



SAFETY DATA SHEET

1. Identification

Product identifier	TAK-788 capsules, 20 mg and 40 mg
Other means of identification	
Synonyms	Mobocertinib succinate capsules, TAK-788 drug product, AP32788, Exkivity™
Recommended use	Final drug product.
Recommended restrictions	None known.
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	Category 2
	Specific target organ toxicity, single exposure	Category 1
	Specific target organ toxicity, repeated exposure	Category 1
OSHA defined hazards	Not classified.	
Label elements		



Signal word	Danger
Hazard statement	Suspected of damaging fertility or the unborn child. Causes 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: 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.

3. Composition/information on ingredients

Mixtures

Chemical name	CAS number	%
Gelatin	9000-70-8	Proprietary
TAK-788	2305022-81-3	Proprietary
Titanium dioxide	13463-67-7	Proprietary
Iron oxide	1309-37-1	Proprietary

Composition comments Black ink is optionally used for imprint on capsule shells.
The manufacturer has claimed the exact percentage as trade secret under the OSHA Hazard Communication Standard.

4. First-aid measures

Inhalation Contact with dust: Move to fresh air. Call a physician if symptoms develop or persist.

Skin contact Contact with dust: Wash off with soap and water. Get medical attention if irritation develops and persists.

Eye contact Contact with dust: Do not rub eyes. 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 In clinical use, adverse effects may include: Diarrhoea, nausea, vomiting, decreased appetite, fatigue, rash, dry skin, rash maculo-papular, paronychia, and dermatitis acneiform.

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 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.

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. Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. 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.

Large Spills: Shovel the material into waste container. Following product recovery, flush area with water.

Small Spills: Sweep up or vacuum up spillage and collect in suitable container for disposal.

Never return spills to original containers for re-use. 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. Should be handled in closed systems, if possible. 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 in a well-ventilated place. Store away from incompatible materials (see Section 10 of the SDS).

8. Exposure controls/personal protection

Occupational exposure limits

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

Components	Type	Value	Form
Iron oxide (CAS 1309-37-1)	PEL	10 mg/m3	Fume.
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
Iron oxide (CAS 1309-37-1)	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	Form
Iron oxide (CAS 1309-37-1)	TWA	5 mg/m3	Respirable fraction.
Titanium dioxide (CAS 13463-67-7)	TWA	10 mg/m3	

US. NIOSH: Pocket Guide to Chemical Hazards

Components	Type	Value	Form
Iron oxide (CAS 1309-37-1)	TWA	5 mg/m3	Dust and fume.

Biological limit values

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

Exposure guidelines

TAK-788: OEL - 12 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. If engineering measures are not sufficient to maintain concentrations of dust particulates below the Occupational Exposure Limit (OEL), suitable respiratory protection must be worn. If material is ground, cut, or used in any operation which may generate dusts, use appropriate local exhaust ventilation to keep exposures below the recommended exposure limits.

Individual protection measures, such as personal protective equipment

Eye/face protection

Wear safety glasses with side shields (or goggles).

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

Wear suitable protective clothing. Use of an impervious apron is recommended.

Respiratory protection

In case of inadequate ventilation or risk of inhalation of dust, use suitable respiratory equipment with particle filter. Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits.

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	Swedish orange (reddish orange) for 20 mg. White for 40 mg.

Odor No data available.

Odor threshold Not available.

pH Property has not been measured.

Melting point/freezing point Property has not been measured.

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

Flash point Not applicable, material is a solid.

Evaporation rate Not applicable, material is a solid.

Flammability (solid, gas) Capable of catching on fire.

Upper/lower flammability or explosive limits

Explosive limit - lower (%) Not applicable. Not combustible.

Explosive limit - upper (%) Not applicable. Not combustible.

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 for mixtures.

Auto-ignition temperature Not applicable, material is a solid.

Decomposition temperature Property has not been measured.

Viscosity Not applicable, material is a solid.

Other information

Density Property has not been measured.

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 May cause discomfort if swallowed.

Symptoms related to the physical, chemical and toxicological characteristics In clinical use, adverse effects may include: Diarrhoea, nausea, vomiting, decreased appetite, fatigue, rash, dry skin, rash maculo-papular, paronychia, and dermatitis acneiform.

Information on toxicological effects**Acute toxicity** Not expected to be acutely toxic.

