SAFETY DATA SHEET

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

1.1. Product identifier

Product Name Ritlecitinib Capsule

Product Code(s) PF00075
Trade Name: LITFULO
Compound Number PF-06651600-15
Chemical Family: Not determined

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
66 Hudson Boulevard East
New York, New York 10001
1-800-879-3477

Pfizer Ireland Pharmaceuticals
OSG Building
Ringaskiddy, Co. Cork.
Ireland
+353 21 4378701

E-mail address pfizer-MSDS@pfizer.com

1.4. Emergency telephone number

Emergency Telephone Chemtrec 1-800-424-9300 International Chemtrec (24 hours):+1-703-527-3887

Section 2: HAZARDS IDENTIFICATION

2.1. Classification of the substance or mixture

GHS - Classification: Regulated according to Regulation (EC) 1272/2008 and/or other applicable regulations.

Skin corrosion/irritation Category 2 - H315
Serious eye damage/eye irritation Category 2 - H319
Reproductive toxicity Category 2 - H361d

2.2. Label elements

Signal word Warning

Hazard statements
H315 - Causes skin irritation
H319 - Causes serious eye irritation
H361d - Suspected of damaging the unborn child

Precautionary Statements
P201 - Obtain special instructions before use
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
P332 + P313 - If skin irritation occurs: Get medical advice/attention

Supplemental Hazard Compound, not fully tested, additional hazards may exist.

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

Substances Not applicable

3.2 Mixtures

Hazardous

Chemical name	Weight-%	REACH Registration Number	EC No	Classification according to Regulation (EC) No. 1272/2008 [CLP]	Specific concentration limit (SCL)	M-Factor	M-Factor (long-term)
Ritlecitinib Tosylate (CAS #: 2192215-81-7)	55 - 65		Not Listed	Repr.2 (H361d) Skin Irrit.2 (H315) Eye Irrit.2 (H319)	Not Listed	No data available	No data available

NonHazardous

Chemical name	Weight-%	REACH Registration Number	EC No	Classification according to Regulation (EC) No. 1272/2008 [CLP]	Specific concentration limit (SCL)	M-Factor	M-Factor (long-term)
Lactose Monohydrate (CAS #: 89466-76-2)	*	-	Not Listed	Not classified as hazardous	Not Listed	No data available	No data available
Microcrystalline cellulose (CAS #: 9004-34-6)	*	-	232-674-9	Not classified as hazardous	Not Listed	No data available	No data available
Glyceryl behenate (CAS #: 18641-57-1)	*		242-471-7	Not classified as hazardous	Not Listed	No data available	No data available
Crospovidone	*	-	No information	Not classified	Not Listed	No data	No data

(CAS #:)			available	as hazardous		available	available

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

Acute Toxicity Estimate

Chemical name	Oral LD50	Dermal LD50	Inhalation LC50 - 4 hour - dust/mist - mg/L	Inhalation LC50 - 4 hour - vapor - mg/L	Inhalation LC50 - 4 hour - gas - ppm
Microcrystalline cellulose 9004-34-6	5000	2000	5.8	No data available	No data available
Crospovidone	100000	No data available	No data available	No data available	No data available

Additional information

* Proprietary
Non-hazardous ingredients provided for completeness. 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

Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion

Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

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 and nitrogen and products of sulfur

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 Remove all sources of ignition. Contain the source of the spill if it is safe to do so. Collect spilled material by a method that controls dust generation. Avoid use of a filtered vacuum 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 thoroughly after handling. 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 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.

Ritlecitinib Tosylate

Pfizer OEL TWA-8 Hr: 30 µg/m³

Microcrystalline cellulose

ACGIH TLV	10 mg/m³
Denmark	1 mg/m³
Estonia	10 mg/m³
	2 mg/m³
Finland	2 mg/m³
France	10 mg/m³
	1 mg/m³
Hungary	3 mg/m³
Ireland	10 mg/m³
	STEL: 30 mg/m³
Latvia	2 mg/m³
	6 mg/m³
Poland	3 mg/m³
Romania	10 mg/m³
Russia	TWA: 6 mg/m³
	MAC: 10 mg/m³
Spain	10 mg/m³
Switzerland	3 mg/m³
	2 mg/m³
OSHA PEL	15 mg/m³
	5 mg/m³
	(vacated) TWA: 15 mg/m³ total dust
	(vacated) TWA: 5 mg/m³ respirable fraction
	(vacated) TWA: 5 mg/m³
	(vacated) STEL: 10 mg/m³
United Kingdom	TWA: 10 mg/m³
	TWA: 4 mg/m³
	STEL: 20 mg/m³
	STEL: 12 mg/m³

Crospovidone

Russia	MAC: 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 gloves (e.g. Nitrile, etc.) are 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 Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (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 half mask, P3 filter). (Respirators must meet the standards in accordance with EN140, 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	solid
Color	White to pale color
Odor	No information available.
Odor threshold	No information available
Molecular formula	Mixture
Molecular weight	Mixture

