

**ATTACHMENT C: JOURNAL INFORMATION PIECE FOR  
EMERGENCY MEDICINE PHYSICIANS AND EMERGENCY  
MEDICAL SERVICES PROFESSIONALS**

**Important Safety Information for Emergency Medicine Physicians  
About Potential Risks of Infection and Gastrointestinal  
Perforation With ACTEMRA®**

ACTEMRA® (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor that has been approved by the Food and Drug Administration (FDA) for two indications:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) with a recommended ACTEMRA® dosing interval of every 4 weeks.
- Children 2 years of age and older with active *Systemic Juvenile Idiopathic Arthritis (sJIA)* with a recommended ACTEMRA® dosing interval of every 2 weeks.

The safety and efficacy of ACTEMRA® for conditions other than RA and sJIA have not yet been established.

**Emergency medicine physicians** should be aware of important safety information regarding ACTEMRA®.

**Serious infections:** Patients treated with ACTEMRA are at increased risk for developing serious infections leading to hospitalization or death. These infections include tuberculosis (TB), bacterial, invasive fungal, viral and other opportunistic infections.

**Gastrointestinal perforations:** Gastrointestinal (GI) perforations have been reported in Phase 3 clinical trials, primarily as complications of diverticulitis. Reported perforations have involved generalized purulent peritonitis, lower GI perforation, fistula and abscess. Most patients who developed GI perforations were taking concomitant nonsteroidal anti-inflammatory medications (NSAIDs), corticosteroids or methotrexate. Patients presenting with new-onset abdominal symptoms should be evaluated promptly for early identification of GI perforation.

In addition to these adverse events, patients treated with ACTEMRA may have elevated hepatic transaminases (ALT, AST) and lipids, and decreased neutrophils and platelet counts. Dosage modifications may be required if laboratory abnormalities occur. Please see the full Prescribing Information for more information.

**Hypersensitivity reactions, including anaphylaxis:** Hypersensitivity reactions, including anaphylaxis and death, have been reported in association with infusion of ACTEMRA. Anaphylaxis and other hypersensitivity reactions that required treatment discontinuation were reported in 0.1% (3 out of 2644) of patients in the 6-month controlled trials, and in 0.2% (8 out of 4009) of patients in the all-exposure

rheumatoid arthritis population; and in the sJIA controlled trial, 1 out of 112 patients (0.9%).

In the postmarketing setting, events of clinically significant hypersensitivity, and anaphylaxis, including events with a fatal outcome, have occurred in patients treated with a range of doses of ACTEMRA, with or without concomitant arthritis therapies. Events have occurred in patients who received premedication. Clinically significant hypersensitivity and anaphylaxis events have occurred both with and without previous hypersensitivity reactions and as early as the first infusion of ACTEMRA.

ACTEMRA should only be infused by a healthcare professional with appropriate medical support to manage anaphylaxis. If anaphylaxis or other clinically significant hypersensitivity reaction occurs, administration of ACTEMRA should be stopped immediately and ACTEMRA should be permanently discontinued. Do not administer ACTEMRA to patients with known hypersensitivity to ACTEMRA.

Please see full Prescribing Information for more information.

### ***Reporting Adverse Events***

It is important that you report all serious adverse events that occur in patients being treated with ACTEMRA, even if you do not think there is a causal relationship. The information that you provide about these events may inform therapy and monitoring decisions for future patients.

**Reporting is easy and maintains patient confidentiality.** Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.* You can report your cases to Genentech or directly to the FDA:

- Genentech at 1-800-ACTEMRA (1-800-228-3672)
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

**Please visit [www.ACTEMRA.com](http://www.ACTEMRA.com) for full Prescribing Information and Medication Guide.**

**ATTACHMENT D: JOURNAL INFORMATION PIECE FOR  
GASTROENTEROLOGISTS AND HEPATOLOGISTS**

### **Important Safety Information for Gastroenterologists and Hepatologists About Potential Risks of Gastrointestinal Perforation and Transaminase Elevations With ACTEMRA®**

ACTEMRA® (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor that has been approved by the Food and Drug Administration (FDA) for two indications:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) with a recommended ACTEMRA® dosing interval of every 4 weeks.
- Children 2 years of age and older with active *Systemic Juvenile Idiopathic Arthritis (sJIA)* with a recommended ACTEMRA® dosing interval of every 2 weeks.

The safety and efficacy of ACTEMRA® for conditions other than RA and sJIA have not yet been established.

