Janssen Pharmaceuticals, LLC
800 Ridgeview Drive
Horsham PA, 19044
(215) 325-2082

IMPORTANT DRUG WARNING

June 20, 2022

Subject: Serious Risks With CARVYKTI™ (ciltacabtagene autoleucel) Suspension for Intravenous Infusion:
• Fatal Covid-19 Infection

Dear Health Care Provider:

The purpose of this letter is to inform you of important safety information for CARVYKTI™, a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This letter is being distributed to all prescribers at CARVYKTI™-Certified Treatment Centers (CTCs) and physicians referring patients for treatment at the CTCs.

Serious Risks of Covid-19 Infection Associated With Use of CARVYKTI™

- Patients treated with CARVYKTI™ are likely at an increased risk of severe/fatal COVID-19 infections compared to myeloma patients receiving standard of care
- In an ongoing clinical trial, 7 patients aged 50-71 years old died from COVID-19 infection, (5 of the 7 died in 2022) after treatment with ciltacabtagene autoleucel (cilta-cel). Six of the seven patients were diagnosed with COVID-19 within 4 months after cilta-cel infusion
  - Three patients did not receive any COVID-19 vaccines prior to cilta-cel infusion
    - One of these patients received one dose of COVID-19 vaccine after cilta-cel infusion
  - Three patients received 2 doses of COVID-19 vaccine prior to cilta-cel infusion
    - One of these patients received a third COVID-19 vaccine after cilta-cel infusion
  - One patient received 3 doses of COVID-19 vaccine prior to cilta-cel infusion
- Risk factors for fatal COVID-19 infection include comorbidities associated with severe/fatal COVID-19, such as diabetes and obesity and concomitant use of immune-suppressant medications

Prescriber Action

Consider the recommendations set forth by professional bodies, eg ASH-ASTCT (https://www.hematology.org/covid-19/ash-astct-covid-19-vaccination-for-hct-and-car-t-cell-recipients), EBMT (https://www.ebmt.org/covid-19-and-bmt) and published guidance, and counsel your patients accordingly, on prevention and treatment of COVID-19 infection in patients treated with CARVYKTI™, including:

1. Remind your patients, particularly those who are less than 9 months from CARVYKTI™ infusion, that the ongoing pandemic is still putting them at risk of contracting COVID-19. Ask your patients to continue to limit their risk of exposure to infected individuals as much as possible and strictly adhere to prevention measures such as proper masking, hand hygiene, social distancing, and avoiding travel and public transportation to the extent possible
2. Patients should assume that any vaccination administered prior to lymphodepletion and CARVYKTI™ infusion no longer provides protection. For this reason, it is strongly recommended that all patients receive a full COVID-19 vaccination series (eg, a primary series of 3 vaccines and a 4th booster dose for mRNA vaccines; note: mRNA vaccines are recommended), at least three months after CARVYKTI™ infusion, regardless of vaccination status prior to CARVYKTI™. In addition, if not already vaccinated, caregivers, family, and household contacts should receive COVID-19 vaccination as well
3. Please consider offering Evusheld for pre-exposure prophylaxis to reduce patients' risk of developing severe/fatal COVID-19 infection during the first 6-9 months after infusion of CARVYKTI™. Inform your patient that they may not have sufficient levels of immunity until after the 3rd vaccine dose and that as a result they may remain at a very high risk of severe COVID-19 infection for at least 2-3 months after starting vaccination (Aleman A, Van et. al. Augmentation of humoral and cellular immune responses after third-dose SARS-CoV-2 vaccination and viral neutralization in myeloma patients. *Cancer Cell.* 2022 May 9;40(5):441-443). For this reason, in many parts of the world, Evusheld has received emergency use authorization for patients who have recently received CAR-T therapy
4. Please consider prescribing antivirals, eg, Paxlovid or other available agents, early after COVID-19 diagnosis, keeping in mind that patients may remain asymptomatic or have minimal symptoms for a period of time prior to deteriorating. If you have access to antivirals, please make sure that your patients are aware that these drugs may potentially significantly lower their risk of severe COVID-19 infection

Consistent with the US Prescribing Information for CARVYKTI™, monitor immunoglobulin levels after treatment with CARVYKTI™ and administer IVIG for IgG <400 mg/dL. Manage hypogammaglobulinemia in accordance with local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

Advise your patients to contact their doctor immediately to report any symptom consistent with respiratory tract infection or in case of a positive COVID-19 test.

Reporting Adverse Events

Health care providers and patients are encouraged to report any serious adverse event and any suspected adverse events associated with CARVYKTI™ to Janssen Biotech, Inc., at 1-800-Janssen (1-800-526-7736) or FDA at 1-800-FDA-1088.

This letter is not intended as a complete description of the benefits and risks related to the use of CARVYKTI™. Please refer to the enclosed full prescribing information and medication guide.

Sincerely,

Imran Khan, MD, PhD
Vice President,
Medical Affairs Hematology
Janssen Pharmaceuticals, LLC