Emergency Use Authorization (EUA) for tocilizumab, FOR THE UNAPPROVED USE OF AN APPROVED PRODUCT

Identifying Information

Application Type (EUA or Pre-EUA) If EUA, designate whether pre-event or intra-event EUA request.	EUA
EUA Application Number(s)[1]	99
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Hoffmann-La Roche Ltd. C/O Genentech, Inc. 1 DNA Way, Bldg 45-1 South San Francisco, CA 94080 Dhushy Thambipillai Regulatory Program Management Phone: (b) (6) Fax: (b) (6) Email: (b) (6)
Submission Date(s)	December 7, 2022
Receipt Date(s)	December 7, 2022
OND Division / Office	Division of Pulmonology, Allergy, and Critical Care / Office of Immunology and Inflammation
Proprietary Name	Actemra
Established Name/Other names used during development	Tocilizumab
Dosage Forms/Strengths	Intravenous Infusion; 80 mg/4 mL, 200 mg/10 mL, and 400 mg/20 mL
Therapeutic Class	IL-6 receptor antagonist
Intended Use or Need for EUA	Treatment of coronavirus disease 2019 (COVID-19)
Intended Population(s)	Hospitalized pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)

I. Issue Summary

The June 24, 2021 Emergency Use Authorization (EUA) 99 authorized use of Actemra (tocilizumab) for the treatment of coronavirus disease 2019 (COVID-19) in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

[1] If a Pre-EUA is in existence at the time of the EUA request submission and has been assigned an EUA number, the EUA request should use the same EUA number and electronic archive file.

Based on the review of the Biologics License Application (BLA) 125276 supplement 138 for tocilizumab, the Agency has concluded that the data support approval of tocilizumab for the treatment of COVID-19 in hospitalized adults who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. The BLA indication will not include pediatric patients less than 18 years of age at this time.

At the time of BLA approval, the Agency will issue a Pediatric Research Equity Act (PREA) post-marketing requirement (PMR) for the conduct of a clinical trial in pediatric patients and the submission of the results from that trial to the Agency. The aforementioned pediatric trial is currently ongoing, and once completed the data may support revising the BLA indication to include use in pediatric patients.

Upon approval of the BLA 125276 supplement 138, the Agency will revise the EUA for tocilizumab to remove the authorized uses covered under the approved BLA. The Agency will continue to authorize tocilizumab for emergency use to treat COVID-19 in hospitalized pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. No new clinical data was submitted to the EUA as part of this continued authorization. The Agency has determined that retaining this authorized use is appropriate to protect public health or safety under section 564 of the Federal Food, Drug and Cosmetic Act.[2]

Maintaining the EUA for pediatric patients 2 years of age and older will ensure that important information about the recommended use (e.g., dosing recommendations) for pediatric patients not covered under the approved labeling for adult patients will continue to be available to health care providers. As noted above, the EUA will be reissued for pediatric patients 2 years of age and older concurrent with the approval of Actemra for the treatment of COVID-19 in adult patients.

II. Summary of Revision to EUA Fact Sheets

Changes to the EUA Fact Sheets were made to reflect the removal of authorized uses covered under the approved BLA 125276 supplement 138 (i.e., use in adult patients), to

[2] On October 22, 2020, Veklury (remdesivir) was initially approved to treat COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization. On April 25, 2022, a supplement to NDA 214787 was approved to expand the indication for Veklury to also include the treatment of COVID-19 in pediatric patients (28 days of age and older and weighing at least 3 kg) with positive results of direct SARS-CoV-2 viral testing, who are hospitalized, or not hospitalized and have mild to moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death. Although Veklury is an approved alternative treatment of COVID-19 in pediatric patients (28 days of age and older and weighing at least 3 kg) with positive results of direct SARS-CoV-2 viral testing, who are hospitalized, FDA does not consider Veklury to be an adequate alternative to tocilizumab for this authorized use. Veklury is a nucleoside ribonucleic acid polymerase inhibitor that has demonstrated antiviral activity against SARS-COV-2. Tocilzumab is an IL-6 receptor antagonist, a class of drugs that blocks IL-6 signaling, which is thought to contribute to inflammation and worsening of COVID-19. This is distinct from Veklury, which acts as an antiviral agent.

reflect additional analyses performed during the BLA review, and editorial changes to improve readability. These changes are summarized below.

- Authorized Use:
    - Revised the scope of the authorized use to the treatment of hospitalized pediatric patients 2 years of age and older who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.
- Dosing:
    - Revised to include only the dosing regimen for the pediatric population covered under the scope of the EUA.
- Adverse Reactions:
    - Revised to match the approved label, which used pooled safety data from the COVID-19 studies.
- Use in Specific Populations:
    - Revised to remove the Geriatric Use subsection.
- Clinical Studies:
    - Revised to match the approved label.
- Fact Sheet for Patients, Parents, and Caregivers
    - Revised to reflect the scope of the EUA being limited to pediatric patients.

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/s/

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