

### SECTION 1: Identification of the substance/mixture and of the company/undertaking

#### 1.1. Product identifier

Product form : Mixture  
Trade Name : Savaysa/Lixiana

#### 1.2. Relevant identified uses of the substance or mixture and uses advised against

##### 1.2.1. Relevant identified uses

Main use category : Pharmaceutical product  
Use of the substance/mixture : Therapeutic medication

##### 1.2.2. Uses advised against

No information available.

#### 1.3. Details of the supplier of the safety data sheet

DAIICHI SANKYO CO., LTD. Supply Chain Division, Supply Chain Planning Department, Administration & Planning Group  
3-5-1, Nihonbashi Honcho, Chuo-ku, Tokyo, 103-8426, Japan  
T +81-(0)3-6225-1111 - F +81-(0)3-3246-6918

#### 1.4. Emergency telephone number

Emergency number : +81-(0)3-3246-7033 (on business days 8:45 AM to 5:30 PM JST)

### SECTION 2: Hazards identification

#### 2.1. Classification of the substance or mixture

##### GHS-US classification

Carc. 2 H351  
STOT RE 2 H373  
Full text of R-phrases: see section 16

##### Adverse physicochemical, human health and environmental effects

No additional information available.

#### 2.2. Label elements

Hazard pictograms :



GHS08

Signal word : Warning

Hazard statements : H351 - Suspected of causing cancer  
H373 - May cause damage to organs through prolonged or repeated exposure

Precautionary statements : P260 - Do not breathe dust/fume/gas/mist/vapours/spray.  
P314 - Get medical advice/attention if you feel unwell  
P501 - Dispose of contents/container with official regulation.  
P201 - Obtain special instructions before use  
P202 - Do not handle until all safety precautions have been read and understood  
P280 - Wear protective gloves/protective clothing/eye protection/face protection.  
P308+P313 - IF exposed or concerned: Get medical advice/attention  
P405 - Store locked up

#### 2.3. Other hazards

Other hazards not contributing to the classification : No information available.

### SECTION 3: Composition/information on ingredients

#### 3.1. Substance

Not applicable

#### 3.2. Mixture

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Chemical name	Product identifier	%	Classification according to HazCom 2012
Edoxaban tosylate hydrate	(CAS number) 480449-71-6 (EC no)	19.2	STOT RE 2; H373
D-Mannitol	(CAS number) 69-65-8 (EC no) 200-711-8	*	Classification not possible
Starch, pregelatinized	(CAS number) 9005-25-8 (EC no) 232-679-6	*	Classification not possible
Polyvinylpyrrolidone	(CAS number) 9003-39-8 (EC no) 201-800-4	*	Classification not possible
Hydroxypropyl cellulose	(CAS number) 9004-64-2 (EC no) 220-971-6	*	Classification not possible
Magnesium stearate	(CAS number) 557-04-0 (EC no) 209-150-3	< 1	Skin Irrit. 3, H316; Eye Irrit. 2B, H320
OPADRY 03F430000 (For orange tablets), OPADRY 03F44145 (For pink tablets), OPADRY 03F42132 (For yellow tablets)	Talc (10-30%)	< 5	Classification not possible
	Titanium dioxide (5-10%)		Carc. 2, H351
Carnauba wax	(CAS number) 8015-86-9 (EC no) 232-399-4	Trace	Classification not possible
Talc	(CAS number) 14807-96-6 (EC no) 238-877-9	Trace	Classification not possible

\*Proprietary information

Full text of R- and H-phrases: see section 16

### SECTION 4: First aid measures

#### 4.1. Description of first aid measures

Inhalation	: Remove the victim to fresh air. Seek medical advice.
Skin contact	: Remove all contaminated clothing and wash the affected area with soap and water for 15 minutes. Consult a doctor.
Eye contact	: Gently rinse the affected eyes with clean water for at least 15 minutes. Consult a doctor.
Ingestion	: Rinse mouth thoroughly with water. Try to induce vomiting by having the victim touch the back of his/her throat with his/her finger. Consult a doctor.

#### 4.2. Most important symptoms and effects, both acute and delayed

Symptoms/injuries : No information available to date.

#### 4.3. Indication of any immediate medical attention and special treatment needed

No information available to date.

### SECTION 5: Firefighting measures

#### 5.1. Extinguishing media

Suitable extinguishing agents : Water spray. Carbon dioxide. Extinguishing powder. Foam. Inert gas.  
Prohibited extinguishing agents : No information available to date.

