

## **Review Memorandum**

**Date:** January 7, 2022

**To:** The File

**From:** Narayan Nair, MD (CBER/OBE)  
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**Through:** Peter Marks, MD, PhD (CBER/OD)

**Applicant:** Janssen Biotech, Inc.

**Application Number:** EUA 27205; amendment 230

**Product:** Janssen COVID-19 Vaccine

**Subject:** CBER Assessment of New Safety Information on Immune Thrombocytopenia (ITP) following Administration of the Janssen COVID-19 Vaccine

This review memorandum documents CBER's determination to provide new safety information regarding the serious risk of Immune Thrombocytopenia (ITP) following administration of the Janssen COVID-19 Vaccine in the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and in the Fact Sheet for Recipients and Caregivers for the Janssen COVID-19 Vaccine.

FDA/CBER has continually monitored the post authorization safety of COVID-19 vaccines through both active and passive surveillance as well as review of safety data submitted by the manufacturers. Information about ITP following administration of the Janssen COVID-19 Vaccine was shared with the Vaccines and Related Biological Products Advisory Committee at the October 15, 2021 meeting. A CBER analysis of reports submitted to the Vaccine Adverse Event Reporting System (VAERS) revealed new safety information on the serious risk of ITP following administration of the Janssen COVID-19 Vaccine. Reports were categorized as cases of ITP if the individual had a platelet count less than 150,000 or had received a diagnosis of ITP. As of September 30, 2021, 150 ITP cases occurring within 28 days following administration of the Janssen COVID-19 Vaccine were reported to VAERS. Reports were not adjudicated by hematologists. Reported cases occurred in males and females over 18 years of age; 134 (89%) of the reports were classified as 'serious,' and 15 reported an outcome of death. Eighty-six (57%) of these reports were in females. An observed-to-expected analysis (O/E) was performed based on vaccine administration data and published background rates of ITP. The overall rate ratio of ITP cases reported to VAERS to expected cases of ITP (O/E ratio) is 4.04 (95% CI 3.42, 4.72). The data from FDA's analysis are summarized in the appended document entitled "Update on Immune Thrombocytopenia (ITP)"

Based on their analysis of postmarketing data, on November 24, 2021, Janssen submitted an EUA amendment that included a request to revise the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) to include ITP in Warnings and Precautions and to revise the Fact Sheets for Recipients and Caregivers to address the risk of ITP. FDA reviewed Janssen's analysis of postmarketing data on ITP in addition to conducting its own analysis of reports of ITP submitted to VAERS.

The manufacturer's analysis differed from CBER's analysis in that it utilized a 42-day risk window. In addition, the manufacturer used a different case definition based on the American Society of Hematology definition which excluded reports with platelet counts between 100,000 and 150,000. Based on data through July 31, 2021, the manufacturer reported O/E of 3.557 (95% CI 3.042,4.134) for individuals 18-59 years of age and O/E of 3.060 (95% CI 2.441, 3.788) in those 60 years of age and older.

Based on CBER's analysis of VAERS data and CBER's review of Janssen's analysis, CBER determined that the currently available data suggest an increased risk of ITP following administration of the Janssen COVID-19 Vaccine. Considering the limitations of VAERS data, the seriousness of COVID-19, and the clear and compelling evidence that the Janssen COVID-19 Vaccine may be effective in preventing COVID-19, CBER has determined that the new safety information on ITP does not necessitate a formal reevaluation of the benefit-risk profile of the Janssen COVID-19 Vaccine. CBER has determined that the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) should be revised to include ITP in Warnings and Precautions. CBER also determined that the Fact Sheet for Recipients and Caregivers should be revised to include information on the occurrence of ITP following administration of the Janssen COVID-19 Vaccine, instructions for potential vaccine recipients to inform vaccination providers of a history of thrombocytopenia, and instructions for vaccine recipients to seek medical attention for symptoms of ITP. The revisions to the Fact Sheets are detailed below.

### **Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers)**

Addition of a new Warning and Precaution for ITP, as follows:

#### **Immune Thrombocytopenia (ITP)**

“Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of immune thrombocytopenia (ITP) during the 42 days following vaccination. Individuals with a history of ITP should discuss with their healthcare provider the risk of ITP and the potential need for platelet monitoring following vaccination with the Janssen COVID-19 Vaccine.”

### **Fact Sheet for Recipients and Caregivers**

Revisions to convey the following:

- Instruction for individuals who “have ever had a low level of platelets” to convey that information to the vaccination provider before receiving the Janssen COVID-19 Vaccine.
- “Immune Thrombocytopenia (ITP) is a disorder that can cause easy or excessive bruising and bleeding due to very low levels of platelets. ITP has occurred in some people who have received the Janssen COVID-19 Vaccine. In most of these people, symptoms began within 42 days following receipt of the Janssen COVID-19 Vaccine. The chance of having this occur is very low. If you have ever had a diagnosis of ITP, talk to your vaccination provider before you get the Janssen COVID-19 Vaccine. You should seek medical attention right away if you develop any of the following symptoms after receiving the Janssen COVID-19 Vaccine:
  - Easy or excessive bruising or tiny blood spots under the skin beyond the site of the injection,
  - Unusual or excessive bleeding.”

### **Recommendation**

Based on the analysis of VAERS data as well as Janssen's own assessments, CBER determined that safety information regarding ITP should be included in the Fact Sheets for the Janssen COVID-19

Vaccine. At the current time, CBER has determined that the known and potential benefits continue to outweigh the known and potential risks of the Janssen COVID-19 vaccine. As per statute, the benefit-risk profile of this vaccine will continue to be reevaluated at regular intervals while it is being made available under EUA.