

## **Frequently Asked Questions on the Emergency Use Authorization for Actemra (Tocilizumab) for Treatment of COVID-19**

### **Q. What is the difference between an Emergency Use Authorization (EUA) and an FDA approval?**

A. Under section 564 of the Federal Food, Drug & Cosmetic Act (FD&C Act), the FDA may, pursuant to a declaration by the HHS Secretary based on one of four types of determinations, authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, the FDA must determine, among other things, that based on the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits of the product, when used to diagnose, treat, or prevent such diseases or conditions, outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

### **Q. What does this EUA authorize?**

A. Actemra (tocilizumab), manufactured by Genentech, is authorized for emergency use for the treatment of COVID-19 in hospitalized pediatric patients 2 to less than 18 years of age who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

### **Q. Is Actemra approved by FDA to treat COVID-19?**

A. On December 21, 2022, FDA approved Actemra for the treatment of COVID-19 in hospitalized adult patients who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Actemra is also FDA-approved to treat:

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

FDA has determined Actemra is safe and effective for these uses when used in accordance with the FDA-approved labeling.

**Q. Can Actemra be used outside the hospital (i.e., for non-hospitalized patients)?**

A. Actemra is not currently approved or authorized under its EUA for the treatment of non-hospitalized patients with COVID-19.

**Q. Are there data showing Actemra might benefit patients with COVID-19?**

A. The data supporting Actemra's approval in adults as indicated and the EUA in pediatric patients 2 to less than 18 years of age hospitalized with COVID-19 are from four clinical trials. These include one randomized, controlled, open-label, platform trial (Randomised Evaluation of COVID-19 Therapy [RECOVERY]) and three randomized, double-blind, placebo-controlled trials (EMPACTA, COVACTA, and REMDACTA). The largest trial, RECOVERY, showed a benefit in mortality, and EMPACTA also showed a benefit for treatment with Actemra. While COVACTA and REMDACTA did not show a benefit of treatment with Actemra, these trials contributed to the assessment of safety.

- In the RECOVERY trial, 4,116 hospitalized patients with severe COVID-19 pneumonia were randomized, 2,022 patients received Actemra in addition to standard of care and 2,094 patients received standard of care (the routine care patients receive for treatment of COVID-19) alone. The primary outcome evaluated death through 28 days of follow-up, and results of the primary analysis were statistically significant. The probability of death by day 28 was estimated to be 30.7% for patients receiving Actemra and 34.9% for patients receiving standard of care alone.
- In the EMPACTA trial, 389 hospitalized patients with COVID-19 pneumonia were randomized, 249 patients received Actemra and 128 patients received a placebo. The primary endpoint was the cumulative proportion of patients who required mechanical ventilation or died through 28 days of follow-up. For patients receiving Actemra, there was an observed reduction in progression to mechanical ventilation or death compared to patients who received placebo, with the primary analysis results being statistically significant. The proportion of patients who required mechanical ventilation or died by day 28 was estimated to be 12.0% for Actemra and 19.3% for placebo.
- In the COVACTA trial, 452 hospitalized patients with severe COVID-19 pneumonia were randomized, 294 patients received Actemra and 144 patients received a placebo. The primary efficacy endpoint was clinical status through 28 days of follow-up assessed on a 7-category ordinal scale. While there was no statistically significant difference observed in clinical status on the 7-category ordinal scale between treatment groups, the COVACTA trial contributed to the assessment of the safety for Actemra when used for the treatment of COVID-19.
- In the REMDACTA trial, 649 hospitalized patients with severe COVID-19 pneumonia were randomized, 430 received Actemra in combination with remdesivir and 210 received a placebo in combination with remdesivir. The primary efficacy endpoint was time to hospital discharge or "ready for discharge" through 28 days of follow-up. While there were no statistically significant differences observed between treatment groups with respect to time to hospital discharge or

“ready for discharge” through 28 days of follow-up, the REMDACTA trial contributed to the assessment of the safety for Actemra when used for the treatment of COVID-19.

FDA has authorized the emergency use of Actemra in certain children (2 years and less than 18 years of age) hospitalized with COVID-19 based upon the data in adults from RECOVERY, EMPACTA, COVACTA, and REMDACTA clinical trials that supported Actemra’s approval in adults; the similarity of COVID-19 in children to COVID-19 in adults; and extensive safety and dosing information with use of Actemra in pediatric patients for approved indications (i.e., SJIA, PJIA, and CRS).

For additional information, please refer to the [Fact Sheet for Health Care Providers](#) and section 14 of the [prescribing information](#).

**Q. Are clinical trials underway evaluating Actemra for COVID-19?**

A. Yes. [Clinical trials](#) remain ongoing to study Actemra for the treatment of COVID-19.

**Q. Are side effects possible with Actemra?**

A. Yes. Possible side effects of Actemra are:

- Serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections have occurred in patients receiving Actemra. In COVID-19 patients, Actemra should not be administered if patients have any other concurrent active infection, including localized infection.
- Increases in levels of liver enzymes. Actemra is not recommended in COVID-19 patients with elevated alanine aminotransferase (ALT) or aspartate aminotransferase (AST) above 10 times the upper limit of the reference range. When Actemra is used for treatment of COVID-19, ALT and AST should be monitored according to current standard clinical practice.
- Hypersensitivity reactions, including anaphylaxis. Actemra should only be infused by a healthcare professional with appropriate medical support to manage anaphylaxis.
- Common adverse reactions in COVID-19 patients include constipation, anxiety, diarrhea, insomnia, hypertension, and nausea.

See Warnings and Precautions in the FDA-approved [full prescribing information](#) for additional information on risks associated with longer-term treatment with Actemra.

**Q. How can Actemra for use under the EUA be obtained?**

A. Genentech and its authorized distributors distribute Actemra to hospitals for its authorized use under the EUA. Licensed healthcare providers interested in administering Actemra should contact Genentech or visit Genentech’s [website](#).

**Q. Is there a requirement for providers to report side effects as part of the EUA?**

A. Yes. As part of the EUA, FDA is requiring health care providers who prescribe Actemra to treat COVID-19 to report all medication errors and serious adverse events considered to be potentially related to Actemra 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. This requirement is outlined in the EUA's health care provider [Fact Sheet](#). FDA MedWatch forms should also be provided to Genentech.

**Q. Do patient outcomes need to be reported under the EUA?**

A. No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and serious adverse events considered to be potentially related to the emergency use of Actemra occurring during treatment is required.

**Q. Can health care providers share the patient/caregiver fact sheet electronically?**

A. The letter of authorization for Actemra requires that fact sheets be made available to [health care providers](#) and to [patients, parents, and caregivers](#), "through appropriate means." Electronic delivery of the Fact Sheet is an appropriate means. For example, when the patient requests the Fact Sheet electronically, it can be delivered as a PDF prior to medication administration. Health care providers should confirm receipt of the Fact Sheet with the patient.

**Q: Are there clinical data about the use of Actemra in people who are pregnant or breastfeeding?**

A. The limited data available with Actemra in people who are pregnant is not sufficient to determine whether there is a drug-associated risk for major birth defects and miscarriage. No information is available on the presence of Actemra in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. The lack of clinical data during lactation prevents a clear determination of the risk of Actemra to an infant during lactation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Actemra and the potential adverse effects on the breastfed child from Actemra or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.