection
Proposed Indication(s)	treatment of relapsing forms of multiple sclerosis
Action/Recommended Action for NME:	Approval

Material Reviewed/Consulted	Names of discipline reviewers
OND Action Package, including:	
Regulatory Project Manager	Laurie Kelley, PA-C
Medical Officer Review	Larry Rodichok, MD; Lourdes Villalba, MD
CDTL Review	John Marler, MD
Statistical Review	Xiang Ling, PhD
Pharmacology Toxicology Review Supervisory	Dave Carbone, PhD
CMC Review/OBP Review Application Technical Lead	Joel Welch, PhD
Clinical Pharmacology Review	Ta-Chen Wu, PhD
OPDP	Aline Moukhtara, RN, MPH
OSI	Antoine El Hage, PhD
OSE/DMEPA	Justine Harris, BS, RPh
OSE/DRISK	Bob Pratt, PharmD
OMP/DMPP	Nyedra Booker, PharmD
Pediatrics and Maternal Health	Donna Snyder, MD; Leyla Sahin, MD
Other	Lana Shiu, MD (CDRH); Mark Avigan, MD (OSE); John Senior, MD (OSE); Elisa Braver, PhD (OSE)

OND=Office of New Drugs
 OSE= Office of Surveillance and Epidemiology
 DMEPA=Division of Medication Error Prevention and Analysis
 OSI=Office of Scientific Investigations
 DRISK=Division of Risk Management
 CDTL=Cross-Discipline Team Leader
 OPQ=Office of Pharmaceutical Quality

Please refer to Dr. Dunn's review of this 351(a) Biologics Licensing Application (BLA) for Zinbryta (daclizumab) 150 mg/mL injection, for the treatment of relapsing forms of multiple sclerosis, for the details, findings, and conclusions regarding this application. I have discussed these matters extensively with Dr. Dunn and others on the review team, and examined all clinical, statistical, and non-clinical reviews and agree with the presentation and conclusions in Dr. Dunn's review. Daclizumab was shown primarily to reduce annualized relapse rate in comparison to both placebo (Study 201) and to Avonex (Study 301), with a 54% reduction compared to Avonex, an active agent that itself reduces relapse rate. The effect on disability trended favorably in the placebo-controlled study and in the Avonex (a drug with known effect on disability) study.

Dr. Dunn recommends that Zinbryta be approved, with labeling clearly describing both benefits and important safety concerns. Labeling will discuss all important safety concerns, emphasizing in a Box Warning the need to assess liver chemistries before each dose and the risk of immune-related disorders. Daclizumab will be indicated "generally for patients who have had inadequate response to two or more prior therapies indicated for the treatment of MS." In these patients, daclizumab represents a valuable alternative. There will be required Risk Evaluation and Mitigation Strategy (REMS), which will be critical to managing Zinbryta's risks of hepatotoxicity including autoimmune hepatitis, and a variety of immune-mediated disorders, and to obtaining further data about these risks. Post-marketing requirements for study will assess drug-induced liver injury, the rate of serious infections and immune-related disorders and the risk of breast cancer. I agree with Dr. Dunn's assessment of this application and his conclusion that the application should be approved and will not elaborate further on the application or regulatory action in this memo.

At the time of submission, Zinbryta (BLA 761029) was identified for review under the Program for Enhanced Review Transparency and Communication for NME NDAs and original BLAs (known as the Program and described in the PDUFA V goals letter). Further review of the application during the review cycle has indicated that BLA 761029 may not qualify for the Program; however, consistent with FDA policy, the review of the BLA has continued to be managed under the Program for process reasons. According to CDER's review process, the signatory authority for applications managed under the Program is generally at the office level. Because this application was managed under the Program, it has been signed at the office level to be consistent with OND practice.

The agency has decided the proper name for this product is daclizumab. We note that an alternative name (b) (4) was not adopted by USAN. (b) (4) (b) (4) we have considered the status of the agency's policies on the nonproprietary naming of biological products, the previous approval by FDA of daclizumab in BLA 103749 and the current status of BLA 103749.

Regarding the agency's current policies on the nonproprietary naming of biological products, we note that the draft guidance for industry, Nonproprietary Naming of Biological Products has not been finalized. Consistent with FDA's good guidance practices (see 21 CFR 10.115), FDA has provided an opportunity for public comment before the guidance is finalized. Before the guidance is finalized, FDA continues to make decisions on nonproprietary names on a product-specific basis.

A key factor in FDA's current thinking regarding the (b) (4) proper name of certain biological products is the Agency's determination that (b) (4) lower the risk of confusing different products and assist with FDA's product-specific pharmacovigilance efforts. Daclizumab was approved under BLA 103749 and that BLA has subsequently been revoked. Thus, because the biological product licensed under the current BLA (BLA 761029) will be the only daclizumab product licensed in the U.S., there appears to be no risk of product confusion at this time.

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/s/

YUET L CHOY
05/27/2016

ROBERT TEMPLE
05/27/2016