SAFETY DATA SHEET

Section 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1. Product identifier

Product Name Tofacitinib Citrate Modified Release Tablets

Product Code(s) PZ01959
Trade Name: Xeljanz XR
Chemical Family: Janus kinase 3 (JAK3) inhibitor

1.2. Relevant identified uses of the substance or mixture and uses advised against

Recommended Use Pharmaceutical product

1.3. Details of the supplier of the safety data sheet

Pfizer Inc
235 East 42nd Street
New York, New York 10017
1-800-879-3477

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

1.4. Emergency telephone number

Emergency Telephone Chemtrec 1-800-424-9300 International Chemtrec (24 hours):+1-703-527-3887
E-mail address pfizer-MSDS@pfizer.com

Section 2: HAZARDS IDENTIFICATION

2.1. Classification of the substance or mixture

Reproductive toxicity Category 1B

2.2. Label elements

Signal word Danger

Hazard statements H360Df - May damage the unborn child. Suspected of damaging fertility

Precautionary Statements
P202 - Do not handle until all safety precautions have been read and understood
P281 - Use personal protective equipment as required
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations

2.3. Other hazards

Other hazards An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

Section 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Hazardous

Chemical Name	EC No	CAS No	Weight-%	Classification according to Regulation (EC) No. 1272/2008 [CLP]	REACH Registration Number
Tofacitinib citrate	Not Listed	540737-29-9	8-10	Acute Tox.4 (H302) Repr.1B (H360Df)	
Magnesium Stearate	209-150-3	557-04-0	*	Not Listed	

NonHazardous

Chemical Name	EC No	CAS No	Weight-%	Classification according to Regulation (EC) No. 1272/2008 [CLP]	REACH Registration Number
Sorbitol	Not Listed	6706-59-8	*	Not Listed	
Hydroxyethyl cellulose	Not Listed	9004-62-0	*	Not Listed	
Polyvinyl pyrrolidone-Vinyl acetate copolymer	Not Listed	25086-89-9	*	Not Listed	
Cellulose acetate	Not Listed	9004-35-7	*	Not Listed	
Opadry Pink	Not Listed	MIXTURE	*	Not Listed	
Hydroxypropyl cellulose	Not Listed	9004-64-2	*	Not Listed	
Black ink	Not Listed	NOT ASSIGNED	*	Not Listed	

Full text of H- and EUH-phrases: see section 16

Additional information * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety. In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

Section 4: FIRST AID MEASURES

4.1. Description of first aid measures

Inhalation Remove to fresh air. Seek immediate medical attention/advice.

Eye contact	Rinse thoroughly with plenty of water for at least 15 minutes, lifting lower and upper eyelids. Consult a physician.
Skin contact	Wash skin with soap and water. In the case of skin irritation or allergic reactions see a physician.
Ingestion	Clean mouth with water and drink afterwards plenty of water.

4.2. Most important symptoms and effects, both acute and delayed

Most important symptoms and effects	For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

4.3. Indication of any immediate medical attention and special treatment needed

Note to physicians	None.

Section 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing media

Suitable Extinguishing Media	Dry chemical, CO2, alcohol-resistant foam or water spray.

5.2. Special hazards arising from the substance or mixture

Specific hazards arising from the chemical	Fine particles (such as dust and mists) may fuel fires/explosions.
Hazardous combustion products	Formation of toxic gases is possible during heating or fire. May include oxides of carbon, nitrogen.

5.3. Advice for firefighters

Special protective equipment for fire-fighters	Firefighters should wear self-contained breathing apparatus and full firefighting turnout gear. Use personal protection equipment.

Section 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal precautions, protective equipment and emergency procedures

Personal precautions	Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.
For emergency responders	Use personal protection recommended in Section 8.

6.2. Environmental precautions

Environmental precautions	Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

6.3. Methods and material for containment and cleaning up

Methods for containment	Prevent further leakage or spillage if safe to do so.
Methods for cleaning up	Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.
Prevention of secondary hazards	Clean contaminated objects and areas thoroughly observing environmental regulations.

6.4. Reference to other sections

Reference to other sections	See section 8 for more information. See section 13 for more information.

Section 7: HANDLING AND STORAGE

7.1. Precautions for safe handling

Advice on safe handling
Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken,. avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash hands and any exposed skin after removal of PPE. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

General hygiene considerations Handle in accordance with good industrial hygiene and safety practice.

7.2. Conditions for safe storage, including any incompatibilities

Storage Conditions Store as directed by product packaging.

7.3. Specific end use(s)

Specific use(s) Pharmaceutical drug product.

