Pediatric Focused Safety Review
Update –
Exjade (deferasirox)

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FDA Update

Outline

• September 2015 Pediatric Advisory Committee presentation and request
• Safety issues under evaluation
  – Fever
  – Dehydration/ Hypovolemia
  – Kidney injury
  – Liver injury
• Data sources
Case presented at Sept. 2015 PAC

• Death of a 2 11/12 y.o. girl in association with an acute illness and respiratory syncytial virus (RSV) while receiving deferasirox (DFS) for β-thalassemia and iron overload.

• The patient presented with acute renal and hepatic failure, along with metabolic acidosis. Her immediate cause of death was cerebral edema with herniation.
PAC request and FDA interpretation

• The Pediatric AC members requested that FDA review “any data regarding safety of continued medication to children who have fever, and report back to the PAC”

• FDA ongoing comprehensive review plan
  – Focus broadened to fever and hypovolemia
  – Identify cases from available sources
  – Examine adverse events, possible predisposing factors, and potentially preventable causes
  – Analyze role of interrupting or continuing DFS during acute illness
Acute illness events

Fever

• At least 1 fever occurred among 45% of children (ages 2-15, all indications) in clinical trials (Exjade Investigator Brochure)

• Viral infection, hypovolemia, anorexia, and liver injury may occur without fever

• Is fever a reliable indicator for interrupting DFS dosing?
Acute illness events

Hypovolemia

• Potential for acute volume loss to produce labeled renal criteria for dose modification
• Potential for volume loss to produce excess exposure
• Limitations to methods of volume status assessment from data sources
Safety issues under evaluation for continuation of DFS with acute illness

• Acute illness events
  – Fever
  – Hypovolemia or dehydration

• Associated adverse effects
  – Kidney Injury
  – Liver Injury
Data sources

• A 5 year observational study (registry) of children aged 2 to less than 6 years at enrollment with transfusional hemosiderosis treated with deferasirox (ENTRUST) FDA receipt of data: January 29, 2016

• Pooled analysis of safety data from 17 pediatric clinical trials with Exjade (age <16 years)

• FAERS (FDA Adverse Event Reporting System)

• Published literature
Conclusion

• Final report to PAC expected March 2017 meeting
• Presentation will include discussion of possible label changes