#### 5.2. Special hazards arising from the substance or mixture

Specific hazard level under fire conditions : Hazardous combustion products include carbon monoxide and carbon dioxide.  
Explosion hazard : No information available to date.  
Reactivity : No information available to date.

#### 5.3. Advice for firefighters

Protection during firefighting : Fire fighters should wear appropriate personal protective equipment (protective clothing, chemical safety goggles or rubber gloves).

### SECTION 6: Accidental release measures

#### 6.1. Personal precautions, protective equipment and emergency procedures

General measures : Wear proper protecting equipment to prevent contact with skin and inhalation of vapour. Keep non-essential and unprotected persons away from the area.

##### 6.1.1. For non-emergency personnel

Emergency procedures : Prevent further leakage if safe to do so.

##### 6.1.2. For emergency responders

Emergency procedures : Ventilate area. Stop leak if safe to do so. Keep away from open flame and source of ignition.

#### 6.2. Environmental precautions

Ventilate the area after cleaning is completed. Avoid raising the dust. Do not allow material to be released to the environment without proper governmental permits.

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### 6.3. Methods and material for containment and cleaning up

Methods for cleaning up : Carefully sweep up and remove the contaminant. Do not wash away into sewer or waterways. Ventilate the area after the cleaning is complete.

### 6.4. Reference to other sections

For disposal see section 13. For exposure controls see section 8.

## SECTION 7: Handling and storage

### 7.1. Precautions for safe handling

Precautions for safe handling : Do not breathe the dust. Wear proper protective equipment to avoid contact with skin and eyes.  
Handling temperature : Room temperature  
Appropriate hygiene measures : Practice good personal hygiene after handling this product, especially before eating, drinking, smoking or using the toilet.

### 7.2. Conditions for safe storage, including any incompatibilities

Technical measures : Use in well-ventilated areas.  
Storage conditions : Store in a light-resistant, tight container.  
Incompatible materials : Oxidizing agents, strong  
Storage temperature : Room temperature

### 7.3. Specific end use(s)

Therapeutic medication

## SECTION 8: Exposure controls/personal protection

### 8.1. Control parameters

D-Mannitol (69-65-8)	
Non specific total dusts	AEL <= 10 mg/m <sup>3</sup>
Respirable dust fractions	STEL <= 5 mg/m <sup>3</sup>

Starch, pregelatinized (9005-25-8)	
OSHA permissible exposure limit (PEL)	Total dust: 15 mg/m <sup>3</sup> TWA Respirable fraction: 5 mg/m <sup>3</sup> TWA
ACGIH threshold limit value (TLV)	10 mg/m <sup>3</sup> TWA

Polyvinylpyrrolidone (9003-39-8)	
Not aware of any national exposure limit.	

Hydroxypropyl cellulose (9004-64-2)	
Not listed according to TLV/ACGIH (2010).	

Magnesium stearate (557-04-0)			
Occupational exposure limits	Type	Value	Form
ACGIH	TWA	10.0000 mg/m <sup>3</sup>	-
U.S. - OSHA	PEL	15.0000 mg/m <sup>3</sup>	Total dust
		5.0000 mg/m <sup>3</sup>	Respirable fraction for nuisance dusts

OPADRY 03F430000 (For orange tablets), OPADRY 03F44145 (For pink tablets), OPADRY 03F42132 (For yellow tablets)	
Talc (14807-96-6)	EH40/2005 WELs. TWA: 1 mg/m <sup>3</sup> 8 hr (Respirable dust) OSHA PEL 20 mppcf, NIOSH, ACGIH TWA 2mg/m <sup>3</sup>
Titanium dioxide (13463-67-7)	EH40/2005 WELs. TWA: 10 mg/m <sup>3</sup> 8 hr (inhalable dust) TWA: 4 mg/m <sup>3</sup> 8 hr (Respirable dust) OSHA PEL 15mg/m <sup>3</sup> , NIOSH TWA 2.4mg/m <sup>3</sup> (fine), ACGIH TWA 1mg/m <sup>3</sup>

OPADRY 03F42132 (For yellow tablets)	
Synthetic yellow iron oxide (51274-00-1)	EH40/2005 WELs. STEL: 10 mg/m <sup>3</sup> , (as Fe) 15 min (Fume) TWA: 5 mg/m <sup>3</sup> , (as Fe) 8 hr (Fume) OSHA PEL 10mg/m <sup>3</sup> (fume), ACGIH TWA 5mg/m <sup>3</sup> (resp)Fume : 10 mg/m <sup>3</sup> (as Fe) 15 min STEL Fume : 5 mg/m <sup>3</sup> (as Fe) 8 hr TWA

Carnauba wax (8015-86-9)	
No information available.	

