

Safety Data Sheet for Drug Products (EU)



Date of issue: 08-MAY-2017

Replaces version of:

KISFE FCT 200+2.5MG (3X21+X28) USS 747094 (MARS)

1. Identification of the substance/preparation and of the company

Product name KISFE FCT 200+2.5MG (3X21+X28) USS
Chemical Class Triazol derivative
Generic Name Letrozole, LEE011-BBA
Pharmacological Action Non-steroid aromatase inhibitor, Antineoplastic
Usage Drug product (pharmaceutical bulk, primary packed, finished product, pharmaceutical intermediate)
Company name Novartis Pharma AG
4002 Basel
Switzerland
Tel: +41 61 324 11 11, email: sds.support@novartis.com
Emergency phone number CHEMTEL (International) +1 813 676 1670 (365/24/7)

2. Hazards identification

For side effects, which could also have impact for people working with this substance, please refer to the Patient Information Leaflet.

3. Composition / information on ingredients

For classification of declared components, see section 15, "Regulatory Information"

Chemical Name	Contains:	CAS Number
Letrozole	0 - 2.5 %	112809-51-5
LEE011-BBA	> 25 %	1374639-75-4

Remaining components are inert ingredients.

For TLV values of declared components, see Section 8, Exposure controls / Personal

4. First aid measures

Eye Contact Immediately rinse eyes thoroughly with running water as long as possible (approx. 15 min). Take injured quickly to factory medical center or call an ambulance (code word: eye accident).
Skin Contact Remove contaminated clothing. Rinse contaminated skin immediately with plenty of water and soap and seek medical advice.
Inhalation Remove the victim from danger zone, avoid further exposure.
Ingestion If swallowed, seek medical advice immediately and show this container or label.
Notes to Physician General measures to eliminate the substance and to reduce absorption.

5. Fire fighting measures

Suitable Extinguishing Media Water spray or fog, foam, dry chemical powder, CO₂, dry sand
Unsuitable Extinguishing Media No restrictions
Dangerous Combustion Products carbon oxides, nitrogen oxides, nitrogen oxides, carbon oxides
Protective equipment for firefighters Wear self-contained breathing apparatus and fire protective suite.

6. Accidental release measures

Personal precautions Avoid contact with skin, eyes and clothing.

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Environmental precautions Must not be released into sewers, drains or wells.

Methods for cleaning Transfer large quantities into a container. Clean up the rest with absorbent material and discharge properly.

7. Handling and storage

No special handling requirements for normal use of this material.

Store in a dry and cool place and observe special instructions from supplier.

8. Exposure controls / Personal protection

Occupational Exposure Limit (OEL)

no data available

TLV values of declared components

Contains:

Letrozole

List type	Value	Unit	
Internal exposure limit	0.1	µg/m ³	HHA Database

Contains:

LEE011-BBA

List type	Value	Unit	
Internal exposure limit	8	µg/m ³	HHA Database

Personal protection for open handling

Health care personnel



Safety glasses (EN166) Disposable fine dust protection mask (EN149); Double disposable gloves (EN374) Disposable dust-proof lab coat

9. Physical and chemical properties

Formulation Tablet

Flash Point not applicable

10. Stability and reactivity

Under the normal conditions of use, the product is stable.

