Closer Look

MEMORANDUM

FDA strengthens label warning on bone fracture risk with J&J's Invokana (canagliflozin) - September 13, 2015

The FDA released a Drug Safety Communication last week noting that it has strengthened the warning about bone fracture risk in the label for J&J's Invokana (canagliflozin) and added new information about decreased bone mineral density. The label now includes a separate Warning and Precaution related to the risk of bone fractures, which was previously mentioned in the Adverse Reactions section. This update came in response to an analysis of nine pooled clinical trials that found significantly higher incidence of bone fractures with Invokana vs. placebo (1.4 and 1.5 events per 100 patient-years with 100 mg and 300 mg Invokana, respectively, vs. 1.1 with placebo). Fractures occurred beginning 12 weeks after treatment initiation and were not typically accompanied by significant trauma. Information about the risk of decreased bone mineral density was also added to the Adverse Reactions section of the label after a two-year trial in 714 older patients (age 55-80) with type 2 diabetes found greater declines in bone mineral density in the hip and lower spine with Invokana vs. placebo. The FDA did not advise any significant changes in prescribing patterns but urged patients and providers to consider factors that may contribute to fracture risk prior to initiating treatment with Invokana. The Agency is currently evaluating the risk of bone fractures with AZ's Farxiga (dapagliflozin) and Lilly/BI's Jardiance (empagliflozin) to determine whether additional studies or label updates are warranted. Our sense is that this warning is unlikely to have a substantial impact on clinical practice; its main effect will likely be to solidify and reinforce the existing hypothesis that patients at high fracture risk are not the best candidates for this drug class.