An Overview of the Rare Pediatric Disease Priority Review Voucher Program

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Disclosures

• No Conflicts of Interest
• Nothing to Report
• Opinions expressed are personal and do not reflect those of the FDA
Outline

• Rare Diseases Program
• Special Challenges for Rare Pediatric Diseases
• Rare Pediatric Disease Priority Review Voucher (RPD PRV) Program -- Background and Processes
CDER Rare Diseases Program

Mission Statement:

• Facilitate
• Support
• Accelerate

…the development of drug and biologic products for the treatment of patients with rare disorders
Challenges for Rare Pediatric Disease Drug Development

- Rare diseases **natural history** is often poorly understood/characterized
- Diseases tend to be progressive, **serious**, life-limiting and life-threatening and lack approved therapy
- **Small populations** often restrict study design and replication
Challenges for Rare Pediatric Disease Drug Development

- **Phenotypic** diversity within a disorder adds to complexity, as do **genetic subsets**
- Well defined and validated **endpoints**, **outcome measures/tools**, and **biomarkers** are often lacking
- Lack of **precedent** for drug development
- **Ethical** considerations for children in clinical trials
Rare Pediatric Disease (RPD) Priority Review Voucher Program: Background

• Established by the 2012 FDA Safety and Innovation Act (FDASIA) [Section 908]
• Provides an incentive to encourage the development of drugs and biologics for the prevention or treatment of rare pediatric diseases
• Upon marketing approval, the sponsor for a RPD drug may be issued a voucher redeemable for a priority review for a subsequent marketing application that may otherwise not have qualified for a priority review.
Priority Review

PRIORITY REVIEW Designation, part of the Prescription Drug User Fee Act of 1992 offers a shorter review clock for marketing applications, 6 months compared with the 10 months standard review time.

A drug may receive priority review designation if the application (original or efficacy supplement) is for a drug that treats a serious condition AND, if approved, would provide a significant improvement in safety or effectiveness.
Rare Pediatric Disease Priority Review Voucher Program

• Section 908: The Secretary shall award a priority review voucher to the sponsor of a rare pediatric disease product application upon approval by the Secretary of such rare pediatric disease product application.
Rare Pediatric Disease Priority Review Voucher Program

• Voucher eligibility:
  • Rare pediatric disease defined as a disease that “primarily affects individuals aged from birth to 18 years” with greater than 50% of the affected US population in this age group
  • Is a rare disease or condition as defined in section 526 of the FD & C Act
Rare Pediatric Disease Priority Review Voucher Program

• Voucher eligibility:
  • The candidate drug or biological product contains no active ingredient (including any ester or salt of the active ingredient) that has been previously approved in any other application
  • FDA deems eligible for priority review
  • Relies on clinical data from pediatric population(s) in doses intended for use in that population
  • Does not seek approval for an adult indication in the original rare pediatric diseases product application
Rare Pediatric Disease Priority Review Voucher Program: Process

- The Office of Orphan Products determines whether a disease is designated as a rare pediatric disease.
- A sponsor may choose to request a rare pediatric disease designation “at the same time” that they submit a request for orphan-drug designation (before the filing of a marketing application) OR a request for fast track designation.
  - The request for designation will be decided upon no later than 60 days after submission.
Rare Pediatric Disease (RPD) Priority Review Voucher Program: Process

• However FDA is willing to accept designation requests as long as FDA receives the designation request before FDA has filed the NDA/BLA. In this case the 60 day deadline does not apply.

• Upon marketing approval, the sponsor for a RPD drug may be eligible for a voucher redeemable for a priority review for a subsequent marketing application which typically would have qualified for a standard review.
Rare Pediatric Diseases Priority Review Voucher Program

- Vouchers awarded to date
  - Vimizim (elosulfase alfa) for the treatment of Mucopolysaccharidosis type IVA (Morquio A syndrome)
  - Unituxin (dinutuximab) as part of first line therapy for pediatric patients with high risk neuroblastoma
  - Cholbam (cholic acid) for treatment of bile acid synthesis disorders due to single enzyme defects and for patients with peroxisomal disorders (including Zellweger spectrum disorders)
  - Xuriden (uridine triacetate) is indicated for the treatment of hereditary orotic aciduria (HOA)
Rare Pediatric Diseases Priority Review Voucher Program

• Voucher used to date
  • Sponsors using a PRV are required to pay a separate fee in addition to the usual user fee
  • Sanofi and Regeneron purchased from Biomarin Vimizim (elosulfase alfa) for the treatment of Mucopolysaccharidosis type IVA (Morquio A syndrome)
• Praluent (alirocumab) Approved 7/24/2015
  PRALUENT is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C
Role of the Rare Diseases Program

• In alignment with its mission of accelerating the development of drug and biologic products for the treatment of patients with rare disorders, the RDP has taken on administrative and operational responsibilities for the Rare Pediatric Diseases Priority Review Voucher (PRV) program within the Office of New Drugs (OND)/CDER.

• RDP tracks all requests for vouchers, their status, awarded vouchers and maintains a tracking system for this program.
Role of the Rare Diseases Program

• Coordinated the development of an SOP for OND to process incoming requests for PRVs from initial submission to eventual regulatory decisions and determination of qualification for vouchers

• Serves as the point of communication with the OND review division Regulatory Project Managers (RPMs)

• Drafted template language for the review divisions to use in written response to inquiries from sponsors
Rare Pediatric Disease Priority Review Voucher Program – Designation and Oversight

• GAO will conduct a study of the effectiveness of awarding RPD Priority Review Vouchers after the 3rd voucher is awarded

• Following the award of the 3rd voucher, a one year sunset period began (17 March 2015)

• FR Notice published no later than 30 days after the designated marketing application approval
Rare Pediatric Disease Priority Review Voucher Program – Designation and Oversight

• GAO has initiated its study of the effectiveness of awarding RPD Priority Review Vouchers.

• The 21st Century Cures Act (H.R. 6), passed by the House of Representatives on 7/10/2015 includes a provision to reauthorize the RPD PRV Incentive Program through 12/31/2018.

REFERENCE

Rare Pediatric Disease Priority Review Vouchers, Guidance for Industry DRAFT GUIDANCE

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Thank you very much for your attention!

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Rare Diseases Program/OND/CDER/FDA