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Exploring the Emergency Use Authorization for a Monoclonal Antibody Cocktail for COVID-19

Announcer:
You're listening to The Drug Report on ReachMD, hosted by Linda Bernstein, Pharm.D., Clinical Professor on the Volunteer Faculty of the School of Pharmacy, University of California, San Francisco.

Dr. Bernstein:
Welcome to The Drug Report.

An Emergency Use Authorization or EUA by the Food and Drug Administration was issued to Regeneron on November 21, 2020 for the coadministration of casirivimab and imdevimab, a monoclonal antibody cocktail, also known as REGN-COV2 or REGEN-COV2 for the treatment of mild to moderate COVID-19 in a defined patient population. These monoclonal antibodies are specifically directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells.

FDA Commissioner Stephen M. Hahn, M.D. stated that "Authorizing these monoclonal antibody therapies may help outpatients avoid hospitalization and alleviate the burden on our health care system." These sentiments were echoed by Patrizia Cavazzoni, M.D., acting director of the FDA's Center for Drug Evaluation and Research. "The emergency authorization of these monoclonal antibodies administered together offers health care providers another tool in combating the pandemic. We will continue to facilitate the development, evaluation and availability of COVID-19 therapies."

When given together by intravenous infusion, these two agents were shown in an outpatient clinical trial to decrease COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo.

The FDA's authorization is based on the totality of the evidence of phase 1 and 2 data from the ongoing study, a phase 1/2/3, randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of casirivimab and imdevimab 2400 mg IV or 8000 mg IV or placebo in outpatients (non-hospitalized) with SARS-CoV-2 infection.

The trial results indicated that viral load reduction in patients treated with casirivimab and imdevimab was larger than in patients treated with placebo at day seven. The predefined secondary endpoint was medically attended visits related to COVID-19, particularly hospitalizations and emergency room visits within 28 days after treatment. For patients at high risk for disease progression, hospitalizations and emergency room visits occurred in 3% of casirivimab and imdevimab-treated patients on average compared to 9% in placebo-treated patients. The effects on viral load, reduction in hospitalizations and emergency room visits were similar in patients receiving either of the two doses.

The FDA stated that it is reasonable to believe that casirivimab and imdevimab, administered together, may be effective for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization, and that, when used under the conditions described in this authorization, the known and potential benefits of casirivimab and imdevimab, administered together, outweigh the known and potential risks of such product. Furthermore, there is no adequate, approved, and available alternative to the emergency use of casirivimab and imdevimab, administered together, for this patient cohort.

The evaluation of the safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 is ongoing.

It is suggested that monoclonal antibodies such as REGEN-COV2 have the greatest benefit when given early after diagnosis and in

patients who have not yet mounted their own immune response or who have high viral load.

Casirivimab and imdevimab are not authorized for use in patients:

- Who are hospitalized due to COVID-19, OR
- Who require oxygen therapy due to COVID-19, OR
- Who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Benefit of treatment with these two agents has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

Casirivimab and imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system as necessary.

Under the EUA and as specified in the Fact Sheet, the recommended dose is 1,200 mg of casirivimab and 1,200 mg of imdevimab (2,400 mg total) administered as a single intravenous infusion. It should be prepared by a qualified healthcare professional using aseptic technique.

Possible side effects of casirivimab and imdevimab include: fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, and dizziness. Healthcare professionals will be required to report adverse events to the Food and Drug Administration.

The U.S. government will coordinate with state authorities to allocate REGEN-COV2 on a weekly basis based on the number of COVID-19 cases in each state. The government has committed to providing 300,000 doses at no cost to patients, although healthcare facilities may charge fees related to administration. Regeneron will immediately begin shipping REGEN-COV2 to Amerisource Bergen, a national distributor, which will distribute the therapy as directed by the government.

Regeneron continues to increase in-house production of REGEN-COV2, and the company has partnered with Roche to increase the global supply of REGEN-COV2 beginning in 2021. If REGEN-COV2 proves safe and effective in clinical trials and regulatory approvals are granted, Regeneron will manufacture and distribute it in the U.S. and Roche will develop, manufacture and distribute it outside the U.S. Once both companies are at full manufacturing capacity in 2021, there are expected to be at least 2 million treatment doses available annually.

For The Drug Report, I'm pharmacist, Dr. Linda Bernstein.

Announcer:
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