1. Product and Company Identification

PRODUCT NAME: SOLIQUA 100/33™
Insulin glargine and lixisenatide injection
100 Units/mL and 33 mcg/mL

Solution for injection in a SoloStar® disposable insulin delivery device (3 mL prefilled pen).

Substance name(s): Mixture of lixisenatide and insulin glargine (rDNA origin)

Supplier:
Sanofi-aventis U.S. LLC
A SANOFI COMPANY
55 Corporate Drive
Bridgewater, NJ 08807

24-Hour Transport Emergency, US (Chemtrec):	**(800) 424-9300**
24-Hour Transport Emergency, outside US (Chemtrec):	**(703) 527-3887**
US Customer Service	**(800) 207-8049**
24-Hour Emergency, sanofi-aventis US:	**(908) 981-5550**

Product use: Pharmaceutical product.

2. Hazards Identification

2.1 Classification in accordance with 29 CFR 1910.1200

Classification: Toxic to reproduction, Category 2.

2.2 Label elements in accordance with 29 CFR 1910.1200

Labeling of the finished drug product is not required according to OSHA 29 CFR 1910.1200. The following information is provided for the drug product mixture:

Signal Word: Warning

Hazard Statement(s): Suspected of damaging the unborn child.

Symbol(s): Health hazard

Precautionary Statement(s):

- Prevention: Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Wear eye protection, protective gloves and protective clothing.

- Response: If exposed or concerned: Get medical advice.

- Storage: Store locked up.

- Disposal: Dispose of contents in accordance with local and national regulations.

2.3 Hazards Not Otherwise Classified (HNOC)

Not classified.

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3. Composition/Information on Ingredients

Chemical Name:	**Common Name:**	**CAS #:**	**Percentage or concentration range**
21A-glycine-30Ba-L-arginine-30Bb-L-arginine-insulin(human)	Insulin glargine	160337-95-1	3.6378 mg/mL (< 1.0 %)
Des-Pro36-Exendin-4-(Lys)6-NH2	Lixisenatide	320367-13-3	33 mcg/mL (< 1.0 %)
Phenol, m-Methyl-	m-Cresol	108-39-4	2.7 mg/mL (< 1.0 %)
Zinc chloride	Zinc chloride	7646-85-7	30 mcg/mL (< 2.0 %)
L-methionine	Methionine	63-68-3	3 mg/mL
1,2,3-Propanetriol	Glycerol 85%	56-81-5	20 mg/mL

Non-hazardous excipients: Water for injection.

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4. First Aid Measures

4.1 First aid procedures

Eye contact: In case of contact with product, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lenses if worn. Get medical attention.

Skin contact: In case of contact with product, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if irritation develops and persists.

Ingestion: If swallowed, call a poison center or physician immediately. Do NOT induce vomiting unless directed to do so by a physician. Never give anything by mouth to an unconscious person. Rinse mouth thoroughly with water.

Inhalation: If product is inhaled, remove to fresh air. If breathing is difficult, trained personnel should give oxygen. Get medical attention.

4.2 Most important symptoms and effects, both acute and delayed

Presence of hypoglycemia (sweating, trembling, tachycardia, hunger, anxiety, dizziness, headache, clouding of vision, loss of fine motor skills, combativeness, seizures, mental confusion, and loss of consciousness). Lixisenatide caused mild to moderate nausea and vomiting in clinical trials after subcutaneous administration.

4.3 Indication of any immediate medical attention and special treatment needed

Treat symptomatically and supportively.

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5. Fire Fighting Measures

5.1 Extinguishing media

Suitable extinguishing media: All means: water, carbon dioxide, foam or dry chemical.

Unsuitable extinguishing media: Strong water jet.

5.2 Specific hazards arising from the chemical

Hazardous combustion products: Carbon monoxide, carbon dioxide, oxides of sulfur and nitrogen.

5.3 Special Protective Equipment and Precautions for Fire-fighters

In case of fire, use full firefighting turnout (bunker) gear and self-contained breathing apparatus (SCBA). Keep personnel upwind and away from fire. Move container from fire area if you can do it without risk. Do not scatter spilled material with high-pressure water streams. Dike fire-control water for later disposal.