Talc (14807-96-6)	
ACGIN (TLV)	2 mg/m <sup>3</sup> TWA

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### Talc (14807-96-6)

OSHA

20 mppcf TWA

#### 8.2. Exposure controls

Appropriate technical controls

: Refer to chapter 7. No further action is necessary.

Personal protective equipment

: Gloves. Safety glasses. Protective goggles. Dust formation: dust mask.



Hands

: Wear rubber gloves or chemical resistant gloves.

Eyes

: Wear protective eyeglasses or chemical safety goggles.

Skin and body

: Wear chemical resistant gloves and suitable protective clothing.

Respiratory

: Wear an approved dust respirator.

## SECTION 9: Physical and chemical properties

### 9.1. Information on basic physical and chemical properties

Physical state

: Solid

Description

: Tablets

Colour

: Orange, Pink or Yellow

Odour

: No data available

Odour threshold

: No data available

pH

: No data available

Relative evaporation rate (butylacetate=1)

: No data available

Melting point

: No data available

Freezing point

: Not applicable

Boiling point

: Not applicable.

Flash point

: No data available

Ignition point

: No data available

Decomposition temperature

: No data available

Flammability (solid, gas)

: No data available

Vapour pressure

: No data available

Vapour density

: No data available

Relative density

: No data available

Solubility

: No data available

Log Pow

: No data available

Log Kow

: No data available

Viscosity, kinematic

: No data available

Viscosity, dynamic

: No data available

Explosiveness

: No data available.

Oxidising properties

: No data available.

Explosive limits

: No data available

### 9.2. Other information

No information available.

## SECTION 10: Stability and reactivity

### 10.1. Reactivity

No hazardous reaction when handled and stored according to provisions.

### 10.2. Chemical stability

Stable for 36 months when stored at room temperature under appropriate storage conditions.

### 10.3. Possibility of hazardous reactions

No information available to date.

### 10.4. Conditions to avoid

Keep away from heat and direct sunlight.

### 10.5. Incompatible materials

No information available to date.

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### 10.6. Hazardous decomposition products

Hazardous decomposition products may consist of CO<sub>x</sub> and NO<sub>x</sub> products.

## SECTION 11: Toxicological information

### 11.1. Information on toxicological effects

<b>Edoxaban tosylate (480449-71-6)</b>	
Acute toxicity	Not classified (Conclusive but not sufficient for classification)
Acute toxicity (rat)	MLD >2000 mg/kg
Acute toxicity (monkey)	MLD >400 mg/kg
Skin corrosion/irritation	Not classified.
Serious eye damage/irritation	Not classified.
Respiratory or skin sensitisation	Not classified.
Germ cell mutagenicity	(Based on available data, the classification criteria are not met)
Carcinogenicity	(Based on available data, the classification criteria are not met)
Reproductive toxicity	(Based on available data, the classification criteria are not met)
Specific target organ toxicity (single exposure)	Not classified.
Specific target organ toxicity (repeated exposure)	May cause damage to organs through prolonged or repeated exposure.
NOAEL (oral, rat, 6 months)	54 mg/kg bodyweight/day
NOAEL (oral, monkey, 1 year)	5 mg/kg bodyweight/day
Aspiration hazard	Not classified.
<b>D-Mannitol (69-65-8)</b>	
Acute toxicity (Rat)	LD <sub>50</sub> > 5000 mg/kg Non toxic
Acute toxicity (Mouse)	LD <sub>50</sub> > 5000 mg/kg Non toxic
Repeated dose toxicity (Rat)	No data on possible toxicity effects have been found (Exposure: 94 weeks).
Mutagenesis (In vitro)	Negative (Species: <i>S. typhimurium</i> )
Carcinogenicity	Negative (Oral, mouse, 103 weeks) Not classified as carcinogenic by ACGIH, CIRC, OSHA or NTP.
Reproductive toxicity (Rat)	No treatment related effects (Oral 10 days).
<b>Starch, pregelatinized starch (9005-25-8)</b>	
Acute toxicity (Mouse, intraperitoneal admin.)	LD <sub>50</sub> > 6600 mg/kg
Eye irritation	Not available.
Skin irritation	No irritation to human skin. (300 µg/3 days, intermittent)
Chronic toxicity	Starch is regarded as GRAS (generally recognized as safe) by FDA.
Mutagenicity	Not available.
Carcinogenicity	This product is not considered to be a carcinogen by IARC, NTP, or ACGIH.
<b>Polyvinylpyrrolidone (9003-39-8)</b>	
Acute toxicity (Mouse, intraperitoneal admin.)	LD <sub>50</sub> > 12 g/kg
<b>Hydroxypropyl cellulose (9004-64-2)</b>	
Acute toxicity	Oral LD50 (Rat): >10200 mg/kg Dermal: Not available. Inhalation: Not available, but this material is not reported to be toxic by inhalation.
Skin corrosion/irritation	Dermal (Human): Not irritant.
Serious eye damage/irritation	Eyes (Rabbit): Not irritant.
Respiratory or skin sensitization	Dermal (Human): Negative (10% aq. solution paste) Respiratory: Not available.
Germ cell mutagenicity	Ames test: Negative Chromosomal aberration test: Not available. UDS test: Not available. Micronucleus test: Not available.
Carcinogenicity	This product is not considered to be a carcinogen by IARC, NTP, or OSHA.
Reproductive toxicity	Not available.
SNOT-single exposure	Not available.
SNOT-repeated exposure	Not available.
Aspiration hazard	Not available.
Others	Effect of chronic or sub-acute exposure 90-day sub-acute toxicity for this product (Rat): 0, 0.2, 1.5% (0.100.500. 2500 mg/kg/day) NOAEL for 90-day sub acute toxicity is 2500 mg/kg/day.
<b>Magnesium stearate (557-04-0)</b>	
Local effects	Inhalation of dusts may cause respiratory irritation.
Chronic effects	Lung edema

