Actemra® (tocilizumab)– Emergency use authorization approval

- On June 24, 2021, the FDA announced the emergency use authorization (EUA) approval of Genentech's Actemra (tocilizumab), 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 or invasive mechanical ventilation, or extracorporeal membrane oxygenation.

    - Actemra is not authorized to treat COVID-19 patients outside of the hospital.
    - For this EUA, Actemra may only be administered via intravenous (IV) infusion; the subcutaneous formulation is not part of this EUA.

- Actemra is FDA-approved to treat the following:

    - Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs
    - Adult patients with giant cell arteritis
    - Slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis associated interstitial lung disease
    - Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis
    - Patients 2 years of age and older with active systemic juvenile idiopathic arthritis
    - Adults and pediatric patients 2 years of age and older with chimeric antigen receptor T cell-induced severe or life-threatening cytokine release syndrome.

- Actemra is a monoclonal antibody that reduces inflammation by blocking the interleukin-6 receptor.

- The EUA was approved based on one randomized, controlled, open-label, platform trial [Randomised Evaluation of COVID-19 Therapy (RECOVERY)] and 3 randomized, double-blind, placebo-controlled trials (EMPACTA, COVACTA, and REMDACTA).

    - RECOVERY: 4,116 patients were randomized to Actemra + usual care or usual care alone. The probabilities of dying by day 28 were estimated to be 30.7% and 34.9% in the Actemra and usual care arms, respectively (Hazard ratio [HR] 0.85; p = 0.0028).
    - EMPACTA: 377 patients were randomized to Actemra + standard of care (SoC) or SoC alone. The cumulative proportion of patients who required mechanical ventilation or died by day 28 was 12.0% (95% CI: 8.52, 16.86) in the Actemra arm vs. 19.3% (95% CI: 13.34, 27.36) in the placebo arm (HR 0.56; p = 0.0360).
    - COVACTA: 452 patients were randomized to Actemra + standard of care (SoC) or SoC alone. There were no statistically significant differences observed in the distributions of clinical status on the 7-category ordinal scale (rankings from discharged to death) at day 28 when comparing the Actemra arm to the placebo arm.
    - REMDACTA: 640 patients were randomized to Actemra + remdesivir (RDV) or RDV alone. There were no statistically significant differences between treatment arms with respect to time to hospital discharge or "ready for discharge" through day 28 (HR 0.965; 95% CI: 0.78, 1.19) or time to mechanical ventilation or death through day 28 (HR 0.980; 95% CI: 0.72, 1.34).

- Warnings and precautions for Actemra (based on use in other indications) include serious infections; gastrointestinal perforations; hepatotoxicity; laboratory parameters; hypersensitivity reactions, including anaphylaxis; demyelinating disorders; active hepatic disease and hepatic impairment; and vaccinations.

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- The most common adverse events (≥ 3%) with Actemra use (in other indications) are constipation, anxiety, diarrhea, insomnia, hypertension and nausea.

- The recommended dose of Actemra for this EUA is a single 60-minute intravenous infusion at 12 mg/kg in patients < 30 kg and 8 mg/kg in patients ≥ 30 kg.

    — If clinical signs or symptoms worsen or do not improve after the first dose, one additional infusion of Actemra may be administered at least 8 hours after the initial infusion.
    — Maximum dosage in COVID-19 patients is 800 mg per infusion.

- For this EUA, Actemra 80 mg/4 mL, 200 mg/10 mL, and 400 mg/20 mL single-use vials should be used.