



SAFETY DATA SHEET

1. Identification

Product identifier	Ixazomib citrate capsules 2.3 mg, 3 mg, 4 mg
Other means of identification	
Synonyms	Ninlaro capsules, Ixazomib citrate drug product, MLN9708, MLN2238 citrate ester drug product
Recommended use	Pharmaceutical product. This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to medicinal use of the product. In this instance patients should consult prescribing information/package insert/product label or consult their pharmacist or physician. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate safety data sheet for each ingredient.
Recommended restrictions	All other uses.
Manufacturer/Importer/Supplier/Distributor information	
Main Office	Takeda Pharmaceutical Company Limited 1-1, Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo 103-8668, Japan
US contact:	40 Landsdowne Street, Cambridge, MA, 02139, USA
Phone Number	1-617-679-7000
CH contact:	Takeda Pharmaceuticals International AG Thurgauerstrasse 130, 8152 Glattpark-Opfikon (Zurich), Switzerland
E-mail	Takeda-SDS@takeda.com
Emergency phone number	Call CHEMTREC Day or Night Within USA and Canada: 1-800-424-9300 Outside USA and Canada: +1 703-741-5970 (collect calls accepted) From anywhere in the world: +1 703-527-3887

2. Hazard(s) identification

Physical hazards	Not classified.	
Health hazards	Acute toxicity, oral	Category 2
	Reproductive toxicity	Category 2
	Specific target organ toxicity, repeated exposure	Category 1
OSHA defined hazards	Not classified.	
Label elements		



Signal word	Danger
Hazard statement	Fatal if swallowed. Suspected of damaging fertility or the unborn child. Causes damage to organs through prolonged or repeated exposure.
Precautionary statement	
Prevention	Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Do not breathe dust. Wash thoroughly after handling. Do not eat, drink or smoke when using this product. Wear protective gloves/protective clothing/eye protection/face protection.
Response	If swallowed: Immediately call a poison center/doctor. Rinse mouth. If exposed or concerned: Get medical advice/attention.

Storage	Store locked up.
Disposal	Dispose of contents/container in accordance with local/regional/national/international regulations.
Hazard(s) not otherwise classified (HNOC)	None known.
Supplemental information	Finished Pharmaceutical products in their final packages are not subject to OSHA labeling requirements.

3. Composition/information on ingredients

Mixtures

Chemical name	CAS number	%
Ixazomib citrate	1239908-20-3	3 - 4
Cellulose	9004-34-6	Proprietary
Gelatin	9000-70-8	Proprietary
Iron oxide	1309-37-1	Proprietary
Iron oxide yellow	51274-00-1	Proprietary
Magnesium distearate	557-04-0	Proprietary
Magnetic iron oxide	12227-89-3	Proprietary
Talc	14807-96-6	Proprietary
Titanium dioxide	13463-67-7	Proprietary

Composition comments The specific chemical identity and/or exact percentage of component(s) have been withheld as a trade secret.

4. First-aid measures

Inhalation	Powder: Move to fresh air. Call a physician if symptoms develop or persist.
Skin contact	Wash off with soap and water. Get medical attention if irritation develops and persists.
Eye contact	Rinse with water. Get medical attention if irritation develops and persists.
Ingestion	Large quantities: Call a physician or poison control center immediately. Rinse mouth. Do not induce vomiting without advice from poison control center. If vomiting occurs, keep head low so that stomach content doesn't get into the lungs. Do not use mouth-to-mouth method if victim ingested the substance. Induce artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device.
Most important symptoms/effects, acute and delayed	In clinical use, adverse effects may include: Dose limiting toxicities (DLTs) experienced in the dose-escalation cohorts overall included nausea, vomiting, syncope, rash, and peripheral neuropathy.
Indication of immediate medical attention and special treatment needed	Provide general supportive measures and treat symptomatically. Keep victim warm. Keep victim under observation. Symptoms may be delayed.
General information	IF exposed or concerned: Get medical advice/attention. If you feel unwell, seek medical advice (show the label where possible). Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. Show this safety data sheet to the doctor in attendance.

5. Fire-fighting measures

Suitable extinguishing media	Use fire-extinguishing media appropriate for surrounding materials.
Unsuitable extinguishing media	Do not use water jet as an extinguisher, as this will spread the fire.
Specific hazards arising from the chemical	During fire, gases hazardous to health may be formed.
Special protective equipment and precautions for firefighters	Self-contained breathing apparatus and full protective clothing must be worn in case of fire.
Fire fighting equipment/instructions	Use water spray to cool unopened containers.
Specific methods	Use standard firefighting procedures and consider the hazards of other involved materials.
General fire hazards	No unusual fire or explosion hazards noted.