11. Toxicological information

Acute Toxicity

Data of Letrozole
LD50: > 2000 mg/kg
Route: oral
Species: rat

Data of Letrozole
LD50: > 2000 mg/kg
Route: oral
Species: mouse

Data of Letrozole
LD50: < 200 mg/kg
Route: oral
Species: dog

Data of LEE011-BBA
MTD: 100 mg/kg

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	Route: oral Species: dog
Irritation, Corrosion	Data of Letrozole Eyes (Species: rabbit) non irritant Method: OECD 405 * 1987 * Eye Irritation / Corrosion Data of Letrozole Skin (Species: rabbit) non irritant Method: 92/69/EC (L383) B.4 * Acute toxicity (skin irritation) Data of LEE011-BBA Skin (Species: rabbit) non irritant Method: OECD Guideline 404 (Acute Dermal Irritation / Corrosion)
Sensitisation	Data of LEE011-BBA Skin (Species: mouse) not sensitizing Method: OECD Guideline 429 (Skin Sensitisation - LLNA) Value from salt form
Mutagenicity	Data of Letrozole Negative (AMES-Test (reverse mutation assay)) Cell: Strains of salmonella typhimurium. Data of Letrozole Negative (Gene Mutation Assay in Vitro) Cell: V79 cells (embryonic lung fibroblasts) of the Chinese hamster Method: OECD 476 * 1984 Data of Letrozole Negative (Chromosome Aberration Study) Cell: Chinese hamster ovary (CHO) cells Data of Letrozole Negative (Micronucleus Test) oral, Species: rat Method: 92/69/EC (L383) B.12 * Mutagenicity (micronucleus test) Data of LEE011-BBA Negative with and without metabolic activation (Micronucleus Test) in vitroCell: TK6 cells Method: OECD Guideline 487 (In vitro Mammalian Cell Micronucleus Test) Data of LEE011-BBA Negative with and without metabolic activation (Chromosome Aberration Study) in vitroCell: Cultured peripheral human lymphocytes Method: OECD Guideline 473 (In vitro Mammalian Chromosome Aberration Test) Data of LEE011-BBA Negative (Micronucleus Test) in vivo, Species: rat, Cell: Bone marrow Method: OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test) Data of LEE011-BBA Negative with and without metabolic activation (AMES-Test (reverse mutation assay)) in vitroCell: Strains of salmonella typhimurium. Method: OECD Guideline 471 (Bacterial Reverse Mutation Assay)
Chronic Effects	Data of Letrozole (Repeated Dose Toxicity) NOAEL: 0.3 mg/kg/d Route: oral Species: rat, Organ: Multiple organs Duration: 52 weeks Data of Letrozole (Repeated Dose Toxicity) NOAEL: 0.3 mg/kg/d Route: oral Species: dog, Organ: Multiple organs Duration: 52 weeks

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Data of Letrozole
Carcinogen (Repeated Dose Toxicity)
LOAEL: 0.6 mg/kg/d
Route: oral
Species: mouse, Organ: Female reproductive system
Duration: 104 weeks

Data of Letrozole
No evidence for carcinogenicity (Repeated Dose Toxicity)
LOAEL: 0.6 mg/kg/d
Route: oral
Species: mouse
Duration: 104 weeks
male

Data of Letrozole
Carcinogen (Repeated Dose Toxicity)
LOAEL: 0.1 mg/kg/d
Route: oral
Species: rat, Organ: Female reproductive system
Duration: 104 weeks

Data of Letrozole
No evidence for carcinogenicity (Repeated Dose Toxicity)
LOAEL: 0.1 mg/kg/d
Route: oral
Species: rat
Duration: 104 weeks
male

Data of LEE011-BBA
(Repeated Dose Toxicity)
NOAEL: 25 mg/kg/d
Route: oral
Species: rat, Organ: Multiple organs
Dosage: <= 150 mg/kg/d, Duration: 15 weeks
male

Data of LEE011-BBA
(Repeated Dose Toxicity)
NOAEL: 300 mg/kg/d
Route: oral
Species: rat, Organ: Multiple organs
Dosage: <= 300 mg/kg/d, Duration: 15 weeks
female

Data of LEE011-BBA
(Repeated Dose Toxicity)
LOAEL: 1 mg/kg/d
Route: oral
Species: dog, Organ: Multiple organs
Dosage: <= 10 mg/kg/d, Duration: 15 weeks
male

Data of LEE011-BBA
(Repeated Dose Toxicity)
NOAEL: 10 mg/kg/d
Route: oral
Species: dog, Organ: Multiple organs
Dosage: <= 10 mg/kg/d, Duration: 15 weeks
female

