

**Division of Hematology Products
Clinical Review of NDA/BLA
Post-Marketing Commitment (PMC) or Requirement (PMR)**

BLA Number(s): 125103
Supporting Document Number: 148
Drug Name: Kepivance (palifermin)
Sponsor: Swedish Orphan Biovitrum AB (SOBI)
Type of Submission: Post-Marketing Commitment or Post-Marketing Requirement
Date Received: 1/30/13
Date Completed: 3/30/13

Reviewer: Patricia Dinndorf
Team Leader: Albert Deisseroth

Regulatory History:

The following PMRs and PMCs have not been fulfilled or terminated.

- PMC 2 BLA 125103 original approval January 15, 2004
To complete and submit data from study protocol 960226, a long-term observational follow-up study of subjects previously enrolled in any palifermin study conducted in the myelotoxic therapy setting.
Outstanding milestone: FSR - 6/30/15
Status: Applicant submitting annual interim reports.
- PMC 3 BLA 125103 original approval January 15, 2004
To complete and submit data from study protocol 990123, a long-term observational follow-up study of subjects with head and neck cancer previously enrolled in palifermin studies in the fractionated chemoradiotherapy setting.
Outstanding milestone: FSR - 6/30/15
Status: Applicant submitting annual interim reports.
- PMC 11 BLA 125103 original approval January 15, 2004
To conduct a prospective cohort study using the available International Bone Marrow Transplant Registry (IBMTR) and Autologous Blood and Bone Marrow Registry (ABMTR) databases to evaluate the incidence of secondary malignancies, cancer relapse rates, and survival in patients who receive alifermin compared to a matched patient control group who have not received palifermin. The study protocol will be submitted by July 30, 2005, and will be initiated by January 31, 2006. Interim data will be submitted at 2 year intervals for a period of 10 years, beginning July 31, 2008 and the final study report will be submitted by July 31, 2016.
Outstanding milestone: Study Completion – 9/30/17; FSR - 6/30/15
Status: Applicant submitting annual interim reports.

- PMR 38/1 One of 2 studies in pediatric patients replacing original PMC 1. To conduct a deferred pediatric study under PREA to determine whether well-tolerated and pharmacologically active doses of palifermin in three patient cohorts defined by age (1-2, 3-11, and 12-16 years) with hematologic malignancies treated with myelotoxic therapy and undergoing hematologic stem cell transplant. In study 20010133, "A Phase 1 Dose-escalation Study to Evaluate the Safety and Pharmacokinetics (PK) of Palifermin in Pediatric Subjects with Acute Leukemias Undergoing Myeloablative Therapy and Allogeneic Hematopoietic Stem Cell Transplant (HSCT)," that will be conducted at approximately seven sites registered with the Pediatric Blood and Marrow Transplant Consortium (PBMTTC), 18 to 54 subjects will be treated in the specified age groups. The study will evaluate the safety and pharmacokinetics of palifermin in patients with acute leukemias receiving myelotoxic therapy followed by hematologic stem cell transplant. Three doses (40/mg/kg/day, 60/mg/kg/day, 80/mg/kg/day) will be evaluated in each age cohort in a dose-escalation manner. Age cohorts will be treated simultaneously with the objective to identify a safe, well-tolerated, efficacious dose in each age cohort. Outstanding milestone: FSR – Submitted 12/21/12
Status: Under FDA review. This PMR will be fulfilled when final labeling complete.

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/s/

PATRICIA A DINNDORF
03/30/2013