Xultophy® 100/3.6

Safety Data Sheet

according to Federal Register / Vol. 77, No. 58 / Monday, March 26, 2012 / Rules and Regulations

Revision date: 11/12/18 Version 1.0

SECTION 1: Identification

1.1. Identification

Product name : Xultophy® 100/3.6

Synonyms : IDegLira (100 U/mL insulin degludec 3.6 mg/mL liraglutide)

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

Recommended use : Xultophy® 100/3.6 is a combination of insulin degludec, a long-acting human insulin analog, and liraglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus inadequately controlled on basal insulin (less than 50 units daily) or liraglutide (less than or equal to 1.8 mg daily)

Restrictions on use : Refer to current approved Xultophy® 100/3.6 Prescribing Information for detailed information.

1.3. Details of the supplier of the safety data sheet

Novo Nordisk
800 Scudders Mill Road
Plainsboro, NJ 08536
T 800-727-6500
www.novonordisk-us.com

1.4. Emergency telephone number

Emergency number : 800-727-6500

SECTION 2: Hazard(s) identification

2.1. Classification of the substance or mixture

GHS-US classification

Not classified

2.2. Label elements

GHS-US labeling

No labeling required

2.3. Other hazards

Other hazards not contributing to the classification : Inactive ingredients include: glycerol, phenol, zinc, hydrochloric acid and sodium hydroxide (for pH adjustment) and water for injections. Inadvertent needle stick may pose risk of blood borne pathogens.

2.4. Unknown acute toxicity (GHS US)

Not applicable

SECTION 3: Composition/Information on ingredients

3.1. Substance

Not applicable

3.2. Mixture

Name	Product identifier	%	GHS-US classification
Solution for injection containing Insulin Degludec	(CAS No) 844439-96-9	<= 0.366	Not classified
Solution for injection containing liraglutide	(CAS No) 204656-20-2	<= 0.36	Not classified

Full text of hazard classes and H-statements : see section 16

SECTION 4: First aid measures

4.1. Description of first aid measures

First-aid measures general : If exposed or concerned: Get medical advice/attention. Call a poison center/doctor/physician if you feel unwell.

First-aid measures after inhalation : Remove person to fresh air and keep comfortable for breathing. If experiencing respiratory symptoms: Call a poison center or a doctor.

First-aid measures after skin contact : Wash skin with plenty of water. Take off contaminated clothing. If skin irritation or rash occurs: Get medical advice/attention.

First-aid measures after eye contact : Immediately flush eyes with plenty of water, occasionally lifting the upper and lower eyelids. Check for and remove any contact lenses. Continue to rinse for at least 10 minutes. Get medical attention if irritation occurs.

First-aid measures after ingestion : Rinse mouth. Drink plenty of water. Seek medical advice in case of persistent discomfort. Do NOT induce vomiting. Not expected to be active orally (hypoglycemia).

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

Symptoms/injuries: As packaged, this material does not present significant health hazards. The hazards below apply to the product if pen is broken.

Symptoms/injuries after inhalation: Not investigated. Inhalation of mist/dust containing protein may cause sensitization.

Symptoms/injuries after skin contact: May cause irritation by the active substance or any of the excipients.

Symptoms/injuries after eye contact: May cause irritation. Avoid contact with the eyes.

Symptoms/injuries after ingestion: Not expected to be active orally. Absorption is not expected. Ingestion is not known to cause health effects.

Symptoms/injuries upon injection: None anticipated under normal conditions and use. As with other insulin therapy, patients may experience rash, redness, inflammation, bruising, or itching at the site of Xultrophy®100/3.6 injection.

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

Treat symptomatically.

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media : Use media appropriate for surrounding fire.

5.2. Special hazards arising from the substance or mixture

Reactivity : The product is non-reactive under normal conditions of use, storage and transport.

5.3. Advice for firefighters

Protection during firefighting : Do not attempt to take action without suitable protective equipment. Self-contained breathing apparatus. Complete protective clothing.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

6.1.1. For non-emergency personnel

Emergency procedures : Evacuate unnecessary personnel.