Section 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

Exposure Limits
Refer to available public information for specific member state Occupational Exposure Limits.

Tofacitinib citrate
Pfizer OEL TWA-8 Hr: 15 µg/m³, Skin

Hydroxypropyl cellulose

Russia	MAC: 10 mg/m³

Magnesium Stearate

ACGIH TLV	10 mg/m³
	3 mg/m³
Ireland	10 mg/m³
	STEL: 30 mg/m³
Spain	10 mg/m³

8.2. Exposure controls

Engineering controls Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Environmental exposure controls No information available.

Personal protective equipment Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

Eye/face protection Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.).

Hand protection Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.).

Skin and body protection Wear impervious protective clothing to prevent skin contact – consider use of disposable clothing where appropriate. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.).

Respiratory protection Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL (e.g. particulate respirator with a full mask, P3 filter).

(Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.).

General hygiene considerations Handle in accordance with good industrial hygiene and safety practice.

Section 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Physical state	Tablets
Color	Pink to beige
Molecular formula (MF):	Mixture
Molecular weight	Mixture
Odor	No data available.
Odor threshold	No data available

Property	**Values**
	No data available
Melting point / freezing point	No data available
Boiling point / boiling range	No data available
Flash point	No data available
Evaporation rate	No data available
Flammability (solid, gas)	No data available
Flammability Limit in Air	
Upper flammability limit:	No data available
Lower flammability limit:	No data available
Vapor pressure	No data available
Vapor density	No data available
Relative density	No data available
Water solubility	No data available
Solubility(ies)	No data available
Autoignition temperature	No data available
Decomposition temperature	No data available
Kinematic viscosity	No data available
Dynamic viscosity	No data available
Explosive properties	No information available
Oxidizing properties	No information available
Partition Coefficient: (Method, pH, Endpoint, Value)	
Tofacitinib citrate	
Predicted 7.4 Log D -2.56	

9.2. Other information

Liquid Density	No data available
Bulk density	No data available

Section 10: STABILITY AND REACTIVITY

10.1. Reactivity

Reactivity No data available.

10.2. Chemical stability

Stability Stable under normal conditions.

Explosion data
Sensitivity to Mechanical Impact No data available.
Sensitivity to Static Discharge No data available.

10.3. Possibility of hazardous reactions

Possibility of hazardous reactions No information available.

10.4. Conditions to avoid

Conditions to avoid Fine particles (such as dust and mists) may fuel fires/explosions.

10.5. Incompatible materials

Incompatible materials As a precautionary measure, keep away from strong oxidizers.

10.6. Hazardous decomposition products

Hazardous decomposition products No data available.

Section 11: TOXICOLOGICAL INFORMATION

11.1. Information on toxicological effects

General Information: The information included in this section describes the potential hazards of the individual ingredients
Short term Active ingredient may be harmful if swallowed.
Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on lymphatic system blood and blood forming organs
Known Clinical Effects: Based on clinical trials in humans, possible adverse effects following exposure to this compound may include: nausea, headache, immune-mediated disorders, and hematological effects.

Acute Toxicity: (Species, Route, End Point, Dose)
Tofacitinib citrate
Rat Oral Minimum Lethal Dose 500 mg/kg
Non-human Primate Oral Maximum Asymptomatic Dose 40 mg/kg
Magnesium Stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m ^{3}

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50
Polyvinyl pyrrolidone-Vinyl acetate copolymer	> 630 mg/kg (Rat)	-	-
Cellulose acetate	> 5 g/kg (Rat)	-	-
Hydroxypropyl cellulose	= 10200 mg/kg (Rat)	-	-

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)
Tofacitinib citrate
Skin Sensitization - LLNA Mouse Negative
Eye Irritation Rabbit Non-irritating
Skin Irritation Rabbit Non-irritating

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)
Tofacitinib citrate
6 Week(s) Rat Oral 1 mg/kg/day NOAEL Erythroid cells, Lymphatic system
1 Month(s) Monkey Oral 10 mg/kg/day NOAEL Lymphatic system, Immune system, Erythroid cells
39 Week(s) Monkey Oral 10 mg/kg/day NOAEL Bone Marrow, Erythroid cells, Lymphatic system

6 Month(s) Rat Oral 1 mg/kg/day NOAEL Lymphatic system, Erythroid cells
39 Week(s) Monkey Oral 2 mg/kg/day NOAEL Blood, Blood forming organs, Spleen, Thymus
1 Month(s) Mini Pig Dermal 10 mg/cm2/day NOAEL None identified
3 Month(s) Mini Pig Dermal 10 mg/cm2/day NOAEL Spleen
Magnesium Stearate
13 Week(s) Rat Oral 1092 g/kg LOAEL Liver

