Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***COVID-19 Clinical Update***
-April 2021-

Background:

The Indian Health Service National Pharmacy and Therapeutics Committee provided a panel review of COVID-19 pandemic-related content, including clinical updates on COVID-19 treatment guidelines, vaccines and medication safety efforts at the Spring 2021 NPTC Meeting.

Discussion:

COVID-19 Treatment Guidelines Update:

A review of COVID-19 treatment guidelines focused on pharmacotherapeutic updates from the U.S. National Institute of Health (NIH), the Infectious Diseases Society of America (IDSA) and the World Health Organization. Important changes in recommendations for (1) convalescent plasma, (2) ivermectin, (3) monoclonal antibodies and (4) tocilizumab were nearly universal in the both U.S.-based organizational guidelines. Both the NIH and IDSA guidelines either recommend against use of **convalescent plasma** in most settings (i.e., hospitalized or ambulatory) or state an absence of sufficient data to support its use. As a reminder, low-titer convalescent plasma is no longer authorized through the FDA's Emergency Use Authorization for convalescent plasma as of March 9, 2021. **Ivermectin** remains lacking in sufficient evidence at this time to be recommended for use in any setting, except in the context of a clinical trial. On April 15th, 2021 the FDA revoked its bamlanivimab monotherapy EUA in favor of the authorized **monoclonal antibody combinations**, bamlanivimab and etesevimab or casirivimab and imdevimab. Lastly, in severe/critical patients with COVID-19 exhibiting rapid respiratory decompensation, guidelines supported the use of **tocilizumab**, in combination with corticosteroids.

COVID-19 Vaccines Update:

In March 2021, a third COVID vaccine was authorized for use in the United States. The Janssen vaccine platform differs somewhat from its mRNA predecessors. The Johnson and Johnson vaccine uses a human adenovirus to express the SARS-CoV-2 spike protein in cells.[1] The phase 3 clinical trial, ENSEMBLE, which began September 7, completed its enrollment of 45,000 volunteers on December 17. Study populations included non-pregnant healthy adults. In terms of effectiveness, both co-primary endpoints were met.[2] A single dose of the vaccine protects against moderate to severe/critical COVID-19 in adults ≥18 years of age, with a vaccine effectiveness of 66.9% at least 14 days after vaccination and 66.1% at least 28 days after vaccination.[3] Consistent efficacy is shown across age, race, and ethnicity groups. Safety data from the Phase 3 study from over 43,000 participants with a median of 2 months of follow-up after vaccination demonstrated that a single dose of the Johnson & Johnson vaccine has an acceptable safety and reactogenicity profile in participants ≥18 years of age, including older adults.

The IHS National Pharmacy and Therapeutics Committee (NPTC) distributed a pharmacovigilance drug safety alert on April 15 to ensure that I/T/U clinicians were aware of important information necessary to identify rare thrombotic events potentially related to this vaccine.[4] As of April 12, 2021, following administration of nearly 4 million doses of Janssen vaccine in the United States, a total of 15 confirmed cases of thrombotic thrombocytopenic syndrome (TTS) have been observed, all among women, ages 18-59 years.[5] Twelve of these cases involved cerebral venous sinus thrombosis (CVST) with a median age of 37 years and median time to symptom onset of 8 days (with a range of 6-15 days). Risk factors included obesity, oral contraceptive use, hypothyroidism, and hypertension. The most common initial signs and symptoms were headache (all occurring ≥ 6 days after vaccination), chills, fever, N/V, malaise/lethargy, and abdominal pain. Eleven of the 15 confirmed cases of TTS experienced thromboses in sites other than (either alone or in addition to CVST), including portal, hepatic, internal jugular, brachial, femoral, and/or lower extremity veins and/or superior mesenteric, splenic, carotid, femoral, or iliac artery.

Following a thorough review of available data related to the incidence of TTS after Janssen COVID vaccination, on April 23, the CDC and FDA lifted the pause in use of the Janssen vaccine.[6] The agencies determined that the vaccine is safe and effective in preventing COVID-19 and that known and potential benefits outweigh the potential risks among adults. In response, the NPTC released additional guidance to field-level staff regarding the lifting of the pause and the importance of continued surveillance.[7]

COVID-19 IHS Pharmacovigilance/Safety Update:

The NPTC pharmacovigilance program evaluates the utilization and safety of select COVID-19 medications and COVID-19 vaccine safety through biweekly surveys. To date, 25 medication surveys and 9 vaccine surveys have been completed. These surveys compliment the findings found through other national reporting and safety systems such as MedWatch and the Vaccine Adverse Event Reporting System (VAERS). Many patients have received treatment for COVID-19 infections through outpatient services with monoclonal antibodies (i.e., bamlanivimab & etesevimab and casirivimab & imdevimab) and inpatient services with remdesivir, dexamethasone, and others. Rates of reported adverse drug events is below 2% for all agents with the majority of cases being minor. Adverse vaccine events are reported through three IHS vaccine safety monitoring systems. Most events have been common minor reactogenicity side effects. The IHS encourages reporting of all serious adverse vaccine events to the CDC's VAERS, which is the nation's early warning system for vaccine safety. The acronym "IHS" should be included in item #26 for all VAERS reports. This permits for CDC analysis of all events originating from the I/T/U system.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

References:

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2. U.S. Food and Drug Administration. Letter of Authorization. Janssen COVID-19 Vaccine. February 27, 2021.
3. U.S. Food and Drug Administration. Fact Sheet for Healthcare Providers. Emergency Use Authorization of Janssen COVID-19 vaccine.
4. CDC Advisory Committee on Immunization Practices. Implementation considerations for COVID-19 vaccines. Emergency Meeting, March 1, 2021.
5. Indian Health Service. NPTC Pharmacovigilance Drug Safety Alert- Rare and Serious Adverse Events Potentially Associated with the Johnson & Johnson/Janssen COVID-19 Vaccine.
6. U.S. Centers for Disease Control and Prevention. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-04-23/03-COVID-Shimabukuro-508.pdf
7. U.S. Food and Drug Administration. www.fda.gov/news-events/press-announcements/joint-cdc-and-fda-statement-johnson-johnson-covid-19-vaccine
8. Indian Health Service. NPTC Pharmacovigilance Drug Safety Alert- FDA and CDC Lift Recommended Pause on Johnson & Johnson (Janssen) COVID-19 Vaccine Use Following Thorough Safety Review