FDA Advisory Committee for exagamglogene autotemcel (Exa-cel) Gene Therapy for SCD

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Sick Cells Webinar - October 9th, 2023

Housekeeping

- Today's webinar is being recorded.
- During the meeting, please minimize your distractions.
- Mute your mic when you aren't speaking.
- We are encouraging video participation to make our group feel more engaged during discussions.
- The recording will be available on the Sick Cells YouTube Channel.

Agenda

- Background of FDA Advisory Committees
- The Importance of FDA Advisory Committees
- History of FDA Advisory Committees for Sickle Cell Disease
- FDA Advisory Committee for Exa-cel Gene Therapy

Background

What is an FDA Advisory Committee?

- The Food and Drug Administration (FDA) is responsible for evaluating the **efficacy and safety** of new therapies.
  - Sometimes requires outside expertise
- The FDA Advisory Committee (Ad Comm) is composed of **outside experts** to help the FDA come to a conclusion of therapy approval.
  - Provide advice on the **safety, efficacy, and appropriate use of products**.
- There are **49** FDA Advisory committees.

Background

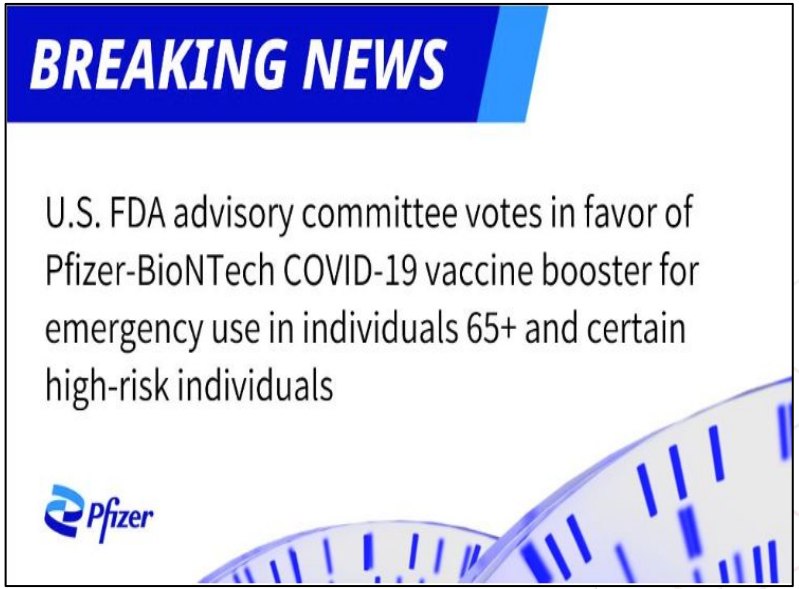
Why does the FDA use advisory committees?

- To include independent experts that work outside of the government
- Work towards an open government by giving the public a voice
- **Encourages patients, caregivers, healthcare professionals, and many more from the public to share their experiences and submit comments.**

Background

When does the FDA use advisory committees?

- The FDA can choose any time during or after the **approval process** to convene an advisory committee.
- When there is **insufficient** scientific evidence of a therapy during clinical trials.
- When a pharmaceutical company applies for accelerated approval or **Fast Track**.



Vaccine Related Biological Products Advisory Committee (VRBPAC)

FDA Applications and Designations

- **Application Types**
- Investigational New Drug (IND) Application.
- New Drug Application (NDA)
- Abbreviated New Drug Application (ANDA)
- **Biologics License Applications (BLA)**
- Drug Applications for Over-the-Counter (OTC) Drugs.

Designations

- **Priority Review**
  - The FDA's goal is to decide on an application within 6 months.
- Breakthrough Therapy
- Accelerated Approval
- Fast Track

Background

Who makes up the FDA advisory committees?

- **Scientific Experts**
  - Researchers, biologists, chemists, clinician-researchers
- **Consumer Representative**
  - Knowledge of consumer rights and needs
- **Industry Representative**
  - May or may not have the ability to vote
  - Present how specific issues can affect the industry
- **FDA Patient Representative**
  - Recruited through the FDA Patient Representative Program
  - Provide input and share disease and treatment experiences

The Importance of an FDA Advisory Committee

“These meetings often represent the FDA's first public discussion of a new medical product and can be an invaluable source of information for patients, health care providers, and others who are interested in the product.”

