SAFETY DATA SHEET

1. Identification

Product identifier **Iclusig**

Other means of identification

Synonyms Ponatinib tablets 10 mg / 15 mg / 30 mg / 45 mg, Iclusig film-coated tablets, Ponatinib hydrochloride tablets, Ponatinib drug product, AP24534

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

SDS Information

US Office 500 Kendall Street, Cambridge, MA 02142, USA

CH Office 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

Note) When calling Chemtrec for emergency, first tell the product name on SDS along with the SDS date.

Note) When transcribing the Chemtrec number to GHS label or others, the above note must be transcribed together.

2. Hazard(s) identification

Hazards for the product as sold

Physical hazards Not classified.

Hazards for the product as sold

Health hazards	Acute toxicity, oral	Category 4
	Carcinogenicity	Category 2
	Reproductive toxicity	Category 2
	Specific target organ toxicity, single exposure	Category 1
	Specific target organ toxicity, repeated exposure	Category 1

Hazards for the product as sold

Environmental hazards	Hazardous to the aquatic environment, acute hazard	Category 2

Hazards for the product as sold

Hazardous to the aquatic environment, long-term hazard	Category 1

Hazards for the product as sold

OSHA defined hazards Not classified.

Label elements

Signal word Danger

Hazard statement Harmful if swallowed. Suspected of causing cancer. Suspected of damaging fertility or the unborn child. Causes damage to organs. Causes damage to organs through prolonged or repeated exposure. Toxic to aquatic life. Very toxic to aquatic life with long lasting effects.

Precautionary statement

Prevention Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Do not breathe dust/fume. Wash thoroughly after handling. Do not eat, drink or smoke when using this product. Avoid release to the environment. Wear protective gloves/protective clothing/eye protection/face protection.

Response If swallowed: Call a poison center/doctor if you feel unwell. Rinse mouth. IF exposed or concerned: Call a POISON CENTER/doctor. Collect spillage.

Storage Store locked up.

Disposal Dispose of contents/container in accordance with local/regional/national/international regulations.

Hazard(s) not otherwise classified (HNOC) No additional hazards are known to be associated with the expected conditions of use at the time of publication. This document does not address hazards that may arise from uses not reasonably anticipated by the manufacturer.

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	%
Lactose monohydrate	10039-26-6	*
Microcrystalline cellulose	9004-34-6	*
Ponatinib hydrochloride	1114544-31-8	*
Sodium starch glycolate	9063-38-1	*
Polyethylene oxide	25322-68-3	*
Polyvinyl alcohol	9002-89-5	*
Talc	14807-96-6	*
Titanium dioxide	13463-67-7	*
Colloidal silicon dioxide	7631-86-9	*
Magnesium stearate	557-04-0	*

Composition comments * Proprietary.

The exact percentage (concentration) of composition has been withheld as a trade secret.

4. First-aid measures

Inhalation 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 Rinse mouth. If vomiting occurs, keep head low so that stomach content doesn't get into the lungs. Get medical advice/attention if you feel unwell.

Most important symptoms/effects, acute and delayed	Prolonged exposure may cause chronic effects.
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	Water fog. Foam. Dry chemical powder. Carbon dioxide (CO2).
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. Water runoff can cause environmental damage.
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. Ensure adequate ventilation. 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	Prevent product from entering drains. Large Spills: Stop the flow of material, if this is without risk. Following product recovery, flush area with water. Small Spills: 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 release to the environment. Inform appropriate managerial or supervisory personnel of all environmental releases. Prevent further leakage or spillage if safe to do so. 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. Avoid prolonged exposure. 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. Avoid release to the environment. 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). When quality control required, follow the storage condition specified separately.

8. Exposure controls/personal protection

Occupational exposure limits

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

Components	Type	Value	Form
Microcrystalline cellulose (CAS 9004-34-6)	PEL	5 mg/m3	Respirable fraction.
		15 mg/m3	Total dust.

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

Components	Type	Value	Form
Titanium dioxide (CAS 13463-67-7)	PEL	15 mg/m3	Total dust.

