Susan McCune, M.D.
Director, Office of Pediatric Therapeutics
Office of Clinical Policy and Programs
Office of the Commissioner, FDA

PEDIATRIC ADVISORY COMMITTEE OPENING REMARKS

Pediatric Advisory Committee Meeting
September 15, 2020

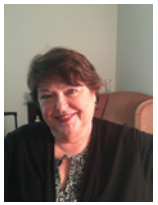
Opening Remarks

- Personnel Update
- Web-posted reviews
- Update for Montelukast (Singulair)
- Non-Compliance Letters

Personnel Update

- PAC
  - Jennifer Goldman, MD

- OPT
  - Sheila Reese, RN



  - Ester Hatton

  - Jeanine Best, MSN, RN, PNP

  - CDR Margaret V. Caulk, MPH

Web Posted Reviews

- **Center for Drug Evaluation and Research (N=15)**
  - BUTRANS (buprenorphine transdermal system)
  - CANASA (mesalamine suppositories for rectal use)
  - DESCOVY (emtricitabine and tenofovir alafenamide)
  - DRAXIMAGE DTPA (technetium TC-99m pentetate kit) injection and inhalation
  - DYSPORT (abobotulinumtoxinA)
  - GENVOYA (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) oral tablets
  - LUMASON (sulfur hexafluoride lipid-type A microspheres) injectable suspension
  - LUMIFY (brimonidine tartrate) OTC
  - LUZU (luliconazole) cream, 1%
  - OMIDRIA (phenylephrine and ketorolac intraocular solution)
  - SENSIPAR (cinacalcet)
  - STELARA (ustekinumab) injection
  - SYMFI LO (efavirenz 400 milligram (mg) + lamivudine 300 mg + tenofovir disoproxil fumarate 300 mg) and SYMFI (efavirenz 600 mg + lamivudine 300 mg + tenofovir disoproxil fumarate 300 mg)
  - TRIUMEQ (abacavir, dolutegravir, and lamivudine)
  - XEPI (ozenoxacin)
- **Center for Biologics Evaluation and Research (N=9)**
  - AFSTYLA (antihemophilic factor (recombinant), single chain)
  - EPICEL (cultured epidermal autografts)
  - FLUCELVAX QUADRIVALENT (influenza vaccine)
  - FLUCELVAX (influenza vaccine)
  - FLULAVAL (influenza vaccine)
  - FLULAVAL QUADRIVALENT (influenza vaccine)
  - HIBERIX (Haemophilus b conjugate vaccine (tetanus toxoid conjugate))
  - KOVALTRY (antihemophilic factor (recombinant))
  - Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted
- **Center for Devices and Radiological Health (N=7)**
  - CONTEGRA PULMONARY VALVED CONDUIT (Humanitarian Device Exemption (HDE))
  - ELANA SURGICAL KIT (HDE)
  - ENTERRA THERAPY SYSTEM (HDE)
  - LIPOSORBER LA-15 SYSTEM (HDE)
  - MEDTRONIC ACTIVA DYSTONIA THERAPY (HDE)
  - PLEXIMMUNE IN-VITRO DIAGNOSTIC TEST (HDE)
  - PULSERIDER ANEURYSM NECK RECONSTRUCTION DEVICE (HDE)

Medwatch Safety Alerts for Human Medical Products
https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/default.htm

Montelukast and Neuropsychiatric Events

- 2008: Warnings and Precautions, Drug Safety Communication, Dear Health Care Provider letters issued
  - Postmarketing reports
  - Wide variety of events, including behavior changes and completed suicide
- 2008 – 2019: Additional neuropsychiatric events included in label
- September 2019: Joint Meeting of the Pediatric Advisory Committee and the Drug Safety and Risk Mitigation Advisory Committee
  - Response to stakeholder requests
  - Review of FAERS data, published literature and results from observational study in Sentinel

https://www.fda.gov/advisory-committees/pediatric-advisory-committee/fda-briefing-materials-september-27-2019-joint-meeting-pediatric-and-drug-safety-and-risk-management

Slide courtesy of Dr. Stacy Chin

Montelukast and Neuropsychiatric Events

- Re-assessed benefit-risk for asthma and allergic rhinitis
  - Benefits may not outweigh the risks for treatment of allergic rhinitis
    - New safety information
    - Nature of disease
    - Context of available therapies
- March 4, 2020: Issue safety labeling changes
  - Boxed Warning
  - Limitation of use for allergic rhinitis → reserve use for patients who have inadequate response or intolerance to alternative therapies
  - Medication Guide
  - Drug Safety Communication and Press Release

Boxed warning required for asthma, allergy drug Singulair

Mar 4 - Mental health side effects include suicidal thoughts or actions

https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-boxed-warning-about-serious-mental-health-side-effects-asthma-and-allergy-drug

Slide courtesy of Dr. Stacy Chin

Non-Compliance Letters

- Center for Biologics Evaluation and Research (n=2)
  - https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cber/ucm448393.htm
- Center for Drug Evaluation and Research (n=46)
  - https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm343203.htm
- The websites list the sponsor, product, a copy of the non-compliance letter, the sponsor's response (if available), and the status of the PREA requirement (e.g., released, replaced, fulfilled)

Non-Compliance Letters

- Center for Biologics Evaluation and Research (n=2)
  - No new letters since the last PAC meeting

- Center for Drug Evaluation and Research (n=46)
  - 15 new letters since the last PAC meeting

Non-Compliance Letters (CDER)

Sponsor	Product	Date of Letter	Date of Sponsor Response
Akebia Therapeutics	Auryxia (ferric citrate) Tablets	1/31/20	3/13/20
Arbor Pharmaceuticals, LLC	Edarbi (azilsartan medoxomil) Tablets, 40 mg & 80 mg	2/10/20	3/26/20
Assertio Therapeutics, Inc	Zipsor (diclofenac potassium) liquid filled-capsules)	11/5/19	12/26/19
AstraZeneca Pharmaceuticals LP	Nexium (esomeprazole magnesium) for delayed release oral suspension	8/21/19	10/3/19
Cumberland Pharmaceuticals, Inc.	Vibativ (televancin) for Injection, 250 mg & 750 mg	12/12/19	1/15/20
Ferring Pharmaceuticals, Inc.	Prepopik (citric acid, magnesium oxide, and sodium picosulfate)	10/4/19	11/19/19
Mylan Ireland Limited	Arixtra (fondaparinux sodium injection) solution	4/27/20	6/16/20