6.1.2. For emergency responders

Protective equipment : Equip cleanup crew with proper protection.

6.2. Environmental precautions

Under normal use, this product is not expected to impact the environment. Prevent entry to sewers and public waters.

6.3. Methods and material for containment and cleaning up

Methods for cleaning up : Take up liquid spill into absorbent material. Notify authorities if product enters sewers or public waters.

Other information : Dispose of materials or solid residues at an authorized site.

6.4. Reference to other sections

For further information refer to section 13.

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Precautions for safe handling : Do not get in eyes, on skin, or on clothing. Prevent contact with needles used to administer Xultophy® 100/3.6. Use personal protective equipment as required. Xultophy® 100/3.6 is for subcutaneous use only.

Hygiene measures : Do not eat, drink or smoke when using this product. Practice good housekeeping. Wash thoroughly after handling. Change contaminated clothing. Do not reuse until laundered.

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions : Storage temperature for Xultophy® 100/3.6, see Prescribing Information for details on storage and handling. Must be kept in original packaging and stored according to Prescribing Information to prevent degradation. Xultophy® 100/3.6 should not be used after the expiration date on the pens.

SECTION 8: Exposure controls/personal protection

Phenol (CAS 108-952)		
U.S. OSHA	OSHA PEL (TWA) mg/m^3	19 mg/m^3
U.S. OSHA	OSHA PEL (TWA) ppm	5 ppm
ACGIH	ACGIH TLV (TWA) mg/m^3	19 mg/m^3 (skin)
ACGIH	ACGIH TLV (TWA) ppm	5 ppm (skin)

8.1. Control parameters

Solution for injection containing liraglutide [rDNA origin] (204656-20-2)
Not applicable

Solution for injection containing Insulin degludec [rDNA origin] (844439-96-9)
Not applicable

8.2. Exposure controls

Appropriate engineering controls : Work must be done with effective mechanical ventilation (e.g. local extractor fan). There must be access to running water and eye wash.

Personal protective equipment : Avoid all unnecessary exposure.

Hand protection Polyvinylchloride (PVC) / Nitrile rubber gloves.

Eye protection : Eye protection such as chemical splash goggles and/or face shield must be worn when possibility exists for eye contact due to splashing or spraying liquid. Contact lenses should not be worn.

Skin and body protection : PVC gloves, nitrile rubber or similar protection are recommended for waste clear-up and manufacturing operations. Avoid contact with sharps used to administer Xultophy® 100/3.6.

Respiratory protection : Not normally required.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state : Liquid

Color : Colorless.

Odor : Smell of phenol and m-cresol (sweetish, sickening odor)

Odor threshold : No data available

pH : No data available

Melting point : No data available

Freezing point : No data available

Boiling point : No data available

Flash point : No data available

Relative evaporation rate (butyl acetate=1) : No data available

Flammability (solid, gas) : No data available

Vapor pressure : No data available

Relative vapor density at 20 °C : No data available

Relative density : No data available

Solubility : No data available

Log Pow : No data available

Auto-ignition temperature	:	No data available
Decomposition temperature	:	No data available
Viscosity, kinematic	:	No data available
Viscosity, dynamic	:	No data available
Explosion limits	:	No data available
Explosive properties	:	No data available
Oxidizing properties	:	No data available

SECTION 10: Stability and reactivity

10.1. Reactivity

The product is non-reactive under normal conditions of use, storage and transport.

10.2. Chemical stability

Stable under normal conditions.

10.3. Possibility of hazardous reactions

No dangerous reactions known under normal conditions of use.

10.4. Conditions to avoid

None under recommended storage and handling conditions (see section 7). Not recommended for use in combination with any other product containing liraglutide or another GLP-1 receptor agonist.

