Pediatric Focused Safety Review
Orencia (abatacept)
Pediatric Advisory Committee Meeting
September 15, 2020

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Outline

- Background Information
  - Previous Pediatric Advisory Committee (PAC) Meeting
- Relevant Pediatric Labeling
- Drug Use Trends
- Adverse Events
- Summary

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Background Information

- **Drug:** Orencia® (abatacept)
- **Original Market Approval:** December 23, 2005
- **Sponsor:** Bristol Myers Squibb
- **Therapeutic Category:** Immunosuppressant agent
- **Indications:**
  - Adult rheumatoid arthritis (RA)
  - Polyarticular juvenile idiopathic arthritis (JIA)
  - Adult psoriatic arthritis (PsA)
- **Formulation:**
  - Lyophilized powder for intravenous (IV) infusion
  - Prefilled syringe and ClickJect Autoinjector for subcutaneous (SC) administration

Background Information

- **Pediatric Research Equity Act (PREA) labeling change:**
  - JIA ages 6 years and older (IV formulation): April 7, 2008
- **PAC Meeting September 2009:**
  - No new safety concerns identified
  - Recommended routine monitoring
- **PREA labeling change:**
  - JIA ages 2 years and older (SC formulation): March 30, 2017*
  - Supported by open-label study evaluating pharmacokinetics, efficacy, and safety of SC abatacept in 205 pediatric patients (age 2-17 years) with active polyarticular JIA

*Initiated current review

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Labeling: Warnings and Precautions

- **5.1 Concomitant Use with Tumor Necrosis Factor (TNF) Antagonists, Other Biologic RA/PsA Therapy, or Janus Kinase Inhibitors is Not Recommended**
- **5.2 Hypersensitivity**
- **5.3 Infections**
- **5.4 Immunizations**
- **5.5 Use in Patients with Chronic Obstructive Pulmonary Disease**
- **5.6 Immunosuppression**

Labeling: Adverse Reactions—Pediatric

6.2 Clinical Trials Experience in Pediatric Patients with Polyarticular JIA

- In general, the adverse events in pediatric patients were similar in frequency and type to those seen in adult patients
- Frequently reported adverse events
  - Infections: 36% (upper respiratory tract infections and nasopharyngitis)
  - Headache: ≥ 5%
  - Nausea: ≥ 5%
  - Diarrhea: ≥ 5%
  - Cough: ≥ 5%
  - Pyrexia: ≥ 5%
  - Abdominal pain: ≥ 5%

Adverse Reactions in Patients with polyarticular JIA Treated with SC Abatacept

- Adverse reaction profile consistent with IV abatacept in pediatric clinical trials
- Frequently reported adverse events
  - Local injection-site reactions: 4.4%

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Abatacept Utilization Data

- Abatacept utilization in patients younger than 18 years of age was low

- In 2018, pediatric patients accounted for 2% of a total of 37,388 patients who had a prescription or medical claim for abatacept

- In 2018, 72% of pediatric patients were ages 12 - <18 years

Source: Symphony Health Integrated Dataverse, 2015-2018. Data extracted July 2019.

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FDA Adverse Event Reporting System (FAERS) Pediatric Case Selection July 7, 2009,* to December 18, 2019

Total pediatric reports with a serious outcome retrieved (N=368)
- Pediatric reports with the outcome of death (n=9)

Excluded Reports† (n=366)
(Including 9 deaths)

- Duplicates (n=196, including 2 deaths)
- Unassessable (n=52)
- Adverse events unlikely related to abatacept (n=45, including 3 deaths)
- Labeled adverse event reported (n=35, including 3 deaths)
- No adverse event described with abatacept (n=24)
- Transplacental exposure (n=12)
- Miscoded age (n=2, including 1 death)

Pediatric Cases for Discussion (n=2) (Including 0 deaths)

*Prior abatacept pediatric review assessed from drug approval to July 7, 2009

† DPV reviewed these cases, but they were excluded from the case series for the reason listed

Serious Unlabeled Adverse Events in Pediatric Patients

- Inflammatory bowel disease (n=1)
  - Did not constitute a safety signal because the report contained potential alternative cause (concomitant leflunomide)
- Angioedema (n=1)
  - Led to full safety review that identified 83 adult (n=82) and pediatric (n=1) patients
  - Safety Labeling Change approved on June 17, 2020
    - Warnings and Precautions Section 5.2 Hypersensitivity
    - Includes information about early and delayed onset

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Summary: Pediatric Safety Review

- Angioedema was identified as a potential signal, assessed in a concurrent signal review, and added to labeling in June 2020
- Low use of abatacept in pediatric population
- Pediatric reported adverse events are consistent with known adverse events described in labeling
- **FDA recommends to continue ongoing, postmarketing safety monitoring**
- **Does the Pediatric Advisory Committee concur?**

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