



1700 K Street, NW | Suite 740 | Washington, DC 20006
T 202.293.2856
www.agingresearch.org
@Aging_Research

March 10, 2021

Mara L. Becker, MD, MSCE
Chairperson
Arthritis Advisory Committee
Food and Drug Administration
Vice Chair, Faculty
Department of Pediatrics
Division of Pediatric Rheumatology
Duke University School of Medicine
Duke Clinical Research Institute
2301 Erwin Road, T901
Durham, North Carolina 27705

Sonia Hernandez-Diaz, MD, MPH, DrPH
Chairperson
Drug Safety and Risk Management Advisory
Committee
Food and Drug Administration
Professor of Epidemiology
Department of Epidemiology
Harvard T.H. Chan School of Public Health
677 Huntington Avenue, Room 816
Boston, Massachusetts 02115

Docket No. FDA-2021-N-0134 for "Joint Meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments."

Dear Dr. Becker and Dr. Hernandez-Diaz,

The [Alliance for Aging Research](http://www.agingresearch.org) (Alliance) is the leading nonprofit organization dedicated to accelerating the pace of scientific discoveries and their application to vastly improve the universal human experience of aging and health. The Alliance believes that research-enabled advances help people live longer, happier, more productive lives and reduce healthcare costs over the long term. Further, access to the latest scientific information empowers people to take control of their health. The Alliance strives to advance science and enhance lives through a variety of activities and initiatives – from policy issues to provider and consumer health programs – that generate knowledge and action on age-related matters.

On March 24-25, 2021, the Food and Drug Administration's Arthritis Advisory Committee and Drug Safety and Risk Management Advisory Committee will meet to discuss the biologics license application (BLA) 761130, tanezumab subcutaneous injection for the proposed indication of relief of signs and symptoms of moderate to severe osteoarthritis in adult patients for whom the use of other analgesics are ineffective or inappropriate. As an organization representing older adults' healthcare interests, the Alliance has engaged in educational activities to inform older adult consumers on the potential risks of pain management

Alliance for Aging Research

Docket No. FDA-2021-N-0134 for “Joint Meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments.”

medications while advocating that older adults have access to appropriately prescribed medications to address pain. While the Alliance does not take a position on whether the evidence provided by the sponsor company is sufficient to meet the gold standard of the FDA, we urge you to holistically consider the current absence of medications to address chronic pain, the side effects of existing medications to address pain in osteoarthritis, and benefit-risk preferences of patients with severe pain associated with osteoarthritis.

The burden of persistent pain for older adults is significant

Nearly 100 million Americans live with persistent pain.¹ As adults age, they are more likely to report suffering from pain, resulting in reduced mobility, avoidance of activity, falls, depression, anxiety, isolation, and sleep impairment.² The incidence of persistent pain increases with age. Approximately 65 percent of adults 65 years of age and older report suffering from pain, and 30 percent report suffering from chronic pain, which is defined as persistent pain lasting over three months.³

Older patients with persistent pain are too often undertreated or do not receive the appropriate therapy. Psychosocial factors, like the tendency of older adults to underreport their pain and the lower adherence rates to prescribed pain medications, complicate pain assessment and treatment. Older adults are also more likely to have comorbidities and are more susceptible to polypharmacy, impacting choices and consequences of therapies.⁴

Additionally, prescribing treatment can be complicated since opioids in older adults increase fall risk and confusion and can produce other negative side effects. Treatment is often further complicated by the fact that opioid medications, while highly effective for many patients, do carry the risk of addiction and must be managed in a manner best suited for the individual.

Osteoarthritis is one of the most common conditions causing pain in older adults

Osteoarthritis, affecting an estimated 32.5 million individuals in the United States, is one of the most common conditions causing persistent pain in older adults, significantly reducing quality of life.⁵ However, there are no treatments available to slow or reverse the destruction of joint structures that lead to pain and disability for the condition.⁶ The chronic nature of the condition

¹ Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. Relieving pain in America: a blueprint for transforming prevention, care, education, and research. National Academies Press (US), 2011.

² Ibid.