US. OSHA Table Z-3 Permissible Exposure Limits (PEL) for Mineral Dusts (29 CFR 1910.1000)

Components	Type	Value	Form
Microcrystalline cellulose (CAS 9004-34-6)	TWA	5 mg/m3	Respirable fraction.
		15 mg/m3	Total dust.
		50 mppcf	Total dust.
		15 mppcf	Respirable fraction.
Talc (CAS 14807-96-6)	TWA	0.1 mg/m3	Respirable.
		20 mppcf	
		2.4 mppcf	Respirable.
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 (TLV)

Components	Type	Value	Form
Microcrystalline cellulose (CAS 9004-34-6)	TWA	10 mg/m3	
Talc (CAS 14807-96-6)	TWA	2 mg/m3	Respirable fraction.
Titanium dioxide (CAS 13463-67-7)	TWA	2.5 mg/m3	Respirable finescale particles
		0.2 mg/m3	Respirable nanoscale particles

NIOSH. Immediately Dangerous to Life or Health (IDLH) Values, as amended

Components	Type	Value
Talc (CAS 14807-96-6)	IDLH	1000 mg/m3
Titanium dioxide (CAS 13463-67-7)	IDLH	5000 mg/m3

US. NIOSH: Pocket Guide to Chemical Hazards

Components	Type	Value	Form
Microcrystalline cellulose (CAS 9004-34-6)	TWA	5 mg/m3	Respirable.
		10 mg/m3	Total
Talc (CAS 14807-96-6)	TWA	2 mg/m3	Respirable.

US. OARS. Workplace Environmental Exposure Level (WEEL) Guide

Components	Type	Value
Polyethylene oxide (CAS 25322-68-3)	TWA	10 mg/m3

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

Exposure guidelines Ponatinib hydrochloride (CAS 1114544-31-8): OEL - 9 µg/m3 (Takeda internal value).

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	If contact is likely, safety glasses with side shields are recommended.
Skin protection	
Hand protection	Wear appropriate chemical resistant gloves. Impervious oil/water/chemical-resistant gloves (nitrile, etc.). Gloves meeting EN374, ASTM F1001 or international equivalent standard are recommended.
Skin protection	
Other	Use of an impervious apron is recommended.
Respiratory protection	In case of insufficient ventilation, wear suitable respiratory equipment. In the United States of America, if respirators are used, a program should be instituted to assure compliance with OSHA 29 CFR 1910.134. Seek advice from supervisor on the company's respiratory protection standards.
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

Physical state	Solid.
Form	Film-coated tablets.
Color	No data available.
Odor	No data available.
Odor threshold	Property has not been measured.
Melting point/freezing point	Property has not been measured.
Boiling point or initial boiling point and boiling range	Property has not been measured.
Flammability	Will burn if involved in a fire.
Upper/lower flammability or explosive limits	
Explosive limit - lower (%)	Not applicable, material is a solid.
Explosive limit - upper (%)	Not applicable, material is a solid.
Flash point	Property has not been measured.
Auto-ignition temperature	Not applicable, material is a solid.
Decomposition temperature	Property has not been measured.
pH	Property has not been measured.
Kinematic viscosity	Not applicable, material is a solid.
Solubility	
Solubility (water)	Property has not been measured.
Partition coefficient (n-octanol/water)	Not applicable, product is a mixture.
Vapor pressure	Not applicable, material is a solid.
Density and/or relative density	
Density	Property has not been measured.
Relative density	Property has not been measured.
Vapor density	Not applicable, material is a solid.
Particle characteristics	
Particle size	Property has not been measured.
Other information	
Evaporation rate	Not applicable, material is a solid.
Explosive properties	Not explosive.

Oxidizing properties	Not oxidizing.
Viscosity	Not applicable, material is a solid.

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 acids, alkalis and oxidizing agents.
Hazardous decomposition products	No hazardous decomposition products are known.

11. Toxicological information

Information on likely routes of exposure

Inhalation	No adverse effects due to inhalation are expected.
Skin contact	Prolonged skin contact may cause temporary irritation.
Eye contact	Direct contact with eyes may cause temporary irritation.
Ingestion	Harmful if swallowed.
Symptoms related to the physical, chemical and toxicological characteristics	Prolonged exposure may cause chronic effects.