***-**Linda Ann Sherman, M.D., M.P.A., former director of the FDA's Advisory Committee Oversight and Management Staff.*

Center for Drug Evaluation and Research. “Advisory Committees: Critical to the FDA’s Product Review Process.” *U.S. Food and Drug Administration*, FDA, 4 May 2016, www.fda.gov/drugs/information-consumers-and-patients-drugs/advisory-committees-critical-fdas-product-review-process.

Primary Roles of the FDA Advisory Committee

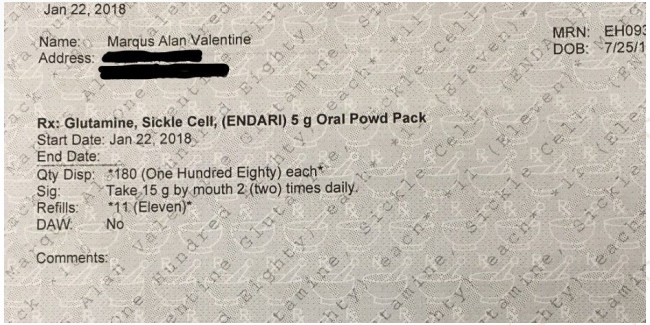
- Provide **independent** expert advice as the FDA evaluates products.
- **Review** and **evaluate** safety, effectiveness, and appropriate use data.
- Discussions are to help ensure the public is clear about the **FDA's expectations**.
- This process and **transparent**, **independent**, and **open to the public**.

History of FDA Advisory Committees for Sickle Cell Disease

- Hydroxyurea®
- Endari™ (L-glutamine)
- FDA Advisory Committee information for other SCD therapies

FDA Advisory Committee Recommends Approval of Endari™ from Emmaus Life Sciences for the Treatment of Sickle Cell Disease

Thursday, May 25, 2017


Jan 22, 2018

Name: Marqus Alan Valentine
Address: [redacted]

MRN: EH093
DOB: 7/25/1

Rx: Glutamine, Sickle Cell, (ENDARI) 5 g Oral Powd Pack
Start Date: Jan 22, 2018
End Date:
Qty Disp: *180 (One Hundred Eighty) each*
Sig: Take 15 g by mouth 2 (two) times daily.
Refills: *11 (Eleven)*
DAW: No

Comments:

Hydroxyurea®: December 1997

The first FDA advisory committee convening for SCD therapy.

- The advisory committee voted on a **unanimous** decision on recommended approval of hydroxyurea.
- The panel advised on conducting further studies on carcinogenicity.
  - FDA added on the label to require blood counts to be measured every 2 weeks.

Alicia Ault, US FDA approves first drug for sickle-cell anaemia, The Lancet, Volume 351, Issue 9105, 1998, Page 809, ISSN 0140-6736, https://doi.org/10.1016/S0140-6736(05)78941-8. (https://www.sciencedirect.com/science/article/pii/S0140673605789418)

Endari™: May 24, 2017

First SCD drug to be approved after 20 years and for pediatrics.

- **Marqus and Ashley Valentine, Juanita G, and Mary Brown** were speakers for the Oncologic Drug Advisory Committee (ODAC).
- The committee voted 10-3.
- **Approved** July 7th, 2017.

FDA Ad Comm not required for Oxbryta®

- Oxbryta® (voxelator) applied for accelerated approval on June 26, 2019.
  - Approved November 25, 2019.
- Advisory Committee was not required due to **significant evidence on safety and efficacy** during clinical trials.

FDA Ad Comm not required for Adakveo®

- Adakveo® (crizanlizumab-tmca) applied for priority review on May 16, 2019.
  - Approved November 15, 2019.
- Advisory Committee was not required due to **significant evidence on safety and efficacy** during clinical trials.

Lovo-cel from BlueBird Bio will not require an FDA Advisory Committee

- Bluebird Bio's gene therapy for SCD, **Lovo-cel**, applied for **priority review** for FDA approval.
- Advisory committee is not recommended from the FDA.
  - Previous FDA committees have **unanimously** recommended on the approval of BlueBird Bio gene therapies for Beta-Thalassemia.
- Prescription Drug User Fee Act (**PDUFA**) date: Deadlines for the FDA to respond to the application.
  - 10 months after the drug application has been accepted by the FDA
  - 6 months, if the drug is given a priority review.
  - **PDUFA date for Lovo-cel: December 20, 2023.**

FDA Advisory Committee for exagamglogene autotemcel (Exa-cel) Gene Therapy

The **Cellular, Tissue, and Gene Therapies Advisory Committee** will convene for the Vertex Pharmaceuticals, Inc. **priority** review for exagamglogene autotemcel (**Exa-cel)** on **October 31, 2023.**