Reproduction Toxicity Data of Letrozole
Embryotoxicity (Embryo-Fetal Development)
LOAEL: 0.003 mg/kg/d
Route: oral
Species: rat

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Data of Letrozole
Teratogenicity at maternally toxic dose (Embryo-Fetal Development)
LOAEL: 0.03 mg/kg/d
Route: oral
Species: rat

Data of Letrozole
Female fertility decreased (Fertility and early Embryonic Development)
Route: oral
Species: rat, Sex: female

Data of Letrozole
Male fertility decreased (Fertility and early Embryonic Development)
Route: oral
Species: rat, Sex: male

Data of Letrozole
Maternal toxicity / embryotoxicity - no teratogenicity (Embryo-Fetal Development)
NOAEL: 0.002 mg/kg/d
Route: oral
Species: rabbit

Data of LEE011-BBA
Effect on embryo-fetal development (Embryo-Fetal Development)
NOEL: 50 mg/kg/d
Route: oral
Species: rat

Data of LEE011-BBA
Maternal toxicity (Embryo-Fetal Development)
NOAEL: 300 mg/kg/d
Route: oral
Species: rat

Data of LEE011-BBA
Effect on embryo-fetal development (Embryo-Fetal Development)
NOEL: 10 mg/kg/d
Route: oral
Species: rabbit

Data of LEE011-BBA
Maternal toxicity (Embryo-Fetal Development)
NOEL: 30 mg/kg/d
Route: oral
Species: rabbit

Human Pharmacokinetics
Data of Letrozole
Half Life ($T_{1/2}$): 2 days
Tmax: 1 hours
Availability: 99.9 %
Route: oral

12. Ecological information

Biological Elimination Data of Letrozole
Degradation: 1 % (CO2)
Not readily degradable
Initial conc.: 23.4 mg/l
Method: OECD 301B * 1981

Data of Letrozole
Degradation: 1 % (CO2)
Not readily degradable
Initial conc.: 26.3 mg/l
Method: OECD 301B * 1981

Data of LEE011-BBA
Degradation: 5 - 14 % (Temperature: 21.7 - 22.3 °C)

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Not readily degradable
Initial conc.: 12 mg/l, Duration: 28 days
Method: OECD 301B * 1992; EC No 440/2008 C.4-C * 2008; ISO 9439 * 1999
ISO 10634

Fish acute toxicity

Data of Letrozole
LC0: 37 mg/l
LC50: > 37 mg/l
LC100: > 37 mg/l
Species: rainbow trout (*salmo gairdneri*, *oncorhynchus mykiss*)
Exp. time: 96 hours
Method: OECD 203 * 1984 * acute toxicity
Not toxic with reference to the 7th Amendment to Directive 67/548/EEC, 92/32/EEC
Data of LEE011-BBA
LC50: 38 mg/l
Species: common carp (*cyprinus carpio*)
Exp. time: 96 hours
Method: OECD 203 * 1992 * acute toxicity
EC 440/2008 C.1
ISO 7346-1&2, 1996

Fish chronic toxicity

Data of Letrozole
LOEC: 0.025 mg/l
NOEC: NOEC: 0.005 mg/l
Species: red killifish (*oryzias latipes*), jap. killifish
Exp. time: 21 days
Method: unvalidated test method.
Information from other sources (e.g. literature)
Data of LEE011-BBA
LOEC: 2.2 mg/l
NOEC: NOEC: 1 mg/l
Species: fathead minnow (*pimephales promelas*)
Exp. time: 33 days
Method: OECD Guidelines 210: Fish, Early-life Stage Toxicity Test