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures

Keep unnecessary personnel away. Keep people away from and upwind of spill/leak. Wear appropriate protective equipment and clothing during clean-up. Local authorities should be advised if significant spillages cannot be contained. For personal protection, see section 8 of the SDS.

Methods and materials for containment and cleaning up

Large Spills: Stop the flow of material, if this is without risk. Sweep up and shovel material into suitable container for disposal. Following product recovery, flush area with water.

Small Spills: Pick up with suitable appliance and dispose of. Clean surface thoroughly to remove residual contamination.

Never return spills to original containers for re-use. Put material in suitable, covered, labeled containers. For waste disposal, see section 13 of the SDS.

Environmental precautions

Avoid discharge into drains, water courses or onto the ground.

7. Handling and storage

Precautions for safe handling

Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Do not taste or swallow. When using, do not eat, drink or smoke. Pregnant or breastfeeding women must not handle this product. Should be handled in closed systems, if possible. Provide adequate ventilation. Wear appropriate personal protective equipment. Wash hands thoroughly after handling. Observe good industrial hygiene practices.

Conditions for safe storage, including any incompatibilities

Store locked up. Store in tightly closed container. Store away from incompatible materials (see Section 10 of the SDS).

8. Exposure controls/personal protection

Occupational exposure limits

U.S. - OSHA Components

Type

Value

Ixazomib citrate (CAS
1239908-20-3)

TWA

0.5 µg/m³

Comments: Takeda internal value

US. OSHA Table Z-1 Limits for Air Contaminants (29 CFR 1910.1000)

Components

Type

Value

Form

Cellulose (CAS 9004-34-6)

PEL

5 mg/m³

Respirable fraction.

15 mg/m³

Total dust.

Titanium dioxide (CAS
13463-67-7)

PEL

15 mg/m³

Total dust.

US. OSHA Table Z-3 (29 CFR 1910.1000)

Components

Type

Value

Form

Titanium dioxide (CAS
13463-67-7)

TWA

5 mg/m³

Respirable fraction.

15 mg/m³

Total dust.

50 mppcf

Total dust.

15 mppcf

Respirable fraction.

US. ACGIH Threshold Limit Values

Components

Type

Value

Cellulose (CAS 9004-34-6)

TWA

10 mg/m³

Titanium dioxide (CAS
13463-67-7)

TWA

10 mg/m³

US. NIOSH: Pocket Guide to Chemical Hazards

Components

Type

Value

Form

Cellulose (CAS 9004-34-6)

TWA

5 mg/m³

Respirable.

10 mg/m³

Total

Biological limit values

No biological exposure limits noted for the ingredient(s).

Appropriate engineering controls	Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels to an acceptable level.
Individual protection measures, such as personal protective equipment	
Eye/face protection	Not normally needed. If contact is likely, safety glasses with side shields are recommended.
Skin protection	
Hand protection	Wear appropriate chemical resistant gloves. Nitrile gloves are recommended. Suitable gloves can be recommended by the glove supplier.
Skin protection	
Other	Wear suitable protective clothing.
Respiratory protection	Not normally needed. In case of insufficient ventilation, wear suitable respiratory equipment.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.
General hygiene considerations	Observe any medical surveillance requirements. Keep away from food and drink. Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment to remove contaminants.

9. Physical and chemical properties

Appearance

Physical state	Solid.
Form	Hard capsules.
Color	No data available.
Odor	No data available.
Odor threshold	Not applicable.
pH	Not available.
Melting point/freezing point	Not available.
Initial boiling point and boiling range	Not applicable.
Flash point	Not applicable.
Evaporation rate	Not applicable.
Flammability (solid, gas)	No data available.
Upper/lower flammability or explosive limits	
Flammability limit - lower (%)	Not available.
Flammability limit - upper (%)	Not available.
Vapor pressure	Not applicable.
Vapor density	Not applicable.
Relative density	Not available.
Solubility(ies)	
Solubility (water)	Not available.
Partition coefficient (n-octanol/water)	Not available.
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
Viscosity	Not applicable.
Other information	
Explosive properties	Not explosive.
Oxidizing properties	Not oxidizing.

10. Stability and reactivity

Reactivity	The product is stable and non-reactive under normal conditions of use, storage and transport.
Chemical stability	Material is stable under normal conditions.

Possibility of hazardous reactions	No dangerous reaction known under conditions of normal use.
Conditions to avoid	Contact with incompatible materials.
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition products	No hazardous decomposition products are known.