10.5. Incompatible materials

No additional information available

10.6. Hazardous decomposition products

Under normal conditions of storage and use, hazardous decomposition products should not be produced.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute Toxicity

Solution for injection containing liraglutide (204656-20-2)	
LD50 oral rat	980 mg/kg

Phenol (108-95-2)	
LD50 oral rat	317 mg/kg Proceedings of the Society for Experimental Biology and Medicine. Vol. 32, Pg. 592, 1935.
LD50 dermal rabbit	630 mg/kg Union Carbide Data Sheet. Vol. 1/6/1966
LC50 inhalation rat (ppm)	81 ppm Nagonznyi 1976
ATE CLP (oral)	100,000 mg/kg body weight
ATE CLP (dermal)	300,000 mg/kg body weight
ATE CLP (gases)	700,000 ppmV/4h
ATE CLP (vapors)	3,000 mg/l/4h
ATE CLP (dust, mist)	0.500 mg/l/4h

Skin corrosion/irritation	:	Not classified
Serious eye damage/irritation	:	Not classified
Respiratory or skin sensitization	:	May cause an allergic skin reaction.
Germ cell mutagenicity	:	Not classified (Liraglutide was negative with and without metabolic activation in the Ames test for mutagenicity and in a human peripheral blood lymphocyte chromosome aberration test for clastogenicity. Liraglutide was negative in repeat-dose in vivo micronucleau tests in rats.)
Carcinogenicity	:	Liraglutide causes dose-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Xultophy® 100/3.6 causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or non-clinical studies.

Phenol (108-95-2)	
IARC	Group 3 – Not classifiable

Reproductive toxicity : Not classified

Specific target organ toxicity – single exposure : Not classified

Specific target organ toxicity – repeated exposure : Not classified

Phenol (108-95-2)	
LOAEL (oral, rat, 90 days)	1.8 mg/kg body weight/day

Aspiration hazard : Not classified

Potential Adverse human health effects and symptoms : Refer to current approved Xultophy® 100/3.6 Prescribing Information for detailed information.

Symptoms/injuries after inhalation : Not classified

Symptoms/injuries after skin contact : May cause an allergic skin reaction.

Other information : Xultophy® 100/3.6 pen must never be shared between patients, even if the needle is changed. Sharing of the pen poses a risk for transmission of blood-borne pathogens. Xultophy® 100/3.6 contains two drugs: insulin degludec and liraglutide. Administration of more than 50 units of Xultophy® 100/3.6 daily can result in overdose of the liraglutide component. Do not exceed the 1.8 mg maximum recommended dose of liraglutide or use with other glucagon-like peptide-1 receptor agonists. Accidental mix-ups between insulin products have been reported. To avoid medication errors between Xultophy® 100/3.6 (an insulin containing product) and other insulin products, instruct patients to always check the label before each injection.

SECTION 12: Ecological information

12.1. Toxicity

Ecology - general : Avoid discharge to drain or surface water.

Phenol (108-95-2)	
LC50 fish	20.5 mg/l Carins, J. Jr. and A. Scheier 1959. The Relationship of Bluegil Sunfish Body Size to Tolerance for Some Common Chemicals. Proc. 13th Ind. Waste Conf. Purdue Univ. Eng. Bull 96:243-252. Smith, S., V.J. Furay, P.J. Layiwola, and J.A. Menzes-Filho 1994. Ev
EC50 Daphnia	20 mg/l Kamshilow, M.M., and B.A. Flerov 1976. Experimental Research on Phenol Intoxication of Aquatic Organizations and Destruction of Phenol in Model Communities. In: D.I. Mount, W.R. Swain, N.K. Ivanikiw (Eds.), Proc. 1st and 2nd USA-USSR Symp on Effects of Polutantants on Acquatic Ecosystems, Duluth, MN: 181 – 192 (U.S. NTIS PB-287-219) (Author communication used); Cowgill, U.M., and D.P. Milazzo 1991. The Sensitivity of Ceriodaphnia dubia and Daphnia magna to Seven Chemicals Utilitizing the Three-Blood Test. Arch. Environ. Contam. Toxicol. 20(2): 211 – 217.
EC50 Daphnia	12.6 mg/l Holcombe, G.W., G.L. Phipps, A.H. Sulaiman, and A.D. Hoffman 1987. Simultaneous Multiple Species Testing: Acute Toxicity of 13 Chemicals to 12 Diverse Freshwater Amphibian, Fish, and Invertebrate Families. Arch. Environ. Contam. Toxicol. 15:697-710 (OECDG Data File)
ErC50 (algae)	229 mg/l (72 hours) Tisler, T. and J. Zagorc-Koncan 1995. Relative Sensitivity of Some Selected Aquatic Organisms to Phenol. Bull Environ. Contam. Toxicol. 54(5): 717-723
ErC50 (other aquatic plants)	84.5 mg/l (96 hours) Thellen, C., C. Blaise, Y. Roy, and C. Hickey 1989. Round Robin Testing with the Selenastrum Capricomutum Microplate Toxicity Assay. Hydrobiologia 188189: 259 – 268.