**Gastroenterologists** and **hepatologists** should be aware of important safety information regarding ACTEMRA.

**Gastrointestinal perforations:** Gastrointestinal (GI) perforations have been reported in Phase 3 clinical trials, primarily as complications of diverticulitis, including generalized purulent peritonitis, lower GI perforation, fistula and abscess. Most patients who developed GI perforations were taking concomitant nonsteroidal anti-inflammatory medications (NSAIDs), corticosteroids or methotrexate. ACTEMRA should be used with caution in patients who may be at increased risk for GI perforation. Patients presenting with new-onset abdominal symptoms should be evaluated promptly for early identification of GI perforation.

**Transaminase elevations:** Treatment with ACTEMRA was associated with a higher incidence of transaminase elevations (ALT, AST) in Phase 3 clinical trials. These elevations did not result in apparent permanent or clinically evident hepatic injury with modification of the treatment regimen, which resulted in a decrease or normalization of liver enzymes. Patients receiving ACTEMRA should be monitored for elevated transaminase levels and dose modifications may be necessary. When clinically indicated, other liver function tests, such as bilirubin, should be considered. Please see the full Prescribing Information for more information.

#### ***Reporting Adverse Events***

It is important that you report any serious gastrointestinal adverse events, including GI perforation, hepatic disease or hepatic impairment, that occur in a patient being treated with ACTEMRA, even if you do not think there is a causal relationship. The information that you, as a gastroenterologist or hepatologist, provide about these events may inform therapy and monitoring decisions for future patients.

**Reporting is easy and maintains patient confidentiality.** Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.* You can report your cases to Genentech or directly to the FDA:

- Genentech at 1-800-ACTEMRA (1-800-228-3672)
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

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**ATTACHMENT E: JOURNAL INFORMATION PIECE FOR  
INFECTIOUS DISEASE SPECIALISTS**

### **Important Safety Information for Infectious Disease Specialists About Potential Risks of Infections With ACTEMRA<sup>®</sup>**

ACTEMRA<sup>®</sup> (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor that has been approved by the Food and Drug Administration (FDA) for two indications:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) with a recommended ACTEMRA<sup>®</sup> dosing interval of every 4 weeks.
- Children 2 years of age and older with active *Systemic Juvenile Idiopathic Arthritis (sJIA)* with a recommended ACTEMRA<sup>®</sup> dosing interval of every 2 weeks.

The safety and efficacy of ACTEMRA<sup>®</sup> for conditions other than RA and sJIA have not yet been established.

**Infectious disease specialists** should be aware of important safety information regarding ACTEMRA.

**Serious infections:** Patients treated with ACTEMRA are at increased risk for developing serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral and other opportunistic infections.

ACTEMRA should not be administered during an active infection, including localized infections. If a serious infection develops, ACTEMRA should be interrupted until the infection is controlled.

#### ***Reporting Adverse Events***

It is important that you report all serious infections that occur in patients being treated with ACTEMRA, even if you do not think there is a causal relationship. The information that you, as an infectious disease specialist, provide about these events may inform therapy and monitoring decisions for future patients.

**Reporting is easy and maintains patient confidentiality.** Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.* You can report your cases to Genentech or directly to the FDA:

- Genentech at 1-800-ACTEMRA (1-800-228-3672)
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

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**ATTACHMENT F: JOURNAL INFORMATION PIECE FOR  
INTERNISTS AND INTERNAL MEDICINE SUBSPECIALISTS**

## Important Safety Information for Physicians About Risks in Patients Receiving ACTEMRA®

ACTEMRA® (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor that has been approved by the Food and Drug Administration (FDA) for two indications:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) with a recommended ACTEMRA® dosing interval of every 4 weeks.
- Children 2 years of age and older with active *Systemic Juvenile Idiopathic Arthritis (sJIA)* with a recommended ACTEMRA® dosing interval of every 2 weeks.

The safety and efficacy of ACTEMRA® for conditions other than RA and sJIA have not yet been established.

**Physicians** should be aware of important information regarding safety and laboratory monitoring recommendations for ACTEMRA.

**Serious infections:** Patients treated with ACTEMRA are at increased risk for developing serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral and other opportunistic infections.

**Gastrointestinal perforations:** Gastrointestinal (GI) perforations have been reported in Phase 3 clinical trials, primarily as complications of diverticulitis, including generalized purulent peritonitis, lower GI perforation, fistula and abscess. Most patients who developed GI perforations were taking concomitant nonsteroidal anti-inflammatory medications (NSAIDs), corticosteroids or methotrexate. ACTEMRA should be used with caution in patients who may be at increased risk for GI perforation. Patients presenting with new-onset abdominal symptoms should be evaluated promptly for early identification of GI perforation.