Aquatic invertebrate acute toxicity

Data of Letrozole
EC0: 35 mg/l
EC50: > 35 mg/l
EC100: > 35 mg/l
Species: daphnia magna (water flea)
Exp. time: 48 hours
Method: OECD 202 * 2004
Not toxic with reference to the 7th Amendment to Directive 67/548/EEC, 92/32/EEC
Data of LEE011-BBA
EC50: > 33 mg/l
Species: daphnia magna (water flea)
Exp. time: 48 hours
Method: OECD 202 * 2004; EC 440/2008, Part C.2 * 2008; ISO 6341 * 1996

Aquatic invertebrate chronic toxicity

Data of LEE011-BBA
NOEC: NOEC: 1.4 mg/l
Species: daphnia magna (water flea)
Exp. time: 21 days
Method: OECD Guidelines 211: Daphnia magna Reproduction Test

Algae Toxicity

Data of Letrozole
EC50: > 100 mg/l
Species: *Desmodesmus subspicatus*/*Scenedesmus subspicatus* (Green algae)
Exp. time: 72 hours
Method: OECD 201 * 1984 * Growth inhibition
Not toxic with reference to the 7th Amendment to Directive 67/548/EEC, 92/32/EEC
Data of LEE011-BBA
EC10: 0.71 mg/l

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EC20: 1.21 mg/l
EC50: 3.38 mg/l
NOEC: 0.76 mg/l
Species: Green algae - fresh water (*Pseudokirchneriella subcapitata*)
Exp. time: 72 hours
Method: OECD 201 * 2006 * Growth inhibition; ISO 8692 * 2004
EC 440/2008 C.3
Value from another salt form

Bacterial Respiration Inhibition

Data of Letrozole
EC0: 20.2 mg/l
EC50: > 20.2 mg/l
EC100: > 20.2 mg/l
Species: activated sludge
Exp. time: 696 hours
Method: evaluated
Data of LEE011-BBA
EC50: > 1000 mg/l
Species: activated sludge
Exp. time: 3 hours
Method: OECD 209 * 2010; EC 440/2008, L142 C11 * 1988; ISO 8192 (2007)

Ecotoxicity Summary

Data of Letrozole
Bioaccumulation in water organisms is not likely based on the n-octanol/water partition coefficient (log Pow < 3.0).
Data of Letrozole
When low concentrations are discharged correctly into adapted biological sewage treatment plants, interference with the degradation activity of activated sludge is not likely.
Data of LEE011-BBA
Avoid release into soil, rivers or drains.

13. Disposal considerations

Disposal Requirements Fill into suitable waste receptacles, seal and label them properly. Incineration in an approved, controlled furnace with combustion gas scrubbing and emission gas control. Local regulations should be adhered to.

14. Transport information





Regulation	Class	UN No.	PG	Label	LQ
RID/ADR:	Not restricted	0			N.A.
IMDG-Code:	Not restricted	0			
ICAO/IATA-DGR:	Not restricted	0			

ICAO/IATA-DGR: no dangerous good

Proper shipping name: -

15. Regulatory information

Classifications of components:

Chemical Name	Contains:	CAS Number	Picto	Signal Word	Classification
Letrozole	0 - 2.5 %	112809-51-5	 	D	H360fd, H372, H410
LEE011-BBA	> 25 %	1374639-75-4	 	W	H361, H373, H401, H411

Remaining components are inert ingredients.

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16. Other information

Abbreviations used

H360fd: May damage fertility. May damage the unborn child.

H372: Causes damage to organs through prolonged or repeated exposure.

H410: Very toxic to aquatic life with long lasting effects.

H361: Suspected of damaging fertility or the unborn child.

H373: May cause damage to organs through prolonged or repeated exposure.

H401: Toxic to aquatic life.(in EU not leading to classification as hazardous)

H411: Toxic to aquatic life with long lasting effects.

Recipient

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Product should be stored, handled and used in accordance with good industrial hygiene practices and in conformity with legal regulations. The information contained herein is based on the present state of our knowledge and is intended to describe our products from the point of view of safety requirements. It should therefore not be construed as guaranteeing specific properties.