

ACTEMRA(R) Sterile Concentrate for Injection (200 mg)
Version
0.0Revision Date:
01-29-2020Date of last issue: 06-10-2017
Date of first issue: 12-04-2015**SECTION 1. IDENTIFICATION**

Product name : ACTEMRA(R) Sterile Concentrate for Injection (200 mg)

Product code : RO487-7533/F01

Common name(s), syno- : RoActemra
nym(s) of the substance**Manufacturer or supplier's details**

Company name of supplier : Genentech, Inc.

Address : DNA Way 1
94080 South San Francisco
CA
USA

Telephone : 001-(650) 225-1000

E-mail address : info.sds@roche.com

Emergency telephone

Emergency telephone num- : US Chemtrec phone (800)-424-9300
ber**Recommended use of the chemical and restrictions on use**

Recommended use : Formulated pharmaceutical active substance

Restrictions on use : For professional users only.

SECTION 2. HAZARDS IDENTIFICATION**GHS classification in accordance with 29 CFR 1910.1200**

Not a hazardous substance or mixture.

GHS label elements

Not a hazardous substance or mixture.

Other hazards

None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

Chemical name	CAS-No.	Concentration (% w/w)
Tocilizumab	375823-41-9	2.0
Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.	9005-65-6	0.05
.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl	57-50-1	5.0
di Sodium monohydrogen phosphate,	10039-32-4	0.15

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dodecahydrate		
Sodium dihydrogen phosphate dihydrate	13472-35-0	0.17
Water	7732-18-5	> 92.0

SECTION 4. FIRST AID MEASURES

- General advice : Do not leave the victim unattended.

- If inhaled : Move to fresh air.
 If unconscious, place in recovery position and seek medical advice.
 If symptoms persist, call a physician.

- In case of skin contact : If on skin, rinse well with water.

- In case of eye contact : Immediately flush eye(s) with plenty of water.
 Remove contact lenses.
 Protect unharmed eye.
 If eye irritation persists, consult a specialist.

- If swallowed : Keep respiratory tract clear.
 Do not give milk or alcoholic beverages.
 Never give anything by mouth to an unconscious person.
 If symptoms persist, call a physician.
 Rinse mouth with water.

- Most important symptoms and effects, both acute and delayed : None known.

- Notes to physician : The first aid procedure should be established in consultation with the doctor responsible for industrial medicine.

SECTION 5. FIRE-FIGHTING MEASURES

- Suitable extinguishing media : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

- Specific hazards during fire fighting : No information available.

- Hazardous combustion products : In case of fire hazardous decomposition products may be produced such as:
 Carbon monoxide
 Nitrogen oxides (NOx)
 Sulfur oxides

- Further information : Standard procedure for chemical fires.
 Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

- Special protective equipment for fire-fighters : Wear self-contained breathing apparatus for firefighting if necessary.

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SECTION 6. ACCIDENTAL RELEASE MEASURES

- Personal precautions, protective equipment and emergency procedures : Refer to protective measures listed in sections 7 and 8.
- Environmental precautions : Local authorities should be advised if significant spillages cannot be contained.
- Methods and materials for containment and cleaning up : Wipe up with absorbent material (e.g. cloth, fleece).
Keep in suitable, closed containers for disposal.

SECTION 7. HANDLING AND STORAGE

- Advice on protection against fire and explosion : Normal measures for preventive fire protection.
- Advice on safe handling : For personal protection see section 8.
Smoking, eating and drinking should be prohibited in the application area.
- Conditions for safe storage : Electrical installations / working materials must comply with the technological safety standards.
- Further information on storage conditions : See label, package insert or internal guidelines
- Materials to avoid : No materials to be especially mentioned.
- Storage temperature : Protected from heat and light
- Further information on storage stability : No decomposition if stored and applied as directed.

