March 10, 2025

Dr. Sara Brenner
Acting Commissioner
Dockets Management Staff (HFA-305),
U.S. Food and Drug Administration,
5630 Fishers Lane, Rm. 1061,
Rockville, MD 20852

Submitted electronically via regulations.gov

Re: Accelerated Approval and Considerations for Determining Whether a Confirmatory Trial is Underway (FDA-2024-D-3334)

Dear Dr. Brenner:

The Academy of Managed Care Pharmacy (AMCP) thanks the Food and Drug Administration (FDA) for the opportunity to provide comments in response to the "Accelerated Approval and Considerations for Determining Whether a Confirmatory Trial is Underway" (Draft Guidance).

AMCP is the nation's leading professional association dedicated to increasing patient access to affordable medicines, improving health outcomes, and ensuring the wise use of healthcare dollars. Through evidence and value-based strategies and practices, AMCP's nearly 8,000 pharmacists, physicians, nurses, and other practitioners manage medication therapies for the 270 million Americans served by health plans, pharmacy benefit management firms, emerging care models, and government health programs.

Accelerated approval is an important topic for managed care organizations (MCOs). Providing access to medications for patients is vital. Manufacturers and MCOs alike want to provide access to medications to help patients with unmet medical needs as early as possible. At the same time, MCOs need greater certainty about safety and efficacy and often find that available clinical data falls short. MCOs may face financial risk for covering products subject to accelerated approval, especially if these products prove not to be effective.

Need for Greater Transparency

AMCP commends the FDA for clarifying the accelerated approval process for confirmatory trials, which helps expedite access to life-saving medications. While FDA approval is necessary for patient access to these drugs, it does not guarantee payer coverage. Transparency during confirmatory trials is essential for payers as "the evidence available at product launch is often limited to small, single-arm studies using surrogate or intermediate endpoints with uncertain meaning."[1]

[1] AMCP Partnership Forum: Addressing Evidence Gaps in the FDA Accelerated Approval: Payer Perspectives. (2023) Available at: https://amcp.org/sites/default/files/2024-02/Addressing-Evidence-Gaps-in-Accelerated-Approval-Programs-Payer-Perspectives.pdf

AMCP recommends providing public access to anticipated trial timelines at the time of accelerated approval. AMCP also supports proactive communication of progress data when delays occur during confirmatory trials to enhance transparency and provide important insights into the development of therapies. This interim data could be useful in assessing treatment effectiveness while awaiting more comprehensive results.

AMCP urges the FDA to standardize public reporting of deviations from trial timelines. AMCP is concerned that when timelines are not met, patients' exposure to drugs with insufficient evidence may unreasonably be extended. AMCP is also concerned by the continued availability of accelerated approval therapies after clinical outcomes are not met in confirmatory trial.

Confirmatory Trials

Payers need sufficient information about product effectiveness, safety, offsets of medical costs, and economic endpoints when considering the value of covering a medication approved under the accelerated approval pathway. Payers need sufficient information to correlate surrogate outcomes with expected medical cost offsets. Completion of rigorous confirmatory trials provides valuable data for these stakeholders.

AMCP believes that the FDA should embrace flexibility in the timing of confirmatory studies. Confirmatory trials should begin earlier in the clinical trial program in those cases where an earlier indicator or earlier start could be initiated. Short trial periods may be insufficient to ascertain therapies' long-term value. Many treatments require time to demonstrate their full impact, and follow-up trials often underscore the importance of prolonged observation to reveal significant long-term therapeutic effects.

AMCP also encourages FDA to integrate an expert advisory committee early in the discussions with sponsors and to require correlation of surrogate endpoints with meaningful clinical outcomes to increase payer confidence in the treatment effects of medications. This would serve to strengthen and validate the plan as it relates to trial design, evaluate the strength of surrogate endpoints, and assess the timing of confirmatory trial results.

Conclusion

AMCP appreciates your consideration of these concerns and looks forward to continuing work on these issues with the FDA. If you have any questions regarding AMCP's comments or would like further information, please contact Vicky Jucelin, AMCP's Manager of Regulatory Affairs, at vjucelin@amcp.org or (571) 858-5320.

Sincerely,

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