SAFETY DATA SHEET

1. Identification

Product identifier **Fruquintinib capsules**

Other means of identification

Product code Fruzaqla capsules 1mg, Fruzaqla capsules 5mg, TAK-113 drug product, TAK-113 capsules, Elunate, HMPL-013

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 40 Landsdowne Street, Cambridge, MA, 02139, 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

2. Hazard(s) identification

Physical hazards Not classified.

Health hazards

Reproductive toxicity (the unborn child)	Category 2
Specific target organ toxicity, single exposure	Category 2
Specific target organ toxicity, repeated exposure	Category 1

OSHA defined hazards Not classified.

Label elements

Signal word Danger

Hazard statement Suspected of damaging the unborn child. May cause damage to organs. 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 exposed or concerned: Call a poison center/doctor.
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	%
Fruquintinib	1194506-26-7	*

* Proprietary.

Composition comments The manufacturer has claimed the specific chemical identity and/or exact percentage as trade secret under the OSHA Hazard Communication Standard. Components not listed are either non-hazardous or are below reportable limits.

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. Get medical attention if symptoms occur.
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 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 spray. Foam. 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.
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. 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	Stop the flow of material, if this is without risk. Following product recovery, flush area with water. 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. Avoid prolonged exposure. When using, do not eat, drink or smoke. Pregnant or breastfeeding women must not handle this product. 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). When quality control required, follow the storage condition specified separately.

8. Exposure controls/personal protection

Occupational exposure limits
No exposure limits noted for ingredient(s).

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

Exposure guidelines
Fruquintinib (CAS 1194506-26-7): OEL - 2 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.

Thermal hazards
Wear appropriate thermal protective clothing, when necessary.

General hygiene considerations
Observe any medical surveillance requirements. 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
Capsule.

Color
1 mg: gelatin capsule with standard yellow opaque cap and white opaque body.
5 mg: gelatin capsule with Swedish orange opaque cap and white opaque body.

Odor
Property has not been measured.

Odor threshold
Property has not been measured.

pH
Not applicable, material is a solid.

Melting point/freezing point
Property has not been measured.

Initial boiling point and boiling range
Property has not been measured.

Flash point
Property has not been measured.

Evaporation rate
Not applicable, material is a solid.

Flammability (solid, gas)
Property has not been measured.

Upper/lower flammability or explosive limits

Explosive limit - lower (%)
Property has not been measured.

Explosive limit - upper (%)
Property has not been measured.

Vapor pressure
Not applicable, material is a solid.

Vapor density
Not applicable, material is a solid.

Relative density
Property has not been measured.

Solubility(ies)

Solubility (water)
Property has not been measured.

Partition coefficient (n-octanol/water)	Not applicable to mixtures.
Auto-ignition temperature	Property has not been measured.
Decomposition temperature	Property has not been measured.
Viscosity	Not applicable, material is a solid.

Other information

Explosive properties	Not explosive.
Kinematic viscosity	Not applicable, material is a solid.
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	No adverse effects due to skin contact are expected.
Eye contact	Direct contact with eyes may cause temporary irritation.
Ingestion	Expected to be a low ingestion hazard.
Symptoms related to the physical, chemical and toxicological characteristics	Prolonged exposure may cause chronic effects.

Information on toxicological effects

Acute toxicity Not expected to be acutely toxic.

Fruquintinib (CAS 1194506-26-7)	Result: Dermal LD50 in rats was tested to be >2000 mg/kg.

Skin corrosion/irritation Not classifiable.

Corrosivity

Fruquintinib (CAS 1194506-26-7)	Result: No specific animal studies for irritation were performed.

Serious eye damage/eye irritation Not classifiable.

Eye

Fruquintinib (CAS 1194506-26-7)	Result: No specific animal studies for irritation were performed.

Respiratory or skin sensitization

Respiratory sensitization	No data available.
Skin sensitization	Not classifiable.

Skin sensitization

Fruquintinib (CAS 1194506-26-7)	Result: Skin sensitization was evaluated in a guinea-pig assay which had negative results.

Germ cell mutagenicity Not classifiable.

Fruquintinib:
TAK-113 was not genotoxic based on the results of a standard panel of in vitro and in vivo genotoxicity studies, including Ames assay, an in vitro chromosome aberration assay in Chinese hamster ovary, and an in vivo rat micronucleus test with inclusion of an alkaline comet assay.

Carcinogenicity Not classifiable.

IARC Monographs. Overall Evaluation of Carcinogenicity

Not listed.

NTP Report on Carcinogens

Not listed.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1053)

Not listed.

Reproductive toxicity

Suspected of damaging the unborn child.

Fruquintinib:
In the fertility and early embryonic development/implantation study, the NOAEL for fertility in male and female rats was found to be 3 mg/kg and 0.5 mg/kg, respectively. The NOAEL for early embryonic development was 0.15 mg/kg. In the embryo-fetal development study in rats, the NOAEL for maternal effects and embryo-fetal development was found to be 0.1 and 0.025 mg/kg, respectively.

Specific target organ toxicity - single exposure

May cause damage to organs.

Fruquintinib (CAS 1194506-26-7)	Result: In single-dose toxicity studies, no mortality occurred in rats or dogs at doses of up to 2000 mg/kg (MTD) and 1000 mg/kg (MTD), respectively. Target organs in rats and dogs were the Gastrointestinal tract.

Specific target organ toxicity - repeated exposure

Causes damage to organs through prolonged or repeated exposure.

Fruquintinib:
The main target organs in rats and dogs were liver, kidney, adrenal gland, immune system (thymus, spleen, and lymph nodes), gastrointestinal system, bone marrow (sternum and femur), and skeletal system (femur and teeth). Apart from skeletal effects, all signs of toxicity resolved during the recovery period. The oral LOAEL from a 26-week study in rats is 0.5/0.25 mg/kg/d (lowest dose tested), and the oral NOAEL from a 39-week study in dogs is 0.03 mg/kg/d.

Aspiration hazard

Not relevant, due to the form of the product.

Chronic effects

Causes damage to organs through prolonged or repeated exposure.

Further information

None known.

12. Ecological information

Ecotoxicity

Not expected to be harmful to aquatic organisms.

Persistence and degradability

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

Bioaccumulative potential

No data available.

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. 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

Not regulated as dangerous goods.

IATA

Not regulated as dangerous goods.

IMDG

Not regulated as dangerous goods.

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

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	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. Massachusetts RTK - Substance List

Not regulated.

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

Not listed.

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

Not listed.

US. Rhode Island RTK

Not regulated.

California Proposition 65

California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): This material is not known to contain any chemicals currently listed as carcinogens or reproductive toxins. For more information go to www.P65Warnings.ca.gov.

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

Issue date	20-November-2023
Revision date	-
Version #	01

List of abbreviations

IDLH: Immediately Dangerous To Life or Health.
LD50: Lethal Dose 50%.
LOAEL: Lowest observed adverse effect level.
MTD: Maximum tolerated dose.
NOAEL: No observed adverse effect level.
OEL: Occupational Exposure Limit.

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.