Meeting Materials

- Background material will be available to the public no later than **2 business days** before the meeting (October 31, 2023).
- Background material will be available on the Advisory Committee Calendar (select “Cellular, Tissue, and Gene Therapies Advisory Committee”)

Public Participation

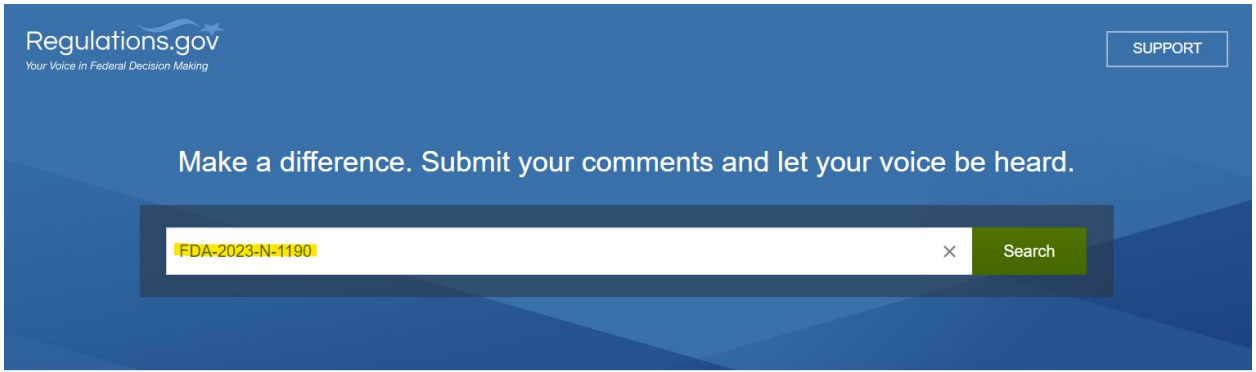
- The meeting will be recorded and broadcasted live from **9:00 am - 5:00 pm EST.**
- The public can submit comments:
  - Comments received **on or before October 24th** will be provided to the committee to be read during the meeting.
  - Comments received after that date until October 30th will go to the FDA and will be taken into consideration.
- **Electronic Submissions**
  - Portal: https://www.regulations.gov/
- **Written/Paper Submissions**
  - Mail: Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Oral Presentations

- Oral presentations from the public will be scheduled between approximately **12:35 p.m. and 1:35 p.m. Eastern Time.**
  - Approximately 3-5 minutes each for each speaker
- Submit a brief statement along with their **names, e-mail addresses, and direct contact phone numbers, and an indication of the approximate time requested** to make their presentation **by 12 p.m. Eastern Time on October 16, 2023.**
  - Speakers will receive a confirmation to speak by October 18, 2023 6 p.m. EST.
  - All submissions (written and oral) **must** include the following information:
  - **Docket No. FDA-2023-N-1190 for Cellular, Tissue, and Gene Therapies Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments-Sickle Cell Disease, Meeting Date: October 31, 2023**
- Speaker registration, please contact **Cicely Reese or Marie DeGregorio** CBERCTGTAC@fda.hhs.gov

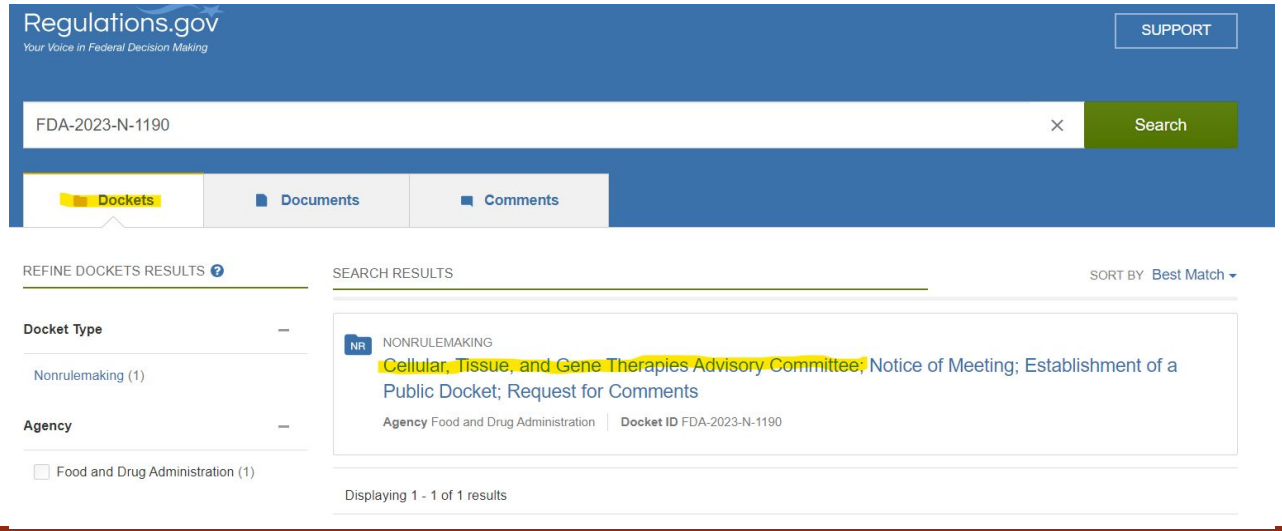
How to Submit an Electronic Submission for Public Comments