Information on toxicological effects

Acute toxicity Harmful if swallowed.

Ponatinib hydrochloride (CAS 1114544-31-8) Result: The oral LD50 in rats is estimated to be 55 mg/kg.

Components	Species	Test Results
Polyethylene oxide (CAS 25322-68-3)		
Acute		
Dermal		
LD50	Rabbit	> 20000 mg/kg
Inhalation		
LC50	Rat	> 1008 mg/m³, 4 Hours
Oral		
LD50	Mouse	6400 mg/kg
	Rat	17300 mg/kg
Ponatinib hydrochloride (CAS 1114544-31-8)		
Acute		
Oral		
LD50	Rat	55 mg/kg Estimate

Skin corrosion/irritation	No data available.
Serious eye damage/eye irritation	No data available.

Respiratory or skin sensitization

Respiratory sensitization	No data available.
Skin sensitization	No data available.
Germ cell mutagenicity	Not classified.

Mutagenicity

Ponatinib hydrochloride (CAS 1114544-31-8) Bacterial Reverse Mutation Test (Ames Assay)
Result: Negative.

Mutagenicity

Ponatinib hydrochloride (CAS 1114544-31-8)	In vitro Chromosome Aberration Result: Negative. Species: Human Organ: Lymphocytes In vivo Micronucleus Result: Negative. Species: Mouse

Carcinogenicity Suspected of causing cancer.

Ponatinib hydrochloride (CAS 1114544-31-8)	Result: 1. In a two-year oral carcinogenicity study in rats, female rats developed squamous cell carcinoma of the clitoral gland at 0.8 mg/kg/day. Result: 2. An increased incidence of sex cord stromal hyperplasia and mixed sex cord stromal benign ovarian tumors was observed at 0.4 and 0.8 mg/kg/day. Result: 3. Ponatinib was not found to be carcinogenic in male rats.

IARC Monographs. Overall Evaluation of Carcinogenicity

Talc (CAS 14807-96-6)	2A Probably carcinogenic to humans.
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.

Reproductivity

Ponatinib hydrochloride (CAS 1114544-31-8)	Result: 1. Oral fertility and early embryonic development study in rats: The NOAEL for reproductive performance and fertility was 1.50 mg/kg/day in males and 0.75 mg/kg/day in females. Result: 2. Ponatinib had no effect on male fertility parameters, but decreased female fertility parameters as indicated by increased pre- and post-implantation embryo-fetal lethality in the rats dosed with 1.50 mg/kg/day ponatinib. Result: 3. Oral embryo-fetal developmental study in rats: The NOAEL for embryo-fetal development impairment was 0.3 mg/kg/day. Result: 4. Embryo-fetal toxicity manifested as post-implantation loss and reduced fetal body weights at 3 mg/kg/day and fetal alterations (soft tissue and skeletal malformations and variations) at 1 and 3 mg/kg/day.

Specific target organ toxicity - single exposure Causes damage to organs.

Ponatinib hydrochloride (CAS 1114544-31-8)	Result: 1. Toxicity studies were conducted in mice, rats, and monkeys. Ponatinib was tolerated up to 450 mg/kg in mice. In rats, lymphoid depletion was noted consistent with bacterial sepsis, skin findings, and hematologic findings. Result: 2. Monkeys presented with follicular atrophy of the thyroid gland and hyperkeratosis. LOAEL estimated <100 mg/kg.

Specific target organ toxicity - repeated exposure Causes damage to organs through prolonged or repeated exposure.

Ponatinib hydrochloride (CAS 1114544-31-8)	Result: 1. Toxicology studies in rats and monkeys indicated the following key target organs of ponatinib toxicity: pancreas, lymphoid organs, bone, skin, thyroid gland, testes, and ovaries. Result: 2. Six months oral study in rat, NOAEL = 0.25 mg/kg/day.

