March 6, 2025

Sara Brenner, Acting FDA Commissioner
Food and Drug Administration
5630 Fishers Lane, Rm.
1061 Rockville, MD 20852

RE: FDA-2024-D-2033 for "Expedited Program for Serious Conditions—Accelerated Approval of Drugs and Biologics"

Dear Acting Commissioner Brenner:

ACHP members are dedicated to providing life-saving treatments to patients with limited options. However, the lack of transparency in the accelerated approval pathway leaves more questions than answers regarding the efficacy of these treatments, which are often the priciest in the U.S. healthcare system. We appreciate the opportunity to comment on the FDA's draft guidance – *Expedited Program for Serious Conditions- Accelerated Approval of Drugs and Biologics* – to address open questions in the program and ensure the right medications reach the right patients under the right conditions and at the right price.

ACHP is the only national organization advancing a unique payer-provider aligned model of health care that fosters true competition, delivering both high-quality coverage and care. As regional, non-profit insurers, ACHP member companies provide affordable coverage options to tens of millions of Americans in nearly 40 states and D.C., remaining in their markets even when other health plans exit. The sustainability of regional health plans is of paramount importance to an innovative and competitive insurance industry, ensuring consumers have robust choices for their health coverage.

Clear and well-defined procedures for drug qualification and withdrawal are essential to building trust in the accelerated pathway and expanding coverage for approved drugs. ACHP strongly recommends that the FDA support reduced pricing for drugs approved through the accelerated approval pathway, establish clear timelines for post-approval confirmatory trials, provide rationale and reassessment of surrogate endpoints and expand use of real-world evidence. Only with these steps can we as a nation ensure that Americans are not wasting precious health care dollars on drugs that do not measure up to the early hype.

ACHP offers the following recommendations to increase data sharing and transparency:

1. **Lower prices for accelerated approval therapies until post-approval confirmatory trials validate the predicted clinical benefit(s).**

ACHP requests that the FDA recognize the cause-effect relationship of the high costs of drugs approved through the accelerated approval pathway, as drugs granted accelerated approval have 26% more price increases over 10 years than other medicines[1]. ACHP strongly recommends the FDA require manufacturers

[1] Bach, P. B. (2022, July 25). 5 things to know about the FDA's flawed approach to accelerated drug approvals. NPR. https://www.npr.org/sections/health-shots/2022/07/25/1113098072/5-things-to-know-about-the-fdas-flawed-approach-to-accelerated-drug-approvals

to charge a substantially reduced price for approved drugs until clinical benefits are confirmed through post-approval confirmatory trials and real-world evidence.

2. **Clear timelines for post-approval confirmatory trials with rationale made public at time of approval.**

The US health care system would benefit from knowing as early as possible if a drug approved through the accelerated pathway actually delivers the predicted clinical benefit. Regulators should publicly provide prompt timelines for post-approval confirmatory trials upon approval, including, but not limited to, patient recruitment requirements, significant trial milestone(s) and trial completion date(s). Post-approval confirmatory trials should be limited to two years after approval to validate the predicted clinical benefit. The rationale for post-approval confirmatory trial conditions – including milestones, enrollment goals, patient recruitment and timelines – should be publicly available at time of approval. Any uncertainty regarding the benefit-risk profile of the approved dosage(s) should be disclosed at the time of approval on the product label.

ACHP recommends that the FDA facilitate data sharing from international regulatory bodies' accelerated approval programs to enhance U.S. approvals. Collaborative and adaptive trial designs enable study modifications based on interim results, ensuring promising therapies are studied more efficiently. Additionally, collaboration between the FDA, pharmaceutical companies, academic institutions and advocacy groups is essential to design trials that are both scientifically rigorous and patient centered.

3. **Clear definition of the evidence required for a drug to be considered 'reasonably likely' to provide clinical benefit.**

ACHP supports the Office of Inspector General roadmap for FDA to improve the integrity of accelerated approval. The December 2022 House Oversight and Reform Committee's investigation into the approval process and pricing of Biogen's Alzheimer's disease drug, Aduhelm, highlights the presence of atypical procedures and deviations from the FDA's own guidance[2].

Prior to approval, the FDA should precisely define how surrogate endpoints used in post-approval confirmatory trials will constitute as "reasonably likely" to demonstrate clinical benefit. ACHP recommends the FDA provide a compendium of the agency's interpretation of the criteria in the accelerated approval pathway over time and across different treatment areas. ACHP also recommends periodically reassessing surrogate endpoints used in post-approval confirmatory trials to ensure they remain 'reasonably likely' to demonstrate clinical benefit to patients with different disease stages, with regulatory requirements updated as new data emerges. Leveraging unclear surrogate endpoints leads to false hope for patients, wasted health care dollars and the diversion of pharmaceutical investment away from effective therapies.

[2] Maloney, E., & Pallone, F. (2022, December 29). Maloney and Pallone release staff report on review, approval, and pricing of Biogen's Alzheimer's drug Aduhelm. House Committee on Oversight and Reform. https://oversightdemocrats.house.gov/news/press-releases/maloney-and-pallone-release-staff-report-on-review-approval-and-pricing-of

4. **Expand use of real-world evidence with standardized methods for collecting and analyzing data.**

Real-world evidence provides insights into how drugs perform in broader, more diverse populations and helps identify long-term outcomes — often significantly different from the initial trial. ACHP recommends the FDA develop a robust framework for ongoing monitoring using both post-approval confirmatory trial data and real-world clinical outcomes to adjust terms of approval based on new evidence. Adjustments should include scaling back indications or revoking accelerated approval when real-world data does not confirm the clinical outcomes in post-approval confirmatory trials.

Until real-world evidence confirms their effectiveness, private plans should not be bound to cover drugs approved through the accelerated approval pathway. Mechanisms such as marginal cost pricing or alternative funding should be considered. If a post-approval confirmatory trial fails to show clinical benefit within the specified timeframe, withdrawal proposals should not be delayed by public comment periods or advisory committee meetings.

Thank you for your consideration of ACHP's recommendations to balance scientific uncertainty, risk acceptance and high prices for treatments coming out of the accelerated approval pathway. We look forward to partnering with the FDA to drive value, quality and competition. Please contact Carmen Witsken, Senior Manager, Pharmacy policy (cwitsken@achp.org) with any questions or to discuss our recommendations further.

Regards,

Ceci Connolly
President and CEO, ACHP