11. Toxicological information

Information on likely routes of exposure

Inhalation	Prolonged inhalation may be harmful.
Skin contact	Prolonged skin contact may cause temporary irritation.
Eye contact	Direct contact with eyes may cause temporary irritation.
Ingestion	Fatal if swallowed.

Symptoms related to the physical, chemical and toxicological characteristics In clinical use, adverse effects may include: Dose limiting toxicities (DLTs) experienced in the dose-escalation cohorts overall included nausea, vomiting, syncope, rash, and peripheral neuropathy.

Information on toxicological effects

Acute toxicity Ixazomib citrate: LD50 – not performed; current SDS applies estimated LD50, <5 mg/kg, derived on the mortality in 2 and 5-Cycle studies in rats (≥ 1 mg/kg). MTD of ixazomib in Sprague-Dawley rats after a single oral gavage administration was 1 mg/kg – no deaths at this dose.

Components	Species	Test Results
Ixazomib citrate (CAS 1239908-20-3)		
Acute		
Oral		
LD50	Rat	< 5 mg/kg (Estimated)
Titanium dioxide (CAS 13463-67-7)		
Acute		
Inhalation		
LC50	Rat	3.43 mg/l, 4 Hours
Oral		
LD50	Rat	> 5000 mg/kg
Skin corrosion/irritation	Prolonged skin contact may cause temporary irritation. Ixazomib citrate and freebase API (MLN2238) caused severe irritation, resulting in irreversible tissue alteration.	
Serious eye damage/eye irritation	Direct contact with eyes may cause temporary irritation. Studies on eye irritancy were not conducted, but Ixazomib is anticipated to be an eye irritant.	
Respiratory or skin sensitization		
Respiratory sensitization	No data available.	
Skin sensitization	No data available.	
Germ cell mutagenicity	No data available to indicate product or any components present at greater than 0.1% are mutagenic or genotoxic. Ixazomib citrate: Test results: Negative.	
Carcinogenicity	Inhalation of titanium dioxide dust may cause cancer, however due to the physical form of the product, inhalation of dust is not likely.	
IARC Monographs. Overall Evaluation of Carcinogenicity		
Titanium dioxide (CAS 13463-67-7)	2B Possibly carcinogenic to humans.	
NTP Report on Carcinogens		
Not listed.		
OSHA Specifically Regulated Substances (29 CFR 1910.1001-1053)		
Not listed.		
Reproductive toxicity	Suspected of damaging fertility or the unborn child. Ixazomib citrate: Embryo-Fetal Development in Rats - oral - rat – NOAEL <0.2 mg/kg/3 days – for general toxicity of dams and NOAEL ≥ 0.6 mg/kg/3 days for reproductive toxicity and EFD effects. Embryo-Fetal Development in Rabbits- oral – rabbit – NOAEL 0.1 mg/kg/3 days – for general toxicity of dams and EFD effects and ≥ 0.1 mg/kg/3 days for reproductive toxicity.	

Specific target organ toxicity - single exposure	Not classified.
Specific target organ toxicity - repeated exposure	Causes damage to organs through prolonged or repeated exposure. Ixazomib citrate: Three-Month (5-Cycle) Intermittent-Dose Toxicology Study of Ixazomib Citrate - oral - rat – NOAEL 0.2 mg/kg - intestine and lymphoid tissue effects. Six-Month (7-Cycle) Intermittent-Dose Toxicology Study of Ixazomib Citrate - oral - rat – NOAEL 0.2 mg/kg -intestine and lymphoid tissue effects. Nine-Month (10-Cycle) Intermittent-Dose Toxicology Study of Ixazomib Citrate - oral - dog – NOAEL 0.1 mg/kg -intestine and lymphoid tissue effects, peripheral nervous system effects. Different dosing regimens were used in studies.
Aspiration hazard	Not an aspiration hazard.
Chronic effects	Prolonged inhalation may be harmful. Causes damage to organs through prolonged or repeated exposure. Prolonged exposure may cause chronic effects.
Further information	No data available.

12. Ecological information

Ecotoxicity The product is not classified as environmentally hazardous. However, this does not exclude the possibility that large or frequent spills can have a harmful or damaging effect on the environment.

Components	Species	Test Results
Titanium dioxide (CAS 13463-67-7)		
Aquatic		
<i>Acute</i>		
Crustacea	EC50	Daphnia magna > 100 mg/l, 48 Hours
Fish	LL50	Oryzias latipes > 100 mg/l, 96 Hours

Persistence and degradability No data is available on the degradability of any ingredients in the mixture.

Bioaccumulative potential No data available for this product.

Partition coefficient n-octanol / water (log Kow)

Ixazomib citrate (CAS 1239908-20-3) 2

Mobility in soil No data available.