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))
Tofacitinib citrate
Embryo / Fetal Development Rat Oral 30 mg/kg/day NOAEL Fetotoxicity
Embryo / Fetal Development Rabbit Oral 100 mg/kg/day NOAEL
Embryo / Fetal Development Rabbit Oral 10
mg/kg/day Developmental toxicity
Fertility & Embryonic Development (Male/Female) Rat Oral 10 mg/kg/day NOAEL Maternal Toxicity
Fertility & Embryonic Development-Females Rat Oral 1.0 mg/kg/day NOAEL Fertility

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)
Tofacitinib citrate
In Vitro Bacterial Mutagenicity (Ames) *Salmonella* , *E. coli* Negative
In Vitro Cytogenetics Human Lymphocytes Positive with activation
Mammalian Cell Mutagenicity Chinese Hamster Ovary (CHO) cells Negative
In Vivo Micronucleus Rat Bone Marrow Negative
In Vivo Unscheduled DNA Synthesis Rat Hepatocyte Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))
Tofacitinib citrate
2 Year(s) Rat Female Oral 10 mg/kg/day NOAEL Benign tumors
2 Year(s) Rat Male Oral 10 mg/kg/day LOAEL Benign tumors
6 Month(s) Mouse Oral 200 mg/kg/day NOEL Not carcinogenic
Carcinogenicity None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

Section 12: ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been thoroughly investigated. Releases to the environment should be avoided.

12.1. Toxicity

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)
Tofacitinib citrate
Activated sludge OECD EC50 3 hours 592.9 mg/l
Mysidopsis bahia (Mysid Shrimp) OECD LC50 96 hours > 1.0 mg/l
Cyprinodon variegatus (Sheepshead Minnow) OECD LC50 96 Hours > 1.0 mg/L
Aquatic Toxicity Comments: A greater than (>) symbol indicates that acute ecotoxicity was not observed at the maximum solubility. Since the substance is insoluble in aqueous solutions above this concentration, an acute ecotoxicity value (i.e. LC/EC50) is not achievable.

12.2. Persistence and degradability

Persistence and degradability No information available.

12.3. Bioaccumulative potential

Bioaccumulation No information available.

Partition Coefficient: (Method, pH, Endpoint, Value)
Tofacitinib citrate
Predicted 7.4 Log D -2.56

12.4. Mobility in soil

Mobility in soil No information available.

12.5. Results of PBT and vPvB assessment

PBT and vPvB assessment No information available.

12.6. Other adverse effects

Other adverse effects No information available.

Section 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

Section 14: TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

Section 15: REGULATORY INFORMATION

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

Sorbitol
- **CERCLA/SARA Section 313 de minimus %** Not Listed
- **California Proposition 65** Not Listed
- **EINECS** Not Listed

Tofacitinib citrate
- **CERCLA/SARA Section 313 de minimus %** Not Listed
- **California Proposition 65** Not Listed
- **EINECS** Not Listed

Hydroxyethyl cellulose
- **CERCLA/SARA Section 313 de minimus %** Not Listed
- **California Proposition 65** Not Listed
- **TSCA** Present

EINECS	Not Listed
AICS	Present

Polyvinyl pyrrolidone-Vinyl acetate copolymer

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
TSCA	Present
EINECS	Not Listed
AICS	Present

Cellulose acetate

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
TSCA	Present
EINECS	Not Listed
AICS	Present

Opadry Pink

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
EINECS	Not Listed

Hydroxypropyl cellulose

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
TSCA	Present
EINECS	Not Listed
AICS	Present

Magnesium Stearate

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
TSCA	Present
EINECS	209-150-3
AICS	Present

Black ink

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
EINECS	Not Listed

15.2. Chemical safety assessment

Chemical Safety Report No information available

Section 16: OTHER INFORMATION

Key or legend to abbreviations and acronyms used in the safety data sheet

Full text of H-Statements referred to under section 3
Acute toxicity, oral-Cat.4; H302 - Harmful if swallowed Reproductive toxicity-Cat.1B; H360Df - May damage the unborn child. Suspected of damaging fertility

Data Sources: Pfizer proprietary drug development information. Safety data sheets for individual ingredients.

Reason for revision Updated Section 9 - Physical and Chemical Properties.

Revision date 09-Jan-2020

Prepared By Product Stewardship Hazard Communication
Pfizer Global Environment, Health, and Safety Operations

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there is no known information at this time.