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6. Accidental Release Measures

6.1 Personal precautions and Protective Equipment:

Eye protection, respiratory protective equipment, and suitable protective clothing should be worn (see Section 8).

6.2 Emergency Procedures:

Follow local workplace procedures. Prevent the product from entering the environment. Avoid discharges to sewers, drains, waterways, or onto the ground.

6.3 Methods for containment:

Absorb spilled liquid with a suitable inert material, place in suitable container for disposal and mop area.

6.4 Methods for clean-up:

Wash the floor with plenty of water, absorb or retain the cleaning water for disposal.

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7. Handling and Storage

7.1 Precautions for Safe Handling

Product should be used in a controlled work area. Use with adequate ventilation. Avoid contact with eyes, skin and clothing. Place a disposable absorbent pad under the product preparation area. Do not eat, smoke or drink while handling product. Wash thoroughly after handling.

7.2 Conditions for Safe Storage

Store refrigerated at 36^{o} – 46^{o} F (2^{o} C – 8^{o} C). Do not freeze. Protect from light. Consult the package insert for additional storage instructions.

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8. Exposure Controls/Personal Protection

8.1 Exposure Limits

Sanofi-aventis occupational exposure limit, insulin glargine: 0.2 mg/m^3, 8-hour TWA.

Sanofi-aventis occupational exposure limit, lixisenatide: 0.001 mg/m^3, 8-hour TWA.

m-Cresol: OSHA PEL 5 ppm (skin), all isomers. ACGIH TLV: 5 ppm (skin), all isomers.

Zinc chloride: OSHA PEL 1 mg/m^3 (as fume). ACGIH TLV 1 mg/m^3 (as fume).

8.2 Appropriate Engineering Controls

Provide adequate ventilation. No other specific controls are needed under normal handling conditions.

8.3 Individual Protection Measures

Eye/face protection: Safety glasses or safety goggles should be worn if there is a potential for eye contact with the product.

Skin protection: Suitable protective gloves should be worn. Use of a protective or disposable gown or laboratory coat is recommended if there exists a potential for contact with the product.

Respiratory protection: None normally required for routine handling of the product. However, approved respiratory protection should be worn if there is a potential for exposure to the product. A respiratory protection program that meets OSHA 29 CFR 1910.134 and ANSI Z88.2 must be followed whenever workplace conditions warrant respirator usage.

General hygiene considerations: Wash hands before breaks and at the end of the work shift.

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9. Physical and Chemical Properties

Appearance: Clear, colorless liquid.
Odor: None
Odor threshold: Not applicable.
pH: 4.5
Melting point/ Freezing point: Not available.
Initial boiling point/boiling point range: Not available.
Flash point: Not available.
Evaporation rate: Not available.
Flammability: Not available.
Upper/lower flammability or explosive limits: Not available.
Vapor pressure: Not available.
Vapor density: Not available.
Relative density: Not available.
Solubility: Not available.
Partition coefficient: n-octanol/water: Not available.
Auto-ignition temperature: Not available.
Decomposition temperature: Not available.
Viscosity: Not available.

10. Stability and Reactivity

10.1 Reactivity

Not a reactive material under normal handling conditions.

10.2 Chemical Stability

Stable under normal handling conditions.

10.3 Possibility of hazardous reactions

None known.

10.4 Conditions to Avoid

Keep away from heat, sparks and flames.

10.5 Incompatible materials

Strong oxidizing and reducing agents.

10.6 Hazardous decomposition products

Carbon monoxide, carbon dioxide, oxides of sulfur and nitrogen.

11. Toxicological Information

Information on likely routes of exposure: Not expected under normal handling conditions. Insulin is orally non-toxic as it can be broken down in the stomach. If absorbed through mucous membranes such as the respiratory tract or mouth, may exert a systemic hypoglycemic effect. Lixisenatide is a peptide; absorption by the oral route is not expected. Unintended spills or releases could result in exposure to eyes, skin and respiratory tract.

