

**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: $\geq 5\%$
 - Nausea: $\geq 5\%$
 - Diarrhea: $\geq 5\%$
 - Cough: $\geq 5\%$
 - Pyrexia: $\geq 5\%$
 - Abdominal pain: $\geq 5\%$

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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