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<b>Magnesium stearate (557-04-0)</b>	
Carcinogenicity	This product is not considered to be a carcinogen by IARC, ACGIH, NTP, or OSHA.
ACGH Carcinogens	A4 Not classifiable as a human carcinogen.
Skin corrosion/irritation	Not available.
Epidemiology	Not available.
Neurological effects	Not available.

<b>OPADRY 03F430000 (For orange tablets), OPADRY 03F44145 (For pink tablets), OPADRY 03F42132 (For yellow tablets)</b>		
Components		
Hydroxypropyl methylcellulose (9004-65-3)	Acute toxicity	Intraperitoneal LD50 (Rat): 5200 mg/kg
Titanium dioxide (13463-67-7)	Acute toxicity	Intratracheal LD (Rat): > 100 µg/kg
		Intratracheal TD <sub>0</sub> (Rat): 5 mg/kg
		Intratracheal TD <sub>0</sub> (Rat): 1.6 mg/kg
		Intratracheal TD <sub>0</sub> (Rat): 1.25 mg/kg
	Chronic toxicity	Oral TD <sub>0</sub> (Rat): 60 g/kg
		A3 (ACGIH), 2B (IARC)

<b>Carnauba wax (8015-86-9)</b>	
Toxicity	Not available.
Irritation	No data
Mutation	No data
Inhalation toxicity	No data

<b>Talc (14807-96-6)</b>	
Ingestion	Single dose oral toxicity is believed to be very low. May cause choking if swallowed
Skin contact	Essentially nonirritating to the skin. Mechanical injury only. Skin absorption is unlikely due to physical properties.
Eye contact	Solid or dust may cause irritation or corneal injury due to mechanical action.
Inhalation	Dust may cause irritation to upper respiratory tract (nose and throat).
Carcinogenicity	A4 (ACGIH), 3 (IARC)

## SECTION 12: Ecological information

### 12.1. Toxicity

<b>Edoxaban tosylate (480449-71-6)</b>	
LC50 fishes 1	> saturated concentration in water. (himedaka, 96 hr)

<b>D-Mannitol (69-65-8)</b>	
No negative effects on the aquatic environment are known.	

<b>Starch, pregelatinized (9005-25-8)</b>	
Ecotoxicity	Not available.

<b>Polyvinylpyrrolidone (9003-39-8)</b>	
No data available.	

<b>Hydroxypropyl cellulose (9004-64-2)</b>	
Ecological toxicity	Acute toxicity to aquatic life Acute toxicity to Fish: Not available. Acute toxicity to Daphnia: Not available. Acute toxicity to Algae: Not available. No information for animal tests is available, but this material is estimated to have low toxicity to aquatic life from the knowledge in handling.