Symptoms related to the physical, chemical and toxicological characteristics: Presence of hypoglycemia (sweating, trembling, tachycardia, hunger, anxiety, dizziness, headache, clouding of vision, loss of fine motor skills, combativeness, seizures, mental confusion, and loss of consciousness). Lixisenatide caused mild to moderate nausea in clinical trials after subcutaneous administration.

Effects of short-term (acute) exposure: Hypoglycemia.

Effects of long-term (chronic) exposure: Hypoglycemia.

Acute toxicity (LD50):
Insulin glargine: Oral route, rat: > 2,000 mg/kg (OECD 423). No data available for lixisenatide.

Skin corrosion/irritation: No data available for the mixture. Lixisenatide was not an irritant based on in vitro test results.

Serious eye damage/irritation: No data available for the mixture. Lixisenatide was a serious eye irritant based on in vitro test results, classified as Eye Damage/Irritation Category 1.

Sensitization: No data available for the mixture. Lixisenatide was non-sensitizing in the Local Lymph Node Assay (LLNA).

Specific target organ toxicity – single exposure (STOT-SE): No data available for the mixture. No organ toxicity was observed in several animal studies with lixisenatide.

Specific target organ toxicity – repeated exposure (STOT-RE): No data available for the mixture. No organ toxicity was observed in several animal studies with lixisenatide.

Carcinogenicity: No data available for the mixture.

Insulin glargine: In mice and rats, standard two-year carcinogenicity studies with insulin glargine were performed at doses up to 0.455 mg/kg, which was for the rat approximately 10 times and for the mouse approximately 5 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 mg/kg/day), based on mg/m^2. The findings in female mice were not conclusive due to excessive mortality in all dose groups during the study. Histiocytomas were found at injection sites in male rats (statistically significant) and male mice (not statistically significant) in acid vehicle containing groups. These tumors were not found in female animals, in saline control, or insulin comparator groups using a different vehicle. The relevance of these findings to humans is unknown.

Lixisenatide: In 2-year subcutaneous carcinogenicity studies, non-lethal C-cell thyroid tumors were seen in rats and mice and are considered to be caused by a non-genotoxic GLP-1 receptor-mediated mechanism to which rodents are particularly sensitive. C-cell hyperplasia and adenoma were seen at all doses in rats and a no observed adverse effect level (NOAEL) could be not defined. In mice, these effects occurred at exposure ratio above 9.3-fold when compared to human exposure at the therapeutic dose. No C-cell carcinoma was observed in mice and C-cell carcinoma occurred in rats with an exposure ratio relative to exposure at human therapeutic dose of about 900-fold. In 2-year subcutaneous carcinogenicity study in mice, 3 cases of adenocarcinoma in the endometrium were seen in the mid dose group with a statistically significant increase, corresponding to an exposure ratio of 97-fold. No treatment-related effect was demonstrated.

Not listed by NTP, not found to be a potential carcinogen by IARC or OSHA.

Reproductive toxicity and teratogenicity: No data available for the mixture.

Insulin glargine: Subcutaneous reproduction and teratology studies have been performed with insulin glargine and regular human insulin in rats and Himalayan rabbits. Insulin glargine was given to female rats before mating, during mating, and throughout pregnancy at doses up to 0.36

mg/kg/day, which is approximately 7 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 mg/kg/day), based on mg/m2. In rabbits, doses of 0.072 mg/kg/day, which is approximately 2 times the recommended human subcutaneous starting dose of 10 Units/day (0.008 mg/kg/day), based on mg/m2, were administered during organogenesis. The effects of insulin glargine did not generally differ from those observed with regular human insulin in rats or rabbits. However, in rabbits, five fetuses from two litters of the high-dose group exhibited dilation of the cerebral ventricles. Fertility and early embryonic development appeared normal.

Lixisenatide: Studies in animals have shown reproductive toxicity. In embryo-fetal development studies with lixisenatide, malformations, growth retardation, ossification retardation and skeletal effects were observed in rats at all doses and in rabbits at high doses. In both species, there was a slight maternal toxicity consisting of low food consumption and reduced body weight. Neonatal growth was reduced in male rats exposed to high doses of lixisenatide during late gestation and lactation, with a slightly increased pup mortality observed.