Components	Species	Test Results
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Titanium dioxide (CAS 13463-67-7)

Acute**Oral**

LD50

Rat

> 5000 mg/kg

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.

Mobocertinib succinate: Ames assay - not mutagenic.

In vitro mammalian chromosome aberration assay - not clastogenic.

In vivo (rat) micronucleus assay - no chromosome damage.

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

Iron oxide (CAS 1309-37-1)

3 Not classifiable as to carcinogenicity 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.

Mobocertinib succinate: Test type: Embryo-Fetal Development. Route: PO. Species: Rat. NOAEL value: 5 mg/kg. Effect: Embryo-fetal lethality and adverse effects on embryo-fetal development with decreased fetal growth, increased early resorptions and postimplantation loss. There was no clear evidence of teratogenicity at any dose (OECD method).

Fertility: Fertility studies were not conducted in animals with TAK-788; however, an evaluation of the reproductive tract was conducted in the general toxicity studies in rats and dogs.

Specific target organ toxicity - single exposure

Causes damage to organs.

Mobocertinib succinate: Single PO doses up to 100 mg/kg were well tolerated in rats (highest dose tested); target organs included small and large intestine (including atrophy, single cell necrosis, hemorrhage, erosion/ulcer and inflammation), squamous epithelium of various organs (decreased thickness) and male reproductive tract and male mammary gland (single cell necrosis).

Single PO doses up to 10 mg/kg were well tolerated in dogs (highest dose tested); target organs included the gastrointestinal tract (small and large intestines, esophagus, salivary gland and tongue; including atrophy, single cell necrosis, hemorrhage and/or decreased epithelial thickness), and kidney (single cell necrosis).

Specific target organ toxicity - repeated exposure

Causes damage to organs through prolonged or repeated exposure.

Mobocertinib succinate: 3-month-PO-rat NOAEL was 10 mg/kg for males, and 5 mg/kg for females (both highest dose tested). Effects: gastrointestinal and reproductive tracts and the skin and stratified squamous epithelium. Other findings: reduced body weight and food consumption, lymphoid hyperplasia in the lymph node, salivary gland acinar atrophy, and exacerbation of chronic progressive nephropathy in the kidneys of males. Changes generally reversible or partially reversible with 1-month recovery period.

3-month-PO-dog NOAEL 0.25 mg/kg for males (1 mg/kg dose level removed early from study due to clinical toxicity [ulceration of oral cavity]; 1 male at 0.5 mg/kg given a 7-day dose holiday due to body weight loss), and 1 mg/kg (highest dose tested) for females. Effects: oral cavity, hard palate, tongue, esophagus, mandibular lymph node, female reproductive tract, eye, larynx, and skin. Other findings: Changes generally recovered or showed evidence of reversibility with 1 month recovery period.

Aspiration hazard

Due to the physical form of the product it is not an aspiration hazard.

Chronic effects

No other specific acute or chronic health impact noted.

12. Ecological information

Ecotoxicity Not expected to be harmful to aquatic organisms.

Components	Species		Test Results
Titanium dioxide (CAS 13463-67-7)			
Aquatic			
Acute			
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 this product.		
Bioaccumulative potential	Partition coefficient: TAK-788: Log DOW at pH 5: 1.6 Log DOW at pH 7: 2.9 Log DOW at pH 9: 5.2 Log P: 4.65		
Mobility in soil	No data available.		
Other adverse effects	None known.		

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 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

Iron oxide (CAS 1309-37-1)

Titanium dioxide (CAS 13463-67-7)

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

Iron oxide (CAS 1309-37-1)

Titanium dioxide (CAS 13463-67-7)

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

Iron oxide (CAS 1309-37-1)

Titanium dioxide (CAS 13463-67-7)

US. Rhode Island RTK

Iron oxide (CAS 1309-37-1)

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 18-May-2020

Revision date 06-September-2021

Version # 03

List of abbreviations

API: Active pharmaceutical ingredient.
EC50: Effective Concentration 50%.
LD50: Lethal Dose 50%.
LL50: Lethal level, 50%.
NOAEL: No observed adverse effect level.
OEL: Occupational Exposure Limit.
PEL: Permissible Exposure Limit.
PO: Per os (oral administration).
TWA: Time Weighted Average.

References

HSDB® - Hazardous Substances Data Bank
IARC Monographs. Overall Evaluation of Carcinogenicity
In-house data
National Toxicology Program (NTP) Report on Carcinogens
OECD SIDS

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.