Specific target organ toxicity - repeated exposure

Ponatinib hydrochloride (CAS 1114544-31-8) — Result: 3. Six months oral study in monkey, NOAEL <0.25 mg/kg/day.

Aspiration hazard Not relevant, due to the form of the product.

Chronic effects Causes damage to organs through prolonged or repeated exposure.

12. Ecological information

Ecotoxicity Toxic to aquatic life. Very toxic to aquatic life with long lasting effects.

Components		Species	Test Results
Ponatinib hydrochloride (CAS 1114544-31-8)			
Aquatic			
Acute			
Algae	EC50	Pseudokirchneriella subcapitata	0.677 mg/l, 72 hours
	NOEC	Pseudokirchneriella subcapitata	0.14 mg/l, 72 hours
Chronic			
Crustacea	NOEC	Daphnia magna	0.04 mg/l, 21 days
Fish	NOEC	Zebrafish (Danio rerio)	0.0012 mg/l, 30 days

Persistence and degradability No data is available on the degradability of this product.
Ponatinib hydrochloride: Not readily biodegradable.

Bioaccumulative potential

Partition coefficient n-octanol / water (log Kow)

Ponatinib hydrochloride (CAS 1114544-31-8) — 4.5 log Pow @ pH 7 (OECD TG 123)

Mobility in soil No data available.

Other adverse effects No data available.

13. Disposal considerations

Disposal instructions Collect and reclaim or dispose in sealed containers at licensed waste disposal site. Do not allow this material to drain into sewers/water supplies. Do not contaminate ponds, waterways or ditches with chemical or used container. 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.

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 UN3077
UN proper shipping name Environmentally hazardous substances, solid, n.o.s. (Ponatinib hydrochloride)
Transport hazard class(es)
Class 9
Subsidiary hazard -
Label(s) 9
Packing group III
Environmental hazards
Marine pollutant Yes
Special precautions for user Read safety instructions, SDS and emergency procedures before handling.
Special provisions 8, 146, 335, A112, B54, IB8, IP3, N20, T1, TP33
Packaging exceptions 155
Packaging non bulk 213

Packaging bulk	240

IATA

UN number	UN3077
UN proper shipping name	Environmentally hazardous substance, solid, n.o.s. (Ponatinib hydrochloride)
Transport hazard class(es)	
Class	9
Subsidiary hazard	-
Label(s)	9
Packing group	III
Environmental hazards	Yes
ERG Code	9L
Special precautions for user	Read safety instructions, SDS and emergency procedures before handling.

IMDG

UN number	UN3077
UN proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Ponatinib hydrochloride)
Transport hazard class(es)	
Class	9
Subsidiary hazard	-
Label(s)	9
Packing group	III
Environmental hazards	
Marine pollutant	Yes
EmS	F-A, S-F
Special precautions for user	Read safety instructions, SDS and emergency procedures before handling.

Transport in bulk according to IMO instruments	Not applicable.

15. Regulatory information

US federal regulations

This product is a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200.
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.

Toxic Substances Control Act (TSCA)

All components are either listed on the TSCA 8(b) inventory and designated “active” or exempt from listing.

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.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

SARA 302 Extremely hazardous substance

Not listed.

SARA 311/312 Hazardous chemical	No (Exempt)

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

Talc (CAS 14807-96-6)
Titanium dioxide (CAS 13463-67-7)

US. Massachusetts RTK - Substance List

Microcrystalline cellulose (CAS 9004-34-6)
Talc (CAS 14807-96-6)
Titanium dioxide (CAS 13463-67-7)

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

Microcrystalline cellulose (CAS 9004-34-6)
Talc (CAS 14807-96-6)
Titanium dioxide (CAS 13463-67-7)

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

Microcrystalline cellulose (CAS 9004-34-6)
Talc (CAS 14807-96-6)
Titanium dioxide (CAS 13463-67-7)

US. Rhode Island RTK

Microcrystalline cellulose (CAS 9004-34-6)
Talc (CAS 14807-96-6)
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

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

Issue date	02-December-2025
Revision date	-
Version #	01
References	IARC Monographs. Overall Evaluation of Carcinogenicity 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.