No decomposition if stored and applied as directed.
- Packaging material : Suitable material: Stainless steel, glass, Vials

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION
Ingredients with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl	57-50-1	TWA	10 mg/m ³	ACGIH
		TWA (Respirable)	5 mg/m ³	NIOSH REL
		TWA (total)	10 mg/m ³	NIOSH REL
		TWA (total)	15 mg/m ³	OSHA Z-1

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		dust)		
		TWA (respirable fraction)	5 mg/m3	OSHA Z-1
		TWA (Total dust)	15 mg/m3	OSHA P0
		TWA (respirable dust fraction)	5 mg/m3	OSHA P0
Tocilizumab	375823-41-9	IOEL	0.4 mg/m3	Roche Industrial Hygiene Committee (RIHC)

Engineering measures : No data available

Personal protective equipment

Respiratory protection : No personal respiratory protective equipment normally required.

Hand protection

Material : Protective gloves

Remarks : Wear appropriate protective gloves to prevent skin contact. Replace torn or punctured gloves promptly.

Eye protection : Safety glasses

Skin and body protection : Protective suit

Hygiene measures : Handle in accordance with good industrial hygiene and safety practice.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : Aqueous solution, Clear liquid, sterile

Color : light yellow

Odor : No data available

Odor Threshold : No data available

Melting point/range : No data available

Boiling point/boiling range : No data available

Flash point : does not flash

Evaporation rate : No data available

Self-ignition : No data available

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Upper explosion limit / Upper flammability limit	:	No data available
Lower explosion limit / Lower flammability limit	:	No data available
Vapor pressure	:	No data available
Relative vapor density	:	No data available
Relative density	:	No data available
Solubility(ies)		
Water solubility	:	completely miscible
Solubility in other solvents	:	No data available
Partition coefficient: n-octanol/water	:	No data available
Autoignition temperature	:	No data available
Decomposition temperature	:	No data available
Viscosity		
Viscosity, dynamic	:	No data available
Viscosity, kinematic	:	No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity	:	No dangerous reaction known under conditions of normal use.
Chemical stability	:	Stable under normal conditions. Proteins are temperature-sensitive; the thermal denaturation has an impact on quality but does not affect Plant and Process Safety; during decomposition no flammable gas, no organic peroxide and no oxidising substances are created Does not contain any antimicrobial preservative; therefore, care must be taken to ensure the sterility of the prepared solution
Possibility of hazardous reactions	:	Stable under recommended storage conditions. No hazards to be specially mentioned.
Incompatible materials	:	No data available
Hazardous decomposition products	:	No data available

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Not classified based on available information.

Components:**.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl:**

Acute oral toxicity : LD50 Oral (Rat): 29,700 mg/kg
LD50 Oral (Mouse): 14,000 mg/kg

Acute inhalation toxicity : Acute toxicity estimate: > 30 mg/l
Test atmosphere: dust/mist
Method: Expert judgment

Acute dermal toxicity : Acute toxicity estimate: > 5,001 mg/kg
Method: Expert judgment

Tocilizumab:

Acute oral toxicity : Remarks: Not bioavailable by oral administration

Acute toxicity (other routes of administration) : No-observed-effect level (Rat): >= 150 mg/kg
Application Route: i.v.

Skin corrosion/irritation

Not classified based on available information.

Serious eye damage/eye irritation

Not classified based on available information.

Respiratory or skin sensitization**Skin sensitization**

Not classified based on available information.

Respiratory sensitization

Not classified based on available information.

Germ cell mutagenicity

Not classified based on available information.

Components:**Tocilizumab:**

Genotoxicity in vitro : Result: negative
Remarks: In vitro tests did not show mutagenic effects

Carcinogenicity

Not classified based on available information.

Components:**.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl:**

Remarks : No ingredient of this product present at levels greater than or

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equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

IARC No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA No component of this product present at levels greater than or equal to 0.1% is on OSHA's list of regulated carcinogens.

NTP No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity

Not classified based on available information.

STOT-single exposure

Not classified based on available information.