**Hypersensitivity reactions, Including anaphylaxis:** Hypersensitivity reactions, including anaphylaxis and death, have been reported in association with infusion of ACTEMRA. Anaphylaxis and other hypersensitivity reactions that required treatment discontinuation were reported in 0.1% (3 out of 2644) of patients in the 6-month controlled trials, and in 0.2% (8 out of 4009) of patients in the all-exposure rheumatoid arthritis population; and in the sJIA controlled trial, 1 out of 112 patients (0.9%).

In the postmarketing setting, events of clinically significant hypersensitivity, and anaphylaxis, including events with a fatal outcome, have occurred in patients treated with a range of doses of ACTEMRA, with or without concomitant arthritis therapies. Events have occurred in patients who received premedication. Clinically significant

hypersensitivity and anaphylaxis events have occurred both with and without previous hypersensitivity reactions and as early as the first infusion of ACTEMRA.

ACTEMRA should only be infused by a healthcare professional with appropriate medical support to manage anaphylaxis. Please see full Prescribing Information for more information.

**Demyelinating disorders:** The impact of treatment with ACTEMRA on demyelinating disorders is not known, but multiple sclerosis and chronic inflammatory demyelinating polyneuropathy were reported rarely in clinical studies of adults with RA. Patients should be closely monitored for signs and symptoms potentially indicative of demyelinating disorders. Prescribers should exercise caution in considering the use of ACTEMRA in patients with preexisting or recent onset demyelinating disorders.

**Malignancies:** Malignancies were observed in clinical studies of ACTEMRA. The impact of treatment with ACTEMRA on the development of the malignancies is not known, but malignancy is a known risk of biological products that suppress the immune system. ACTEMRA is an immunosuppressant and may increase the risk of malignancies.

**Laboratory abnormalities:** Hepatic transaminases (ALT, AST), lipids, neutrophils, and platelets should be monitored, as abnormalities in these parameters were associated with ACTEMRA treatment in Phase 3 clinical trials. Dosage modifications may be required if laboratory abnormalities occur. Please see the full Prescribing Information for more information.

### ***Reporting Adverse Events***

It is important that you report all serious adverse events that occur in patients being treated with ACTEMRA, even if you do not think there is a causal relationship. As an ACTEMRA-prescribing internist and/or internal medicine subspecialist, such as a rheumatologist, the information you provide about these events may inform therapy and monitoring decisions for future patients.

**Reporting is easy and maintains patient confidentiality.** Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.* You can report your cases to Genentech or directly to the FDA:

- Genentech at 1-800-ACTEMRA (1-800-228-3672)
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

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**ATTACHMENT G: JOURNAL INFORMATION PIECE FOR  
NEUROLOGISTS**

## Important Safety Information for Neurologists About Demyelinating Disorders in Co-managing Rheumatoid Arthritis Patients Receiving ACTEMRA®

ACTEMRA® (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor that has been approved by the Food and Drug Administration (FDA) for two indications:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) with a recommended ACTEMRA® dosing interval of every 4 weeks.
- Children 2 years of age and older with active *Systemic Juvenile Idiopathic Arthritis (sJIA)* with a recommended ACTEMRA® dosing interval of every 2 weeks.

The safety and efficacy of ACTEMRA® for conditions other than RA and sJIA have not yet been established.

**Neurologists** co-managing RA patients should be aware of important safety information regarding treatment with ACTEMRA.

**Demyelinating disorders:** The impact of treatment with ACTEMRA on demyelinating disorders is not known, but multiple sclerosis and chronic inflammatory demyelinating polyneuropathy were reported rarely in clinical studies of adults with RA. Patients should be closely monitored for signs and symptoms potentially indicative of demyelinating disorders. Prescribers should exercise caution in considering the use of ACTEMRA in patients with preexisting or recent onset demyelinating disorders.

### **Reporting Adverse Events**

It is important that you report any serious neurologic adverse event, including demyelinating disorders, that occurs in a patient being treated with ACTEMRA, even if you do not think there is a causal relationship. The information that you, as a neurologist, provide about these events may inform therapy and monitoring decisions for future patients.

