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Questions Surround FDA's Orphan Drug Exclusivity Approach

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On Jan. 24, the U.S. Food and Drug Administration issued a notice to clarify orphan drug exclusivity following the U.S. Court of Appeals for the Eleventh Circuit's 2021 ruling in Catalyst Pharmaceuticals Inc. v. Becerra.

The notice indicates the FDA's intention to continue to apply its orphan drug regulations such that the scope of orphan drug exclusivity is tied to the specific orphan indication for which a drug is approved, not the indication for which the drug was designated.

This contrasts with the Eleventh Circuit's decision in the Catalyst case.

Absent a legislative fix, the FDA's application, or lack thereof, of the Catalyst decision will likely position the agency for future challenges and also lends uncertainty to the ultimate scope of current and future periods of orphan drug exclusivity.

Catalyst Pharmaceuticals v. Becerra

Catalyst Pharmaceuticals v. Becerra involved a dispute regarding the scope of orphan drug exclusivity for two products containing the same active moiety, amifampridine, which were each indicated for a subset of patients with Lambert Eaton Myasthenic Syndrome, or LEMS.

Firdapse received orphan drug designation for the broad indication of LEMS in 2009 and was initially approved for the narrower indication of LEMS in adults in 2018, receiving seven years of orphan drug exclusivity.

Ruzurgi was also designated as an orphan drug for LEMS and was approved in 2019 for the narrower indication of LEMS in pediatric patients.

Because the FDA viewed the adult and pediatric indications to be different product uses, it concluded that the later Ruzurgi approval did not violate the Firdapse orphan drug exclusivity. In doing this, the FDA followed its long-standing policy that the scope of orphan drug exclusivity is tied to the approved product indication.

On appeal, however, the Eleventh Circuit found that the FDA's interpretation of the scope of orphan drug exclusivity contravened the unambiguous language in the Federal Food, Drug and Cosmetic Act.

Specifically, the court found that, under the FFDCA, orphan drug exclusivity prevents the FDA from approving two drugs that are deemed to be the same for the same designated rare disease.

Thus, because Firdapse was broadly designated for LEMS, even though Firdapse was originally approved for use only in adults, the FDA was blocked from approving another amifampridine product for any LEMS indication, absent a demonstration of clinical superiority. The FDA did not appeal this decision.

FDA's Take on Catalyst

Following the Catalyst decision, the FDA issued a statement on its website that outlined the key impacts of the case. The FDA stated that it would "need to consider how the decision affects drugs with active terms of orphan drug exclusivity as well as currently marketed drugs, including generics."

The FDA also stated that it expected "that some drugs that are in late-stage development, or that have already been submitted for marketing application review, would be blocked from approval under the Catalyst decision's interpretation of the Act."

Additionally, as a result of the decision, the FDA stopped posting exclusivity end dates and exclusivity protected indications to its orphan drug database.

In an abrupt about-face, however, the FDA's Jan. 24 Federal Register notice takes a different position.

Specifically, the FDA stated that it viewed the holding in the Catalyst case to be confined to the particular products at issue and that it "intends to continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved."

The FDA provided two main reasons behind its approach: (1) the FDA believes that the statute does not unambiguously require that exclusivity extend to the entire disease or condition which has been designated; and (2) the FDA believes that its statutory interpretation best advances the Orphan Drug Act's purposes, balancing the need to incentivize sponsors to develop drugs for rare diseases with the need to provide patient access to orphan drugs.

While, for at least the time being, the FDA is intent on following its historic approach to orphan drug exclusivity, the FDA's latest announcement raises a number of considerations.

As the FDA has remained silent on orphan drug exclusivities for products approved after the Catalyst decision, there is currently a backlog of exclusivity determinations awaiting FDA response. At this time, it is unclear whether the FDA intends to go back to address this gap or whether it will only make determinations on an as needed basis, e.g., if a second product sponsor submits a marketing application.

Sponsors who either have received approvals without exclusivity determinations or sponsors who have a need for information regarding the scope of existing exclusivities may want to consider formally requesting a decision by the FDA.

Given the split between the FDA's and the court's interpretation of the FFDCA, absent congressional action, it is likely a company whose exclusivity is drawn more narrowly to the approved indication may

challenge the decision.

In view of the decision, companies may reconsider strategies for requesting designations, going with as broad a designation as can be substantiated, in the event of another challenge and court decision adopting the rationale in the Catalyst decision. Whether the FDA will continue to allow broad designations could also be under consideration.

There may be a legislative fix to the FFDCA, to clarify the scope of orphan drug exclusivity. Such a fix was proposed in drafts of the FDA user fee reauthorization bills but did not ultimately make it into the final legislation.

Absent a legislative fix or further court action, there still remains uncertainty regarding the exact scope of orphan drug exclusivity periods. This may cause challenges for product sponsors, for instance, when seeking funding and speaking with investors.

Finally, while this notice provides clarity on the FDA's intention to limit orphan drug exclusivity to a product's approved use or indication, sponsors should monitor further developments as the agency continues to implement its interpretation of the statute.

It is possible that we may see modifications to the FDA's approach to orphan designations and exclusivities. By example, we may begin to see the FDA narrowing the scope of orphan drug designations to the specific indication that is under investigation.

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