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

Completed by Reviewer

Product Name	Human coronavirus mRNA vaccine in lipid nanoparticles (BNT162b2)
Manufacturer	Pfizer-BioNTech
STN #	19736/335
DCC Login ID #	
Submission Type	**PAER** ☐ **PSUR** ☐ **PBRER** ☐ **PADER** ☐
Submission Format	**ELECTRONIC** ☑ **PAPER** ☐
Reporting Period	**FROM** April 1, 2021 **TO** April 29, 2021
Date Received by FDA	May 14, 2021
Date Routed to Reviewer	May 14, 2021
Regulatory Information Specialist (RIS) - Name	Ramachandra Naik
Reviewer - Name	Deborah Thompson
Reviewer Signature (electronic signature)	Deborah L. Thompson -S Dig tally signed by Deborah L Thompson -S DN: c=US o=U S Government ou=HHS ou=FDA ou=Peop e 0 9 2342 19200300 100 1 1=2002552931 cn=Deborah L Thompson -S Date: 2021 05 19 12:26:33 04'00'

COMMENTS

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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) cum / (b) (4) interval

   Not Applicable ☐ Worldwide 415,922,715 cum / 172,777,410 interval

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.

BNT162b2 has received temporary authorization for emergency supply in 32 countries and conditional marketing authorization approval in 42 countries.

The sponsor's Core Data Sheet was updated to include adverse reaction information on adolescents 12 through 15 years of age, including that the most frequent adverse reactions were injection site pain, fatigue, headache, myalgia, chills, arthralgia, and fever.

During this reporting period, asthenia, lethargy, decreased appetite, hyperhidrosis, and night sweats were determined to be risks that will be added to the reference safety information and to local product labels (will not be important risks added to the pharmacovigilance plan).

The following signals were addressed and determined not to be risks: herpes zoster, seizure, myocarditis and pericarditis.

The following safety topics were addressed and determined not to be validated signals: cranial nerve palsy, hemolytic anemia, hepatic events, nephrotic syndrome, optic neuritis, and trigeminal neuralgia.

The sponsor provided an observed to expected (O/E) analysis for adverse events of special interest (AESI). The source for background incidence rates was changed this month for many AESI which resulted in differing/lower expected rates from previous reports. The following AESI had at least one risk period (cumulative, interval) with an upper level of the 95% CI exceeding one: acute disseminated encephalomyelitis (ADEM), ageusia/anosmia, Guillain-Barre syndrome, multisystem inflammatory syndrome (MIS), myasthenia gravis, polyneuropathy, and transverse myelitis. The ADEM O/E signal was new this month and is attributed to the change in background rates from 5.3 per 100,000 person-years (py) to 0.10 per 100,000 py. For next month, the sponsor will evaluate whether the 5.3 per 100,000 py rate is a more appropriate benchmark for signal detection.

The sponsor previously evaluated ageusia/anosmia, myasthenia gravis, and transverse myelitis and determined these events are not a validated signal. MIS is known to be associated with COVID-19 and the sponsor states that background rates of MIS are likely increased; they will continue to seek more contemporaneous event rates for the O/E analysis. The O/E ratio for GBS was modestly increased this month compared to last, partly due to the change in background rates data source; GBS will continue to be monitored. The sponsor evaluated polyneuropathy in this monthly report and concluded that the data do not support a validated signal; the topic will continue to be closely monitored.

Conclusions:

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

☐ Please see the following comments and recommendations:

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