³ https://www.painconsortium.nih.gov/sites/default/files/aging_and_chronic_pain_infographic_508.pdf

⁴ <https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/protocol#2>

⁵ <https://www.cdc.gov/arthritis/basics/osteoarthritis.htm>

⁶ <https://onlinelibrary.wiley.com/doi/full/10.1002/acr.22721>

Alliance for Aging Research

Docket No. FDA-2021-N-0134 for “Joint Meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments.”

and the absence of effective analgesics for late-stage osteoarthritis make this one of the largest areas of unmet medical need for older adults.

Current therapies to address osteoarthritis pain are nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, opioids, and medications that modify central sensitization of pain. However, these therapies have both limited efficacy for late-stage osteoarthritis pain management and toxicity concerns that make them not suitable for all patients.

For example, NSAIDs can cause severe stomach bleeding, which may occur without any noticeable symptoms. Older age is a major risk factor for NSAID-related stomach bleeding. Other risk factors may be associated with age-related conditions, including high blood pressure, heart disease, liver damage, kidney disease, or asthma. The FDA has warned that all NSAIDs, except aspirin, can increase the risk for heart attack and stroke, either of which can lead to death.⁷

The lack of effective pain therapies for osteoarthritis patients means millions of patients live with disabling persistent pain that makes routine activities of daily living nearly impossible. According to survey results of nearly 2,000 osteoarthritis patients conducted by the Arthritis Foundation, only 15 percent of patients report that their condition is "well-managed."⁸ There is a great need for alternative therapies to relieve the disabling chronic pain associated with osteoarthritis.

The overarching goal of chronic pain management is to relieve pain and improve function. The National Pain Strategy report recommends that management be integrated, multimodal, interdisciplinary, evidence-based, and tailored to individual patient needs.⁹ In addition to addressing biological factors when known, it is thought that optimal management of chronic pain also addresses psychosocial contributors to pain while taking into account individual susceptibility and treatment responses.

As the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee review the application for tanezumab for the treatments of moderate to severe osteoarthritis, we urge the consideration of the unmet medical need faced by older adults with pain and osteoarthritis patients. The Committees should first and foremost carefully examine osteoarthritis patients' perspectives on clinical outcomes of importance. Second, the Committees should specifically evaluate benefit-risk considerations of tanezumab to best serve

⁷ <https://www.fda.gov/consumers/consumer-updates/fda-strengthens-warning-heart-attack-and-stroke-risk-non-steroidal-anti-inflammatory-drugs>,

⁸ <https://www.arthritis.org/about-us/news-and-updates/covid-19-survey-of-oa-patients>

⁹ National Pain Strategy Task Force. National Pain Strategy: A Comprehensive Population Health-Level Strategy for Pain. Interagency Pain Research Coordinating Committee (IPRCC), National Institutes of Health (NIH); 1-83. 2015. https://iprcc.nih.gov/National_Pain_Strategy/NPS_Main.htm.

Alliance for Aging Research

Docket No. FDA-2021-N-0134 for “Joint Meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments.”

this patient community's interests. Risk tolerance discussions should include pain management versus the potential for OA disease progression.¹⁰ Recent studies suggest that the risk of rapidly progressive OA with tanezumab was greatest when co-administered with NSAIDs¹¹ or with increased dosage levels,¹² which are both important considerations for clinician and patient shared decision-making. If approved, the health care providers prescribing tanezumab must be well informed about the medication's potential side effects and the patient population for which this treatment is most appropriate.

Thank you for the opportunity to provide comments on the upcoming Advisory Committee meeting. Please contact Ryne Carney, Manager of Public Policy, at rcarney@agingresearch.org with any questions or additional information requests.

Sincerely,



Susan Peschin, MHS
President and CEO
Alliance for Aging Research



Ryne Carney
Public Policy Manager
Alliance for Aging Research

¹⁰ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6613301/>

¹¹ <https://www.dovepress.com/safety-and-efficacy-of-subcutaneous-tanezumab-in-patients-with-knee-or-peer-reviewed-article-JPR>

¹² <https://jamanetwork.com/journals/jama/fullarticle/2737173>