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After the Aduhelm euphoria, reality bites

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The practicalities of actually selling the controversial new Alzheimer's drug are proving increasingly difficult for Biogen.

Before Aduhelm's divisive US approval last month the Alzheimer's drug's 2026 sales forecasts had stood at a puny $1.9bn, according to *Evaluate Pharma's* archived consensus. But the green light prompted several banks to upgrade this to over $7bn.

Now everything could change again as a chaotic week for Biogen comes to a close with the company's stock 12% adrift. Yesterday's slapdown from Icer, which voted 15-0 that Aduhelm was not cost effective, crowned news that the FDA was under investigation over allegations of impropriety in the approval process, and that two major US clinics were refusing to administer the drug to patients.

What does this portend for Biogen? The absolute worst case has Aduhelm's approval rescinded, though analysts see no possibility of this at present. More likely is that the drug generates insignificant sales, at least initially, a scenario backed by comments on yesterday's Icer panel by Mark McClellan, a former head of the FDA.

In a session after Icer's vote Mr McClellan said access to Aduhelm would be "pretty limited" while many payers awaited a coverage decision from Medicare in April 2022. He said most people who qualified for Aduhelm did not "have an easy path" to getting the drug.

No infusion

The issue of clinics refusing to infuse Aduhelm is separate. On Wednesday the New York Times reported that the Cleveland Clinic and Mount Sinai Health System had refused to put the Biogen drug on their formularies, which they can do on the grounds of patient choice; apparently doctors at these hospitals can still prescribe Aduhelm, but patients have to go elsewhere to be infused.

This in itself is no huge deal – unless of course other big clinics follow suit. But the gathering snowball that promoted these formulary decisions should give pause.

It seems that, at least in Mount Sinai's case, the move is not based on Aduhelm's cost but on questions the centre has about the propriety of the approval and the FDA's relationship with Biogen, according to the New York Times.

This refers to the FDA's acting commissioner, Janet Woodcock, a week ago instructing the US Department of Health and Human Services' Office of Inspector General to review the interaction between the FDA and Biogen

during the Aduhelm approval process “to determine whether any of those interactions were inconsistent with FDA policies and procedures”.

And that particular can of worms had been opened up by a Stat exposé, whose most explosive claim was that in 2019 Billy Dunn, director of the FDA’s office of neuroscience, had held an informal and undocumented meeting with Al Sandrock, Biogen’s head of R&D, to discuss Aduhelm’s filing and approval. If true this would likely have violated FDA policy.

Noise and stress

Still, the sellside has largely dismissed the investigation, Stifel opining that it had no “tangible impact on Aduhelm” and calling it “more noise and stress” for investors.

However, the risk to Aduhelm comes not from a single event but from a tsunami of various factors that combine to limit patient access to the drug.

Approval had prompted RBC to put 2026 Aduhelm sales expectations at $7.5bn, while Leerink pencilled in $8.2bn, and consensus peak sales stands at around $9bn. At least some of this must now be at risk, judging by Biogen’s share price, which has drifted 20% since the euphoria around Aduhelm’s approval.

Biogen probably did not help itself when it priced the drug at $56,000 per patient per year, a cost that would have bankrupted the US healthcare system were Aduhelm to be prescribed to all patients captured by its initial label.

It is telling that even Biogen seemed to have been surprised by the approval’s breadth, and quickly recognised the consequences. Just weeks later – apparently at the company’s instigation – the label was narrowed to the early-stage population studied in phase 3 (*Narrowed label for Biogen’s Aduhelm lays bare FDA’s fail, July 8, 2021*).

The controversy has made the FDA in particular look bad, something not helped by the resignations of three members of the adcom that had voted against Aduhelm’s approval.

It is ironic that had the FDA proceeded with more caution, perhaps requesting more data and delaying approval, or giving an initial greenlight in a very narrowly defined population, it would have avoided much of the current mess. The question with which investors now have to grapple is how much of the resulting opprobrium directly hits Biogen and Aduhelm’s sales.

The episode shows that it pays to be careful what you wish for. Aduhelm’s path in the real world will not be as smooth as many analysts had initially thought.