Evaluate Vantage

September 14, 2021

Astellas readies roxadustat for launch

Amy Brown

But winning EU approval for the novel anaemia pill was not straightforward, the Japanese firm says.

Amid the delays and mishandling that marked Fibrogen's attempts to get roxadustat to market in the US, it is easy to forget that a different story lies behind the drug's progress in Europe. Astellas, which owns rights to the novel anaemia pill in that region and Japan, won broad backing from the EMA last month with no hold-ups.

This is not to say that the EU regulators waved roxadustat through. The EMA requested several additional data analyses and subgroup explorations and asked "many tough questions", according to Salim Mujais, senior vice-president and head of medical specialties at Astellas. "In my over 20 years in industry this was one of the most rigorous and meticulous processes with regulators," he told *Evaluate Vantage*.

Mr Mujais said that the company was fully aware that winning approval for a novel mechanism in a tough disorder like chronic kidney disease, with a wide spectrum of severity, would be difficult. Roxadustat was the first HIF stabiliser, a new class of drug that works by stimulating the production of endogenous erythropoietin, to reach regulators.

Before the filing was made the company embarked on a series of scientific consultations with the EMA to clarify what would be required. "And during the approval process we also had intense discussions and communications with the regulators," Mr Mujais said. "This is the beauty of the European process. There really is no delay in the communications, it is always ongoing. That's important when the clinical programme is really quite vast."

Mr Mujais would not comment directly on why he thought the US FDA came to a different conclusion about roxadustat's risks and benefits. But the way Fibrogen handled the disclosure of trial results – including publishing and initially submitting the wrong data to the US regulator – has been widely criticised.

Roadblocks and green lights

In the wake of an FDA advisory committee meeting that refused to overlook roxadustat's potential cardiovascular risks, the US regulator decided not to approve the drug without another trial. Europe, however, gave a green light with a broad label encompassing both populations that had been studied: anaemic kidney disease patients on dialysis, and those that have yet to progress to dialysis. Astellas branded the drug Evrenzo.

The EMA concluded that Evrenzo carried no greater risks than erythropoietin agents (Epo), which have been standard of care for anaemia in CKD for decades. Professor Jonathan Barratt, a consultant nephrologist at the UK's University of Leicester and a principal investigator on several of the roxadustat studies, believes that the

approval marks a big step forward for the treatment of renal anaemia.

“My experience within the trials has been incredibly positive. I see no reason why I would not use roxadustat in line with how it has been approved,” he told *Evaluate Vantage*.

He would also not comment on why the FDA might have adopted such a different stance.

“The EMA have looked at the data, and the way it was put forward, and have [concluded] that this drug is effective and carries no additional risks above what we already use,” he said.

Advantages

Safety arguments aside, Evrenzo does have advantages over infused Epo agents, its oral administration being the most obvious. Astellas believes that this will be particularly important when it comes to use in the pre-dialysis population, where anaemia can sometimes be under-managed.

“This population has a huge unmet need for many of the consequences of kidney disease including anaemia,” said Mr Mujais.

And while safety concerns will be more acute in this less sick population, Professor Barrett is convinced that Evrenzo has a role here.

“There isn’t a patient where I wouldn’t want to treat the anaemia because anaemia is so devastating,” he said. “The decision to use this drug – as with any drug – is based on the individual patient. And while safety is at forefront of everything we do, we also need to think about healthcare utilisation.”

Roxadustat trials have shown that patients need less iron supplementation than those given Epo, Professor Barrett pointed out.

“Here we can give you a tablet that makes you less reliant on iron infusions. In a healthcare system stretched by Covid, having a drug that doesn’t use the same resources as Epo will be a welcome relief,” he said.

The real world

Ultimately, however, the perceived safety profile of Evrenzo will dictate the how quickly physicians turn to the drug. Professor Barratt and Mr Mujais – a former nephrologist – stressed that roxadustat’s label warnings were exactly what physicians already looked out for when treating renal anaemia. However it is not inconceivable that those less closely involved in the development path will take more convincing.

Analysts are expecting a slow launch. Astellas is forecast to book global sales of $542m by 2026, according to *Evaluate Pharma*’s sellside consensus. The company has said it expects sales to peak somewhere between $500m and $1bn a year, a fairly wide range that suggests an outlook that is hard to predict.

What could swing sentiment is data on the next HIF stabiliser in the queue: Glaxosmithkline’s daprodustat. The UK pharma giant has declared the clinical programme a success, and said that the project was non-inferior to Epo agents on the risk of major cardiac events.

Presentation of the full results remains important. A closer look might confirm particular safety signals that would justify the FDA’s caution. Alternatively, the data could lend support to the EMA’s stance, which can be read as a pragmatic attempt to improve the treatment of anaemia in kidney disease, which as things stand is far from perfect.

Having a second HIF stabiliser approved in Europe would certainly help Astellas win the safety argument, albeit increasing competition at the same time. In the meantime all developers working in this space will be watching Evrenzo's reception very closely. Changing the FDA's mind about this class would also provide a big boost, although that is a challenge that lies in other companies' hands.