- **Step 1:** Access the electronic submission portal (https://www.regulations.gov/).
- **Step 2:** Copy the docket number (FDA-2023-N-1190) and enter it into the search function.



How to Submit an Electronic Submission for Public Comments Cont.

Step 3: Click the "Dockets" tab, you will then see the advisory committee *"Cellular, Tissue, and Gene Therapies Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments*".

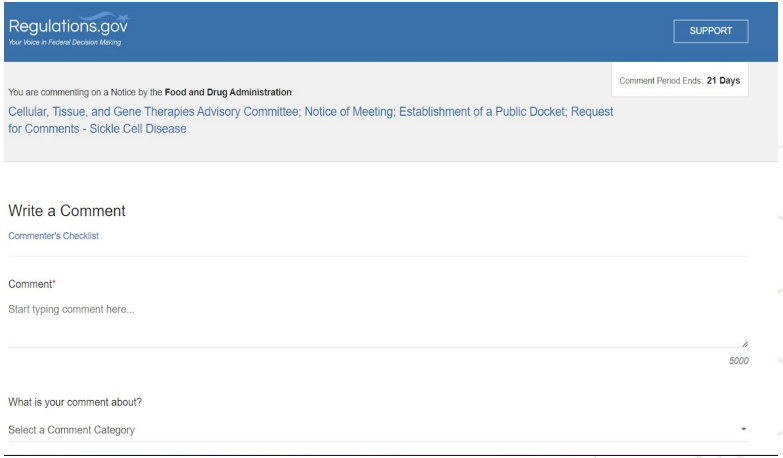


How to Submit an Electronic Submission for Public Comments Cont.

Step 4: Click the "Browse Documents" tab; you will then see the advisory committee "*Cellular, Tissue, and Gene Therapies Advisory Committee; Notice of Meeting; Establishment of a Public Docket; Request for Comments - Sickle Cell Disease*". This is where you will submit public comments.

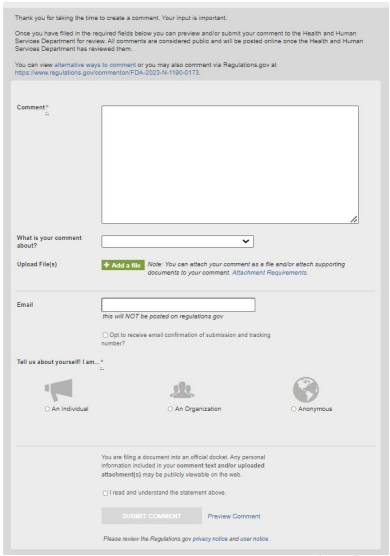
How to Submit an Electronic Submission for Public Comments Cont.

Step 5: After clicking the link, there will be a blue button for "*Comment*". You will see a fillable form to add your comments.



Alternate Way to Submit an Electronic Submission for Public Comments

- **Click the link to the federal register for the "Cellular, Tissue, and Gene Therapies Advisory Committee."**
- **Click the green button "Submit a Formal Comment"**



Additional Information

- **PDUFA date for exagamglogene autotemcel (exa-cel): December 8, 2023.**
- NIH Toolkit: Participate In FDA Advisory Committee Meetings: Providing Testimony
- NIH Toolkit: Participate In FDA Advisory Committee Meetings: Tips for Success
- Public Conduct for FDA Advisory Committee Meetings.
- Sick Cells Toolkit: Submitting Written Comments

Thank You!

Please feel free to contact Mariah Scott (mscott@sickcells.org) for additional questions!