**Reporting is easy and maintains patient confidentiality.** Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.* You can report your cases to Genentech or directly to the FDA:

- Genentech at 1-800-ACTEMRA (1-800-228-3672)
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

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**ATTACHMENT H: JOURNAL INFORMATION PIECE FOR  
ONCOLOGISTS**

### Important Safety Information for Oncologists About Malignancy Risk With ACTEMRA<sup>®</sup>

ACTEMRA<sup>®</sup> (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor that has been approved by the Food and Drug Administration (FDA) for two indications:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) with a recommended ACTEMRA<sup>®</sup> dosing interval of every 4 weeks.
- Children 2 years of age and older with active *Systemic Juvenile Idiopathic Arthritis (sJIA)* with a recommended ACTEMRA<sup>®</sup> dosing interval of every 2 weeks.

The safety and efficacy of ACTEMRA<sup>®</sup> for conditions other than RA and sJIA have not yet been established.

**Oncologists** should be aware of important safety information about ACTEMRA.

**Malignancies** were observed in clinical studies of ACTEMRA. The impact of treatment with ACTEMRA on the development of the malignancies is not known, but malignancy is a known risk of biological products that suppress the immune system. ACTEMRA is an immunosuppressant and may increase the risk of malignancies.

#### ***Reporting Adverse Events***

If you are consulted to see a patient with cancer at any time after receiving ACTEMRA therapy, it is important that you report the case, even if you do not think there is a causal relationship. The information that you, as an oncologist, provide about these events may inform therapy and monitoring decisions for future patients.

**Reporting is easy and maintains patient confidentiality.** Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.* You can report your cases to Genentech or directly to the FDA:

- Genentech at 1-800-ACTEMRA (1-800-228-3672)
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

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**ATTACHMENT I: JOURNAL INFORMATION PIECE FOR  
RHEUMATOLOGISTS**



### Important Safety Information for Rheumatologists About Risks in Patients Receiving ACTEMRA<sup>®</sup>

ACTEMRA<sup>®</sup> (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor that has been approved by the Food and Drug Administration (FDA) for two indications:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) with a recommended ACTEMRA<sup>®</sup> dosing interval of every 4 weeks.
- Children 2 years of age and older with active *Systemic Juvenile Idiopathic Arthritis (sJIA)* with a recommended ACTEMRA<sup>®</sup> dosing interval of every 2 weeks.

The safety and efficacy of ACTEMRA<sup>®</sup> for conditions other than RA and sJIA have not yet been established.

**Rheumatologists** should be aware of important information regarding safety and laboratory monitoring recommendations for ACTEMRA.

**Serious infections:** Patients treated with ACTEMRA are at increased risk for developing serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral and other opportunistic infections.

**Gastrointestinal perforations:** Gastrointestinal (GI) perforation have been reported in Phase 3 clinical trials, primarily as complications of diverticulitis, including generalized purulent peritonitis, lower GI perforation, fistula and abscess. Most patients who developed GI perforations were taking concomitant nonsteroidal anti-inflammatory medications (NSAIDs), corticosteroids or methotrexate. ACTEMRA should be used with caution in patients who may be at increased risk for GI perforation. Patients presenting with new-onset abdominal symptoms should be evaluated promptly for early identification of GI perforation.

**Demyelinating disorders:** The impact of treatment with ACTEMRA on demyelinating disorders is not known, but multiple sclerosis and chronic inflammatory demyelinating polyneuropathy were reported rarely in clinical studies of adults with RA. Patients should be closely monitored for signs and symptoms potentially indicative of demyelinating disorders. Prescribers should exercise caution in considering the use of ACTEMRA in patients with preexisting or recent onset demyelinating disorders.

**Malignancies:** Malignancies were observed in clinical studies of ACTEMRA. The impact of treatment with ACTEMRA on the development of the malignancies is not known, but malignancy is a known risk of biological products that suppress the immune system. ACTEMRA is an immunosuppressant and may increase the risk of malignancies.

**Laboratory abnormalities:** Hepatic transaminases (ALT, AST), lipids, neutrophils and platelets should be monitored, as abnormalities in these parameters were associated with ACTEMRA treatment in Phase 3 clinical trials. Dosage modifications may be required if laboratory abnormalities occur. Please see the full Prescribing Information for more information.

***Reporting Adverse Events***

It is important that you report all serious adverse events that occur in patients being treated with ACTEMRA, even if you do not think there is a causal relationship. As an ACTEMRA-prescribing rheumatologist, the information you provide about these events may inform therapy and monitoring decisions for future patients.

**Reporting is easy and maintains patient confidentiality.** Your patient's name or contact information is not needed. *HIPAA does not apply to this adverse event reporting.* You can report your cases to Genentech or directly to the FDA:

- Genentech at 1-800-ACTEMRA (1-800-228-3672)
- MedWatch (FDA safety information and adverse event reporting program) at 1-800-332-1088 or online at [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

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