CHMP recommends EMA approval of Sanofi/Lexicon's sotagliflozin (Zynquista) for type 1 diabetes - March 2, 2019

In line with opinion for AZ's Forxiga, limited to specialist-treated type 1s with BMI ≥27 kg/m²; FDA PDUFA date March 22; Both 200 and 400 mg recommended for approval

Yesterday, EMA's CHMP recommended approval of Sanofi and Lexicon's SGLT-1/2 dual inhibitor sotagliflozin (commercial name Zynquista) for type 1 diabetes. A final decision is expected "in the coming months" and this is a tremendous win for Sanofi and (especially) Lexicon.

As with last month's positive CHMP opinion on AZ's Forxiga for type 1, the recommendation is limited to people with a BMI ≥27 kg/m² with the drug initiated and supervised by physicians experienced in the treatment of type 1 diabetes. While the (exact) empirical basis for this limitation remains a bit unclear - and was a point of critique at ATTD 2019 - we suspect it's a strategic decision intended to limit initial access to SGLTs among the type 1 community. Moreover, some experts suggest that the risk/benefit profile is more favorable among type 1s with overweight/obesity, who would most benefit from weight loss and may face lower DKA risk due to a higher total daily insulin dose. Some have asked to "see the numbers" on this - we suspect the numbers may be too small overall to "prove" this and we believe that "expert opinion" is quite valuable in this case.

This decision follows January's FDA Advisory Committee meeting on Sanofi/Lexicon's NDA in the US, which ultimately ended in an 8-8 vote on sotagliflozin's approval. Both sotagliflozin and AZ's Farxiga remain under review at FDA. The agency's PDUFA date on sotagliflozin is March 22, while Farxiga was not submitted to FDA until ~4Q18 - however, AZ only needed to submit an sNDA for the additional indication, so it should take proportionally less time for FDA to review the application.

Per CHMP, only the 200 mg tablet of sotagliflozin will be made available; however, the sponsors both announced that both the 200 and 400 mg doses were recommended for approval (i.e., the latter will involve a two-tablet dose). This was a pretty contentious point of discussion during the Ad Comm. One argument certainly did imply that the risk of DKA is higher at the higher dose; we think it's prudent to offer the lower dose to patients initially. Full details on the approval including the prescribing information will not be available until after a positive decision by the European Commission.

Usually, the European Commission's final decisions do fall in lockstep with opinions from CHMP, so we expect final marketing authorization of both Forxiga and Zynquista to come later this year. This decision may be of interest to FDA in showing a way to make this class and all of its benefits - time in range improvements, weight loss, possible CV and renal benefits, and more - available to some people with type 1 while enabling a look at risk "in the real world", which is a limitation of any randomized controlled trial (by design). We are very hopeful about this strategy in that it will create data on actual DKA risk management but in a more conservative style that does not "open the floodgates" to any person with type 1. While we worry about that, we are also very concerned about no approval at all since we believe that would put far more patients at risk who will just "take it anyway," even if unregulated. Without a doubt, more work needs to be done to develop, test, and implement effective DKA risk mitigation strategies (see the recent consensus on this topic), and we both look forward to hearing more granularity on both Sanofi/Lexicon's and AZ's plans to this end and are also excited about the potential to see these move forward. Presumably, ultimately, this class could be made available to a broader group of people with type 1 if the data supported that decision; that is still unknown due to lack of data.

-- by Ann Carracher, Payal Marathe, and Kelly Close