Other adverse effects No other adverse environmental effects (e.g. ozone depletion, photochemical ozone creation potential, endocrine disruption, global warming potential) are expected from this component.

13. Disposal considerations

Disposal instructions Collect and reclaim or dispose in sealed containers at licensed waste disposal site. Dispose of contents/container in accordance with local/regional/national/international regulations.

Local disposal regulations Dispose in accordance with all applicable regulations.

Hazardous waste code The waste code should be assigned in discussion between the user, the producer and the waste disposal company.

Waste from residues / unused products Dispose of in accordance with local regulations. Empty containers or liners may retain some product residues. This material and its container must be disposed of in a safe manner (see: Disposal instructions).

Contaminated packaging Since emptied containers may retain product residue, follow label warnings even after container is emptied. Empty containers should be taken to an approved waste handling site for recycling or disposal.

14. Transport information

DOT

UN number	UN3249
UN proper shipping name	Medicine, solid, toxic, n.o.s. (Ixazomib citrate)
Transport hazard class(es)	
Class	6.1
Subsidiary risk	-
Label(s)	6.1
Packing group	II
Environmental hazards	
Marine pollutant	No.
Special precautions for user	Read safety instructions, SDS and emergency procedures before handling.
Special provisions	T3, TP33
Packaging exceptions	153

Packaging non bulk 212
Packaging bulk 242

IATA

UN number UN3249
UN proper shipping name Medicine, solid, toxic, n.o.s. (Ixazomib citrate)
Transport hazard class(es)
Class 6.1
Subsidiary risk -
Packing group II
Environmental hazards No.
ERG Code 6L
Special precautions for user Read safety instructions, SDS and emergency procedures before handling.

IMDG

UN number UN3249
UN proper shipping name MEDICINE, SOLID, TOXIC, N.O.S. (Ixazomib citrate)
Transport hazard class(es)
Class 6.1
Subsidiary risk -
Packing group II
Environmental hazards
Marine pollutant No.
EmS F-A, S-A
Special precautions for user Read safety instructions, SDS and emergency procedures before handling.

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code Not applicable.

15. Regulatory information

US federal regulations All components are listed on or exempt from the U.S. EPA TSCA Inventory List. This product may only be used for TSCA Exempt purposes such as R&D or Food, Drug or Cosmetic use.

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)

Not regulated.

CERCLA Hazardous Substance List (40 CFR 302.4)

Not listed.

SARA 304 Emergency release notification

Not regulated.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1053)

Not listed.

Toxic Substances Control Act (TSCA) All components are either listed on the TSCA 8(b) inventory and designated "active" or exempt from listing.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

SARA 302 Extremely hazardous substance

Not listed.

SARA 311/312 Hazardous chemical Yes

Classified hazard categories Acute toxicity (any route of exposure)
Reproductive toxicity
Specific target organ toxicity (single or repeated exposure)

SARA 313 (TRI reporting)

Not regulated.

Other federal regulations

Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List

Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)

Not regulated.

Safe Drinking Water Act (SDWA) Not regulated.

US state regulations

US. Massachusetts RTK - Substance List

Cellulose (CAS 9004-34-6)
Titanium dioxide (CAS 13463-67-7)

US. New Jersey Worker and Community Right-to-Know Act

Cellulose (CAS 9004-34-6)
Titanium dioxide (CAS 13463-67-7)

US. Pennsylvania Worker and Community Right-to-Know Law

Cellulose (CAS 9004-34-6)
Titanium dioxide (CAS 13463-67-7)

US. Rhode Island RTK

Cellulose (CAS 9004-34-6)
Titanium dioxide (CAS 13463-67-7)

California Proposition 65



WARNING: This product can expose you to Titanium dioxide, which is known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

California Proposition 65 - CRT: Listed date/Carcinogenic substance

Titanium dioxide (CAS 13463-67-7) Listed: September 2, 2011

US. California. Candidate Chemicals List. Safer Consumer Products Regulations (Cal. Code Regs, tit. 22, 69502.3, subd. (a))

Titanium dioxide (CAS 13463-67-7)

16. Other information, including date of preparation or last revision

Issue date 20-April-2020

Revision date -

Version # 01

HMIS® ratings Health: 2*
Flammability: 0
Physical hazard: 0

List of abbreviations LD50: Lethal Dose 50%.

References In-house data

Disclaimer Takeda Pharmaceutical Company Limited cannot anticipate all conditions under which this information and its product, or the products of other manufacturers in combination with its product, may be used. It is the user's responsibility to ensure safe conditions for handling, storage and disposal of the product, and to assume liability for loss, injury, damage or expense due to improper use. The information in the sheet was written based on the best knowledge and experience currently available.