Office of Biostatistics and Epidemiology/Division of Epidemiology
Periodic Safety Report Review Checklist

Completed by Reviewer

Product Name	Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)
Manufacturer	Pfizer
STN #	19736.366
DCC Login ID #	
Submission Type	**PAER** ☐ **PSUR** ☐ **PBRER** ☐ **PADER** ☐
Submission Format	**ELECTRONIC** ☑ **PAPER** ☐
Reporting Period	**FROM** April 30, 2021 **TO** May 31, 2021
Date Received by FDA	June 15, 2021
Date Routed to Reviewer	June 15, 2021
Regulatory Information Specialist (RIS) - Name	Ramachandra Naik
Reviewer - Name	Deborah Thompson
Reviewer Signature (electronic signature)	Deborah L. Thompson -S Digitally signed by Deborah L. Thompson -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2002552931, cn=Deborah L. Thompson -S Date: 2021.06.24 07:41:45 -04'00'

COMMENTS

Office of Biostatistics and Epidemiology/Division of Epidemiology
Periodic Safety Report Review Checklist

1. Countries where the product is licensed or authorized for distribution:

   Not Reported ☐ US ☐ Worldwide ☑

2. Estimated number of doses distributed by reporting period/cumulative:

   Not Reported ☐ US (b) (4) period / (b) (4) cum

   Not Applicable ☐ Worldwide 220,976,340 period / 639,868,710 cum

3. Does this report describe any actions taken by the manufacturer or other regulatory agency for this product (e.g. labeling changes)? Yes ☑ No ☐

4. Have there been any new safety issues identified by the reviewer in this PSUR? Yes ☑ No ☐

If YES, please provide pertinent information below AND notify/discuss safety issues with the Team Lead and/or Branch Chief.

Safety-related changes to the Core Data Sheet include the addition of asthenia, lethargy, decreased appetite, hyperhidrosis, and night sweats as adverse drug reactions and addi ion of "special warnings and precautions for use" text for vaccine stress-related responses, including dizziness, fain ing, palpitations, increases in heart rate, alterations in blood pressure, feeling short of breath, ingling sensations, swea ing and/or anxiety.

During he reporting period, the following signals were addressed by the company as follows: ongoing evaluation of myocarditis and pericarditis; appendicitis and dizziness were evaluated and determined not to be a risk. The following safety topics were addressed and determined not to be validated signals: abnormal behavior/mental disorder, acquired hemophilia, acute disseminated encephalomyelitis, acute pancreati is, Guillain-Barre syndrome (GBS), menstrual cycle abnormalities, and transverse myelitis (TM).

A review of cumulative reports of hrombosis with hrombocytopenia syndrome (TTS) was provided; among 85 reports of potential TTS two reports met Brighton Level 1 with positive PF4 antibodies, both reports from the UK and post-1st dose (one 31-yr male with no PMH had deep vein hrombosis and platelets=135 and one 47-yr female with PMH of pulmonary embolus and concomitant an icoagulation/anti-platelet medication had cerebral venous sinus hrombosis, mul iple arterial/venous thromboses, and platelets=10. The company stated that given he hundreds of millions of Pfizer-BioNTech vaccine doses administered, it cannot be concluded that the vaccine is causally associated with vaccine induced thrombo ic thrombocytopenia.

Age stratified Observed to Expected (O/E) analyses showed an O/E ra io exceeding 1 for at least one age group for GBS, multisystem inflammatory syndrome, and TM; there were no trends noted across age groups. The company will continue to monitor these events.

Conclusions:

☐ The contents of this PSUR/PAER do not indicate a need for further regulatory action.

☑ Please see the following comments and recommendations:

The Information Request below was sent to the company; await response with the next Summary Monthly Safety Report.
This information request (IR) is in reference to the Pfizer-BioNTech COVID-19 Vaccine Summary Monthly Safety Report (SMSR) for April 30, 2021 to May 31, 2021 (IND 19736.366) and the IR response (IND 19736.367) regarding the Observed to Expected (O/E) analysis for myocarditis and pericarditis. We acknowledge that you aim to refine the O/E analysis to provide smaller age categories for the next reporting period.

We note that in the April SMSR a myocarditis background rate of 4.4 per 100,000 person-years (py) was used for both the 18-64 year and 65+ year age groups. In the May SMSR background rates (per 100,000 py) of 12.38 for 18-24 year, 10.54 for 25-49 year, and 10.05 for 50+ year age groups were used for myocarditis based on data from ACCESS IT_ARS. The ACCESS report indicates that the ARS background rates used in your O/E analysis are relatively high for myocarditis and there are a wide range of reported background rates for myocarditis. Please perform an O/E analysis for myocarditis using various background rates (i.e., lower, mid-range, and higher background rate estimates) to provide a more comprehensive range of O/E results. In addition, please perform an O/E analysis for myocarditis stratified by U.S. vs European vaccination rates (doses), age, gender, and vaccine dose. Please submit these O/E analyses for myocarditis in the SMSR for the next reporting period.

Reference Documents (X:\DE\MEDICAL OFFICER\Guidance Documents):

1. E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs 1996
2. Addendum to E2C Safety Data Management: Periodic Safety Update Reports for Marketed Drugs 2004