<b>Magnesium stearate (557-04-0)</b>	
This product has no known eco-toxicological effects.	

<b>OPADRY 03F430000 (For orange tablets), OPADRY 03F44145 (For pink tablets), OPADRY 03F42132 (For yellow tablets): Toxicity in water</b>	
Titanium dioxide (13463-67-7)	Acute EC50 (Water flea - Daphnia magna): > 1000000 µg/L fresh water 48 hr
	Acute LC50 (Water flea - Daphnia magna): 5.5 ppm fresh water 48 hr
	Acute LC50 (Mummichog - Fundulus heteroclitus): > 1000000 µg/L seawater 96 hr
	Chronic NOEC (Water flea - Daphnia magna): 500 ppm fresh water 48 hr
	Chronic NOEC (Water flea - Daphnia magna): 1 ppm fresh water 48 hr

<b>Talc (14807-96-6)</b>	
In the aquatic environment, this product should not present problems because of extremely low solubility.	

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### 12.2. Persistence and degradability

#### Edoxaban tosylate (480449-71-6)

Residual tendency / decomposability | No information available to date.

#### D-Mannitol (69-65-8)

The product is easily biodegradable.

#### Starch, pregelatinized (9005-25-8)

Inherently biodegradable.

#### Polyvinylpyrrolidone (9003-39-8)

No data available.

#### Hydroxypropyl cellulose (9004-64-2)

Bio-degradability | Not available.

#### Magnesium stearate (557-04-0)

Bio-degradability | Not available.

#### Carnauba wax (8015-86-9)

Biodegradable natural products

#### Talc (14807-96-6)

In the soil compartment, material is inherently very difficult to degrade.

### 12.3. Bioaccumulative potential

#### Edoxaban tosylate (480449-71-6)

Log Pow | 1.72 (at 20°C to 25°C, pH8.0)

Biological accumulativity | No information available to date.

#### D-Mannitol (69-65-8)

Log Pow (n-Octanol/Water Partition Coefficient) | -3, 10

Bioconcentration factor (BCF)/Bioaccumulation | ~ 1

#### Polyvinylpyrrolidone (9003-39-8)

No data available.

#### Hydroxypropyl cellulose (9004-64-2)

Not available.

#### Talc (14807-96-6)

None known.

### 12.4. Mobility in soil

#### Edoxaban tosylate (480449-71-6)

Ecology - soil | No information available to date.

#### D-Mannitol (69-65-8)

Organic Carbon Partition Coefficient (Koc) | ~ 5 (Medium: Soil)

#### Polyvinylpyrrolidone (9003-39-8)

No data available.

#### Hydroxypropyl cellulose (9004-64-2)

Not available.

#### Talc (14807-96-6)

Not available.

### 12.5. Results of PBT and vPvB assessment

No information available.

### 12.6. Other adverse effects

No information available.

## SECTION 13: Disposal considerations

### 13.1. Waste treatment methods

Regional legislation (waste) : Disposal must be done according to official regulations.

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Residual waste : Dispose of waste in accordance with federal, state and local laws.

### SECTION 14: Transport information

In accordance with ADR / RID / IMDG / IATA / ADN

#### 14.1. UN number

None is assigned as compound is not considered dangerous from transportation regulation standpoint

#### 14.2. UN proper shipping name

Not applicable

#### 14.3. Transport hazard class(es)

Not applicable

#### 14.4. Packing group

Not applicable

#### 14.5. Environmental hazards

Other information : No supplementary information available.

#### 14.6. Special precautions for user

##### 14.6.1. Overland transport

No information available.

##### 14.6.2. Transport by sea

No information available.

##### 14.6.3. Air transport

No information available.

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

Not applicable

### SECTION 15: Regulatory information

#### 15.1. Safety, health and environmental regulations specific for the product

##### 15.1.1. US Federal regulations

No information available.

##### 15.1.2. US State regulations

No information available.

#### 15.2. International regulations

No chemical safety assessment has been carried out

### SECTION 16: Other information

Exemption clause : The information in this document is based on the present state of the sponsor's (DAIICHI SANKYO) knowledge and may be revised with new findings. Precautions in this document are only applicable to the product under normal use other than as prescribed. For particular use, appropriate safety and supportive measures should be taken. This document only presents information and does not represent any guarantee.

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*This information is based on our current knowledge and is intended to describe the product for the purposes of health, safety and environmental requirements only. It should not therefore be construed as guaranteeing any specific property of the product*