Closing Comments

Findings of safety review are relevant to the index case

- There is a risk of renal impairment associated with acute illnesses that have risks for volume depletion
- Decreased renal function results in increased DFS exposure, and increased exposure results in decreased renal function, with the potential for an exacerbating cycle and possibly hepatic toxicity
- There is a risk of acute liver failure in children receiving deferasirox

Findings of safety review are relevant to the index case

- The risks of high deferasirox dose and low serum ferritin (as a measure of body iron) are additive for the development of diminished renal function.

- There is a risk of life-threatening adverse events when full dose (20-40 mg/kg/day) Exjade is continued while the body iron burden is approaching or within the normal range

Label updates specific to pediatric patients

- Interrupt dose with hypovolemia and monitor more frequently. Resume when volume is replaced, and normal oral intake resumes, with dose based on renal function (sections BW, 2.1, 2.2, 2.5, 5.1, 5.5, 17)
- DFS exposure increases when eGFR decreases (sections 2.5, 8.4, 12.2)
- Use estimated glomerular filtration rate (eGFR, ml/min/1.73m^2), as the method for monitoring and adjusting drug dose, rather than the current method of creatinine clearance (ml/min) (sections 2.1, 2.4, 2.5, 4, 5.1, 8.4, 8.6)
- There is a risk of kidney and liver failure with continued use of DFS doses 20-40 mg/kg/day, when the body iron burden is approaching or within the normal range (sections 5.2, 5.5, 5.6)

Label updates cont'd

- Adjust dose or increase monitoring when SF < 1,000 mcg/L (sections 2.1, 5.6, 8.4)
- Renal impairment risk increases when DFS > 25 mg/kg/day, while SF < 1,000 mcg/L (sections BW, 5.6, 6.1, 8.4)
- An increased risk of auditory adverse events among pediatric patients was associated with use of Exjade doses greater than 25mg/kg/day, when serum ferritin was less than 1,000 mcg/L (section 5.10)

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