Emergency Use Authorization (EUA) of Tocilizumab (Actemra®)

1. Overview of EUA of Tocilizumab for the Treatment of COVID-19

a. Tocilizumab is an interleukin-6 (IL-6) inhibitor that may block the inflammatory pathway and prevent disease progression
b. Tocilizumab is FDA-approved for many autoimmune and rheumatologic diseases, but is not currently FDA-approved for the treatment of COVID-19
c. FDA has authorized tocilizumab for emergency use for the treatment of 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 ventilation (NIV) or invasive mechanical ventilation (IMV), or extracorporeal membrane oxygenation (ECMO)

2. Which Patients May Benefit from Tocilizumab?

a. Eight RCTs evaluated tocilizumab for COVID-19, but only two RCTs showed mortality reduction in patients with elevated inflammatory markers, and rapidly progressing oxygen requirements to HFNC, NIV, and IMV
b. For more detailed information, please refer to the tocilizumab monograph as well as IDSA and NIH guidelines
c. Parkland Antimicrobial Stewardship subcommittee and Pharmacy &Therapeutics (P&T) Committee approved the following criteria for non-formulary requests based on available literature and guidelines

Approval Criteria
• Confirmed COVID-19 • CRP > 7.5mg/dL • Within 48 hours of commencement of respiratory support (high flow nasal cannula, CPAP, non-invasive ventilation, ECMO, or invasive mechanical ventilation) • Received or concurrently receiving corticosteroids (unless contraindicated)

3. Tocilizumab is NOT Recommended in the Following Patients

a. AST/ALT > 10 x ULN
b. Significant immunosuppression, including recent use of other biologic immunomodulating drugs
c. An uncontrolled, serious bacterial, fungal, or non-SARS-CoV-2 viral infection
d. Absolute neutrophil count < 500 cells/µL
e. Platelet count < 50,000 cells/µL
f. Gastrointestinal perforation
g. Prior hypersensitivity reactions to tocilizumab

4. Dosing and Monitoring

a. Tocilizumab will be limited to a single 60-minute intravenous infusion based on actual body weight
    - >90 kg: 800 mg
    - >65 and ≤90 kg: 600 mg
    - >40 and ≤65 kg: 400 mg
    - ≤40 kg: 8mg/kg

b. Common adverse reactions seen in COVID-19 patients include constipation, anxiety, diarrhea, insomnia, hypertension, and nausea
c. Serious side effects may include serious bacterial infections, elevated AST or ALT levels, and hypersensitivity reactions including anaphylaxis

5. Mandatory FDA Requirements for Prescribing EUA Tocilizumab

a. Patient Communication Requirement
   - Review the information in the "**Fact Sheet for Patients, Parents and Caregivers**"
   - Provide this document to the patient or their caregiver prior to the patient receiving tocilizumab
     - **English Version** / **Spanish Version**

b. Chart Documentation Requirement
   - Use smartphrase **".EUATOCILIZUMAB"** which will document the following:
     - The EUA fact sheet has been given to the patient
     - The patient or caregiver has been informed of alternatives to receiving tocilizumab
     - The patient or caregiver has been informed that tocilizumab is not FDA approved for COVID-19, but is authorized for use under the EUA

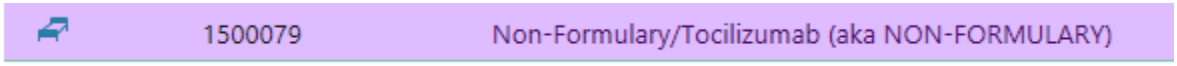
c. Medication errors and serious adverse events considered to be potentially related to tocilizumab must be reported within 7 days from onset of event through FDA's MedWatch Adverse Event Reporting program. Providers can complete and submit the report online; or download and complete the form, then submit it via fax at 1-800-FDA-0178. FDA MedWatch forms should also be provided to Genentech.

d. Additional information can be found in the EUA's Fact Sheet for Healthcare Providers and/or FAQ

6. Ordering EUA Tocilizumab

a. Tocilizumab for COVID-19 must be entered as a non-formulary request

b. Prefilled non-formulary order for tocilizumab can be ordered in Epic by searching "tocilizumab"



c. Dose must be entered in "mg" based on weight. Refer to the section on **Dosing and Monitoring**.

7. Pharmacist Role in Non-formulary Review

a. Decentral pharmacist will page the appropriate on-call pharmacist when a non-formulary request is entered
   - Weekdays (0700 – 1700): Infectious Diseases Pharmacist
   - Weekdays (1700 – 0700): Weekend/Afterhours Pharmacist
   - Weekends or Holidays (24h): Weekend/Afterhours Pharmacist

b. The on-call pharmacist will review the request and follow up with the ordering provider as needed

c. If approved, the on-call pharmacist will write a chart note detailing the outcome of their review

d. If approved, decentral pharmacist will process the non-formulary order and schedule administration

Please direct additional questions to members of the Antimicrobial Stewardship Team:

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