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Jardiance CV label claim is no slam dunk

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Jardiance took a step closer to winning a coveted cardiovascular label claim yesterday at a broadly positive US FDA advisory committee hearing that many, including the drug's owners, Lilly and Boehringer Ingelheim, believe will trigger a jump in demand.

While there is certainly evidence to suggest the FDA will side with its expert panel, there are also areas of doubt; a decision is due by the end of September. The 2% jump in Lilly shares this morning suggests that many will be disappointed should an explicit label claim be rejected. Whether in the end it will make a difference in the market is another question.

Risk reduction

Lilly and Boehringher are hoping to be able to claim that Jardiance can reduce the incidence of cardiovascular death in diabetes patients with established heart disease. On the question of whether the cardiovascular outcomes study, EMPA-REG, provided substantial evidence of this, the vote was close run, with 12 yeas to 11 nays.

Sellside analysts, many of whom now believe that the FDA is more likely to permit a label claim, pointed to the composition of the yes and no camps to support their optimism. Voting in favour were all the cardiologists and "panel heavyweights", according to Leerink, while the FDA reviewers' documents were also supportive and the regulator's representatives at the hearing spoke in favourable terms.

Still, many of the yes voters conceded that it was a tough decision. The main sticking points were the lack of a confirmatory trial and the fact that the claim was only one component of the composite three-point-MACE primary endpoint of the study.

These issues would normally prevent the FDA from allowing such substantial claims, although there are precedents. Leerink wrote that the FDA's Dr Robert Temple, deputy director for clinical science, raised the example of the Life study of Cozaar at the panel hearing. This allowed an indication of stroke risk reduction based on one trial, of which stroke was also a component of a composite endpoint.

Leerink, formerly of the opinion that the EMPA-REG data would only make its way onto the label via the clinical experience section, now reckon a label claim is likely. So do Bernstein analysts, based on the win by the yes votes and the favourable FDA comments.

They also make the point that the mortality claim will not divert patients from diabetes drugs with a better cardiovascular profile because no other drugs have been proven to save lives.

Sales boost

Should the FDA follow through Jardiance will indeed be handed a huge marketing advantage, although Lilly executives have also made clear that treatment guidelines also need to reflect the data. News should follow on this in coming months, and it is hard to imagine anything other than a strong endorsement.

Forecasts already seem to reflect all this – consensus has almost doubled since the EMPA-REG data were released, with analysts pencilling in $2.9bn in 2020. These estimates make Jardiance the third-biggest selling diabetes brand in 2022, according to *EvaluatePharma* (*Jardiance label claim is the next milestone for booming SGLT2 class, June 21, 2016*).

Still, it is notable that the majority of endocrinologists on the panel – eight out of 12 – voted against an explicit label claim. Concerns included the robustness of the signal, lack of clarity on the mechanism of action driving the apparent benefit, as well as the absence of a study to confirm the findings.

This last point could easily be addressed with a request for a second trial. That would take time, although signals might also be gleaned from the second SGLT2 outcomes study to report: Johnson & Johnson's Canvas trial of Invokana should yield results next year. The FDA is due to make its decision on Jardiance before then, however; a September 28 PDFUA date has been set.

Taking into account the split of the panel opinion, and the fact that the FDA remains acutely focused on setting inscrutable cardiovascular safety standards, it would be understandable if the regulator shied away from an explicit endorsement in this case.

However that might not matter in the long term as long as the data are described in the label, as ISI Evercore analysts point out. Few doubt that this will happen, so, claim or no claim, demand for Jardiance looks set to soar.

SGLT2 CV outcome studies		
Jardiance	Empa-Reg Outcome	NCT01131676
Invokana	Canvas	NCT01032629
Farxiga	Declare-Timi58	NCT01730534

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