Property	**Values**
pH	No data available
Melting point / freezing point	No data available
Boiling point / boiling range	
Flash point	No information 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)	Soluble methanol
Partition coefficient	No data available
Autoignition temperature	No data available
Decomposition temperature	No data available
Kinematic viscosity	No data available
Dynamic viscosity	No data available
Particle characteristics	
Particle Size	No information available
Particle Size Distribution	No information available
Explosive properties	No information available

Partition Coefficient: (Method, pH, Endpoint, Value)
Ritlecitinib Tosylate
Measured 4 Log P 0.445
Measured 7 Log P 1.50
Measured 9 Log P 1.40
Ritlecitinib
Predicted 7.4 Log D 0.328

9.2. Other information
No information available

9.2.1. Information with regard to physical hazard classes
No information available

9.2.2. Other safety characteristics
No information 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. As a precautionary measure, keep away from heat sources and electrostatic discharge.

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 hazard classes as defined in Regulation (EC) No 1272/2008

General Information: Toxicological properties have not been thoroughly investigated. The information in this section describes the hazards of various forms of the active ingredient.
Known Clinical Effects: Based on clinical trials in humans, possible adverse effects following exposure to this compound may include: diarrhea, abdominal pain, abdominal discomfort, flatulence, difficult digestion (dyspepsia), inability to swallow (dysphagia), and discolored feces.
Acute toxicity Based on available data, the classification criteria are not met.
Serious eye damage/eye irritation Classification is based on mixture calculation methods based on component data.
Skin corrosion/irritation Classification is based on mixture calculation methods based on component data.
Respiratory or skin sensitization Based on available data, the classification criteria are not met.
STOT - single exposure Based on available data, the classification criteria are not met.
STOT - repeated exposure Based on available data, the classification criteria are not met.
Reproductive toxicity Classification is based on mixture calculation methods based on component data.
Germ cell mutagenicity Based on available data, the classification criteria are not met.
Carcinogenicity Based on available data, the classification criteria are not met.
Aspiration hazard Based on available data, the classification criteria are not met.

Acute Toxicity: (Species, Route, End Point, Dose)
Microcrystalline cellulose
Rat Oral LD50 > 5000 mg/kg
Rabbit Dermal LD50 > 2000 mg/kg
Glyceryl behenate
Rat Oral LD50 5 g/kg
Crospovidone
Rat Oral LD50 100 g/kg
Ritlecitinib
Rat Oral NOAEL 1000 mg/kg

Dog Oral NOAEL 300 mg/kg

Chemical name	Oral LD50	Dermal LD50	Inhalation LC50
Microcrystalline cellulose	> 5 g/kg (Rat)	> 2000 mg/kg (Rabbit)	> 5800 mg/m³ (Rat) 4 h
Crospovidone	= 100 g/kg (Rat)	-	-

Irritation / Sensitization: (Study Type, Species, Severity)

Ritlecitinib Tosylate

Skin Irritation (*In vitro* , RhE) Not applicable Positive
Skin Corrosivity (*In vitro* , RHE) Not applicable Negative
Skin Sensitizarion (*In chemico* , DPRA) Not applicable Positive
Sensitizarion (*In vitro* , KeratinoSens) Not applicable Negative
Skin Sensitization - LLNA Mouse Negative
Eye Irritation Rabbit Mild

Microcrystalline cellulose

Skin irritation Rabbit Non-irritating
Eye irritation Rabbit Non-irritating

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Ritlecitinib Tosylate

6 Month(s) Rat Oral 200 mg/kg/day NOAEL None identified
9 Month(s) Dog Oral 5 mg/kg/day NOAEL Brain, Immune system
9 Month(s) Dog Oral 10 mg/kg/day NOAEL Immune system, Brain, Central Nervous System, Peripheral nervous system

PF-06651600-25

8 Week(s) Rat Oral 175 mg/kg/day NOAEL Blood, Thymus, Spleen, Lymphoid tissue, Bone marrow
8 Week(s) Dog Oral 45 mg/kg/day NOAEL None identified

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Ritlecitinib Tosylate

Embryo / Fetal Development Rat Oral 175 mg/kg/day NOAEL Maternal toxicity
Embryo / Fetal Development Rat Oral 75 mg/kg/day NOAEL Developmental toxicity
Embryo / Fetal Development Rabbit Oral 75 mg/kg/day NOAEL Maternal Toxicity
Embryo / Fetal Development Rabbit Oral 25 mg/kg/day NOAEL Developmental toxicity
Fertility & Embryonic Development (Male/Female) Rat Oral (M) 60 mg/kg/day NOAEL Fertility, Paternal toxicity
Fertility & Embryonic Development (Male/Female) Rat Oral (F) 200 mg/kg/day NOAEL Maternal Toxicity, Fertility, Early embryonic development