Components:**.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl:**

Assessment : The substance or mixture is not classified as specific target organ toxicant, single exposure.

STOT-repeated exposure

Not classified based on available information.

Components:**.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl:**

Assessment : The substance or mixture is not classified as specific target organ toxicant, repeated exposure.

Repeated dose toxicity**Components:****Tocilizumab:**

Species : Rat
NOAEL : mg/kg bw/day, 10
Application Route : i.v.
Exposure time : 28 d
Remarks : Subacute toxicity

Aspiration toxicity

Not classified based on available information.

Components:**.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl:**

No data available

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Remarks : Health injuries are not known or expected under normal use.

Tocilizumab:

Remarks : anaphylactic reactions may occur following the intravenous application of proteins; rare cases of hypersensitivity have been described with other monoclonal antibodies

SECTION 12. ECOLOGICAL INFORMATION**Ecotoxicity****Components:****.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl:**Toxicity to fish : LC50: > 100 mg/l
Exposure time: 96 h**Ecotoxicology Assessment**

Acute aquatic toxicity : This product has no known ecotoxicological effects.

Chronic aquatic toxicity : This product has no known ecotoxicological effects.

Toxicity Data on Soil : Not expected to adsorb on soil.

Other organisms relevant to the environment : No data available

Tocilizumab:Toxicity to fish : LC50 (Brachydanio rerio (zebrafish)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
GLP: yes
Remarks: nominal concentrationNOEC (Brachydanio rerio (zebrafish)): 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
GLP: yes
Remarks: nominal concentrationToxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h
Test Type: Immobilization
Method: OECD Test Guideline 202
GLP: yes
Remarks: nominal concentration

NOEC (Daphnia magna (Water flea)): 100 mg/l

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Exposure time: 48 h
 Test Type: Immobilization
 Method: OECD Test Guideline 202
 GLP: yes
 Remarks: nominal concentration

Toxicity to algae/aquatic plants : EC50 (Desmodesmus subspicatus (green algae)): > 100 mg/l
 Exposure time: 72 h
 Method: OECD Test Guideline 201
 GLP: yes
 Remarks: nominal concentration

NOEC (Desmodesmus subspicatus (green algae)): 100 mg/l
 Exposure time: 72 h
 Method: OECD Test Guideline 201
 GLP: yes
 Remarks: nominal concentration

Toxicity to microorganisms : (activated sludge): 100 mg/l
 Exposure time: 14 d
 Method: OECD Test Guideline 301F
 GLP: yes
 Remarks: no adverse influence on substrate biodegradation

Persistence and degradability**Components:****Tocilizumab:**

Biodegradability : aerobic
 Theoretical oxygen demand
 Result: Readily biodegradable.
 Biodegradation: >= 76 %
 Exposure time: 28 d
 Method: OECD Test Guideline 301F
 GLP: yes

Bioaccumulative potential**Components:****.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl:**

Partition coefficient: n-octanol/water : log Pow: -3.67

Tocilizumab:

Partition coefficient: n-octanol/water : Remarks: No data available

Mobility in soil

No data available

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Other adverse effects

Product:

Ozone-Depletion Potential : Regulation: 40 CFR Protection of Environment; Part 82 Protection of Stratospheric Ozone - CAA Section 602 Class I Substances
 Remarks: This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).

Components:

Tocilizumab:

Additional ecological information : No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

Waste from residues : Can be disposed as waste water, when in compliance with local regulations.
 Contaminated packaging : Empty containers should be taken to an approved waste handling site for recycling or disposal.
 Do not re-use empty containers.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG

Not regulated as a dangerous good

IATA-DGR

Not regulated as a dangerous good

IMDG-Code

Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not applicable

Domestic regulation

49 CFR

Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity

Components	CAS-No.	Component RQ	Calculated product RQ
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SAFETY DATA SHEET

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		(lbs)	(lbs)
di Sodium monohydrogen phosphate, dodecahydrate	10039-32-4	5000	*

*: Calculated RQ exceeds reasonably attainable upper limit.