12.2. Persistence and degradability

No additional information available

12.3. Bioaccumulative potential

Phenol (108-95-2)	
Log Pow	1.5

12.4. Mobility in soil

No additional information available

12.5. Other adverse effects

Effect on the global warming : No known effects from this product.

GWPmix comment : No known effects from this product.

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste treatment methods : The product is not hazardous waste. Dispose in a safe manner in accordance with local/national regulations. Do not throw sharps in the garbage, the toilet or in recycling containers. Refer to http://www.epa.gov/wastes/nonhaz/industrial/medical/med-home.pdf for more information regarding the safe disposal of sharps.

SECTION 14: Transport information

Department of Transportation (DOT)

In accordance with DOT

Not applicable

Transportation of Dangerous Goods

Not applicable

Transport by sea

Not applicable

Air transport

Not applicable

SECTION 15: Regulatory information

15.1. US Federal regulations

Phenol (108-95-2)	
Listed on the United States TSCA (Toxic Substances Control Act) inventory. Listed on the United States SARA Section 313	
RQ (Reportable quantity, section 304 of EPA List of Lists	1,000 lb

Solution for injection containing liraglutide (204656-20-2) and degludec (204656-20-2)
Not listed on the United States TSCA (Toxic Substances Control Act) inventory

15.2. International regulations

CANADA

No additional information available

EU-Regulations

No additional information available

National regulations

No additional information available

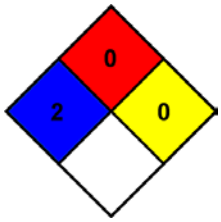
15.3. US State regulations

Phenol (108-95-2)
Idaho – Non-Carcinogenic Toxic Air Pollutants – Acceptable Ambient Concentrations
Maine – Air Pollutants – Hazardous Air Pollutants
Massachusettes – Right to Know List
New Jersey – Right to Know Hazardous Substance List
New York – Reporting of Releases Part 597 – List of Hazardous Substances
Pennsylvania – RTK (Right to Know) List

SECTION 16: Other information

Revision date : 03/02/18

Data sources	:	ChemIDplus [https://chem.nlm.nih.gov/chemidplus/rn/844439-96-9 and https://chem.nlm.nih.gov/chemidplus/rn/204656-20-2]. National Library of Medicine [https://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+113]. Novo Nordisk Medical Information for Health Care Professionals. [https://www.novonordiskmedical.com/our-products.html].
Full text of H-phrases	:	Not applicable
NFPA health hazard	:	2 - Materials that, under emergency conditions, can cause temporary incapacitation or residual injury.
NFPA fire hazard	:	0 - Materials that will not burn under typical dire conditions, including intrinsically noncombustible materials such as concrete, stone, and sand.
NFPA reactivity	:	0 - Material that in themselves are normally stable, even under fire conditions.



HMIS III Rating

Health	:	3 Serious Hazard - Major injury likely unless prompt action is taken and medical treatment is given
Flammability	:	0 Minimal Hazard - Materials that will not burn
Physical	:	0 Minimal Hazard - Materials that are normally stable, even under fire conditions, and will NOT react with water, polymerize, decompose, condense, or self-react. Non-Explosives.

SDS US (GHS HazCom 2012)

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