Ritlecitinib

Prenatal & Postnatal Development Rat Oral 75 mg/kg/day NOAEL Developmental toxicity
Prenatal & Postnatal Development Rat Oral 175 mg/kg/day NOAEL Maternal Toxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

PF-06651600-25

Bacterial Mutagenicity (Ames) *Salmonella* , *E. coli* Negative
In Vitro Micronucleus TK6 cells Positive
In Vivo Micronucleus Rat Bone marrow Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Ritlecitinib Tosylate

1 Month(s) Mouse Oral 450 mg/kg/day NOAEL None identified
6 Month(s) Mouse Oral 300 mg/kg/day NOAEL Not carcinogenic
104 Week(s) Rat Oral 100 mg/kg/day LOAEL Benign tumors

Carcinogenicity None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

Crospovidone

IARC Group 3 (Not Classifiable)

11.2. Information on other hazards

11.2.1. Endocrine disrupting properties

Endocrine disrupting properties No information available.

11.2.2. Other information

Other adverse effects No information available.

Section 12: ECOLOGICAL INFORMATION

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

12.1. Toxicity

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Ritlecitinib Tosylate

Raphidocelis subcapitata (Freshwater alga) OECD ErC50 72 Hours > 20 mg/L
Raphidocelis subcapitata (Freshwater alga) OECD NOEC 72 Hours 8 mg/L

Bacterial Inhibition: (Inoculum, Method, End Point, Result)

Ritlecitinib Tosylate

Activated sludge OECD EC15 1000 mg/L

Chronic Aquatic Toxicity: (Species, Method, Duration, Endpoint, Result, Adverse Endpoint)

Ritlecitinib Tosylate

Pimephales promelas (Fathead Minnow) OECD 33 Day(s) NOEC 1.7 mg/L Survival

12.2. Persistence and degradability

Persistence and degradability

Biodegradation: (Method, Inoculum, Biodeg Study, Result, Endpoint, Duration, Classification)

Ritlecitinib Tosylate

OECD Activated sludge Die-away, Mineralization (CO2 Evolution) 29.3 % in 28 Day(s)
OECD Activated sludge Die-away DT50 1.1 Day(s)

12.3. Bioaccumulative potential

Bioaccumulation

Partition Coefficient: (Method, pH, Endpoint, Value)

Ritlecitinib Tosylate

Measured 4 Log P 0.445
Measured 7 Log P 1.50
Measured 9 Log P 1.40

Ritlecitinib

Predicted 7.4 Log D 0.328

12.4. Mobility in soil

Mobility in soil

Sorption:

Ritlecitinib Tosylate (2192215-81-7)

Method	Inoculum	End Point	Result
OECD	Soil (various)	Kd (Geometric mean)	203
OECD	Soil (various)	Koc (Geometric mean)	10449
OECD	Sediment (various)	Kd (Geometric mean)	79
OECD	Sediment (various)	Koc (Geometric mean)	4209

OECD	Activated sludge	Kd (Geometric mean)	21
OECD	Activated sludge	Koc (Geometric mean)	61

12.5. Results of PBT and vPvB assessment

PBT and vPvB assessment No information available.

12.6. Endocrine disrupting properties

Endocrine disrupting properties No information available.

12.7. 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 wastewater 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.

UN number: Not applicable
UN proper shipping name: Not applicable
Transport hazard class(es): Not applicable
Packing group: Not applicable
Environmental Hazard(s): Not applicable

Special precautions for user: Not applicable

Section 15: REGULATORY INFORMATION

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

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

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

Microcrystalline cellulose

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	carcinogen 12/18/2009
TSCA	Present
EINECS	232-674-9
AICS	Present

Glyceryl behenate

CERCLA/SARA Section 313 de minimus %	Not Listed
California Proposition 65	Not Listed
EINECS	242-471-7
AICS	Present

Crospovidone

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

France

Occupational Illnesses (R-463-3, France)

Chemical name	French RG number	Title
Microcrystalline cellulose 9004-34-6	RG 66	-

European Union

Take note of Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work

Authorizations and/or restrictions on use:

This product does not contain substances subject to authorization (Regulation (EC) No. 1907/2006 (REACH), Annex XIV) This product does not contain substances subject to restriction (Regulation (EC) No. 1907/2006 (REACH), Annex XVII)

Persistent Organic Pollutants

Not applicable

Ozone-depleting substances (ODS) regulation (EC) 1005/2009

Not applicable

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances
AICS - Australian Inventory of Chemical Substances

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

Reproductive toxicity-Cat.2; H361d - Suspected of damaging the unborn child. Skin corrosion/irritation-Cat.2; H315 - Causes skin irritation Serious eye damage/eye irritation-Cat. 2;. H319 - Causes serious eye irritation

Data Sources:	Pfizer proprietary drug development information.
Reason for revision	Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 11 - Toxicology Information. Updated Section 12 - Ecological Information. Updated Section 15 - Regulatory Information.
Revision date	11-Jul-2023
Prepared By	Pfizer Global Environment, Health, and Safety

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