SARA 304 Extremely Hazardous Substances Reportable Quantity

This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity

Components	CAS-No.	Component TPQ (lbs)
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SARA 311/312 Hazards : No SARA Hazards

Clean Air Act

This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).

This product does not contain any hazardous air pollutants (HAP), as defined by the U.S. Clean Air Act Section 112 (40 CFR 61).

This product does not contain any chemicals listed under the U.S. Clean Air Act Section 112(r) for Accidental Release Prevention (40 CFR 68.130, Subpart F).

This product does not contain any chemicals listed under the U.S. Clean Air Act Section 111 SOCM Intermediate or Final VOC's (40 CFR 60.489).

Clean Water Act

The following Hazardous Substances are listed under the U.S. CleanWater Act, Section 311, Table 116.4A:

di Sodium monohydrogen phosphate, dodecahydrate	10039-32-4	>= 0.1 - < 1 %
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The following Hazardous Chemicals are listed under the U.S. CleanWater Act, Section 311, Table 117.3:

di Sodium monohydrogen phosphate, dodecahydrate	10039-32-4	>= 0.1 - < 1 %
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This product does not contain any toxic pollutants listed under the U.S. Clean Water Act Section 307

US State Regulations

Massachusetts Right To Know

.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl	57-50-1
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Pennsylvania Right To Know

Water	7732-18-5
.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl	57-50-1
di Sodium monohydrogen phosphate, dodecahydrate	10039-32-4

Maine Chemicals of High Concern

Vermont Chemicals of High Concern

Washington Chemicals of High Concern

California Permissible Exposure Limits for Chemical Contaminants

.alpha.-D-Glucopyranoside, .beta.-D-fructofuranosyl	57-50-1
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The ingredients of this product are reported in the following inventories:

DSL : This product contains the following components that are not

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on the Canadian DSL nor NDSL.

Tocilizumab

- AICS : Not in compliance with the inventory
- NZIoC : On the inventory, or in compliance with the inventory
- ENCS : Not in compliance with the inventory
- ISHL : Not in compliance with the inventory
- KECI : Not in compliance with the inventory
- PICCS : Not in compliance with the inventory
- IECSC : Not in compliance with the inventory
- TCSI : Not in compliance with the inventory
- TSCA : Substance(s) not listed on TSCA inventory

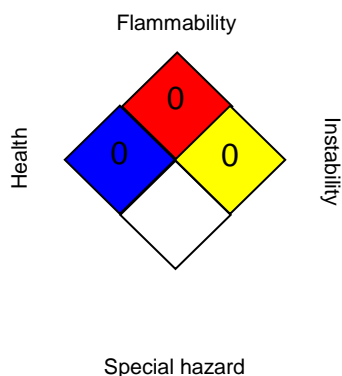
TSCA list

No substances are subject to a Significant New Use Rule.

No substances are subject to TSCA 12(b) export notification requirements.

SECTION 16. OTHER INFORMATION

NFPA:



HMIS® IV:

HEALTH	/	0
FLAMMABILITY		0
PHYSICAL HAZARD		0

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations

- ACGIH : USA. ACGIH Threshold Limit Values (TLV)
- NIOSH REL : USA. NIOSH Recommended Exposure Limits
- OSHA P0 : USA. OSHA - TABLE Z-1 Limits for Air Contaminants - 1910.1000
- OSHA Z-1 : USA. Occupational Exposure Limits (OSHA) - Table Z-1 Lim-

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	its for Air Contaminants
ACGIH / TWA	: 8-hour, time-weighted average
NIOSH REL / TWA	: Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
OSHA P0 / TWA	: 8-hour time weighted average
OSHA Z-1 / TWA	: 8-hour time weighted average

AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; HMIS - Hazardous Materials Identification System; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative

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The information provided in this Material Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

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