Studies with lixisenatide did not indicate direct harmful effects with respect to male and female fertility in rats. Reversible testicular and epididymal lesions were seen in dogs treated with lixisenatide. No related effect on spermatogenesis was seen in healthy men.

Mutagenicity: No data available for the mixture.

Insulin glargine was not mutagenic in tests for detection of gene mutations in bacteria and mammalian cells (Ames- and HGPRT-test) and in tests for detection of chromosomal aberrations (cytogenetics in vitro in V79 cells and in vivo in Chinese hamsters).

Lixisenatide was negative in the Ames test, the in vitro Chromosome Aberration test and the in vivo micronucleus test.

Aspiration hazard: No data available.

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12. Ecological Information

The following information is for the active ingredient insulin glargine unless otherwise noted. No data is available for the mixture or for lixisenatide:

12.1. Ecotoxicity

Fish toxicity (LC50): > 100 mg/l
Species: Zebrafish
Exposure duration: 96 h
Method: OECD 203

Chronic aquatic toxicity: not determined

Toxicity on invertebrates (EC50): > 100 mg/l
Species: Daphnia magna
Exposure duration: 48 h
Method: OECD 202

Toxicity on invertebrates (Chronic toxicity): not determined

Algae toxicity (EC50): 346.1 mg/l
Species: Pseudokirchneriella subcapitata
Exposure duration: 72 h
Endpoint: Biomass
Method: OECD 201

12.2. Persistence and degradability

Biological degradability: 77 - 82 %
Readily biodegradable.
Testing period: 28 d
Method of analysis: Theoretical oxygen demand
Method: OECD 301 F

12.3. Bioaccumulative potential

No data available.

12.4 Mobility in soil

No data available.

12.5 Other adverse effects

No data available.

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13. Disposal Considerations

13.1 Disposal of product waste

Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements. Contains a small amount of m-cresol, which is a RCRA listed waste.

13.2 Disposal of packaging waste

Dispose of in a safe manner in accordance with federal, state and local environmental regulations. Empty packages, containers or liners may contain product residue.

14. Transport Information

14.1 Basic shipping information, finished product

U.S. DOT	Not a regulated material.
ICAO/IATA	Not a regulated material.
IMDG	Not a regulated material.

15. Regulatory Information

US Regulations
CERCLA Hazardous Substance List (40 CFR 302.4): m-cresol (RQ 100 lbs.); zinc chloride (RQ 1,000 lbs.).
Clean Water Act Section 311 Hazardous Substances (40 CFR 117.3): Not listed.
Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130): Not listed.

SARA Title III:
Section 302 Extremely Hazardous Substance (40 CFR 355, Appendix A): Not listed.
Section 313 Toxic Release Inventory (40 CFR 372): m-cresol; zinc chloride.

State Regulations
California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): To the best of our knowledge, this product does not contain any of the listed chemicals, which the state of California has found to cause cancer, birth defects or other reproductive harm.
Massachusetts Right-To-Know List: m-cresol; zinc chloride.
New Jersey Right-To-Know List: m-cresol; zinc chloride.
Pennsylvania Right-To-Know List: m-cresol; zinc chloride.

16. Other Information

Other Information: The information contained herein is based upon data considered true and accurate. Sanofi-aventis U.S. LLC. makes no warranties, express or implied, as to the adequacy of the information contained herein. This information is offered solely for the user's consideration, investigation and verification. Report to the manufacturer any allegations of health effects resulting from handling or accidental contact with this material.

Abbreviations and Acronyms
CAS: Chemical Abstracts Service
DOT: U.S. Department of Transportation
EST: Eastern standard time (U.S.)
IATA: International Air Transport Association
IMDG: International Maritime Dangerous Goods Code
LC50: Lethal concentration, 50%
LD50: Lethal dose, 50%
mcg: Microgram
mg: Milligram
mL: Milliliter
OEL: Occupational Exposure Limit
PPE: Personal Protection Equipment
SDS: Safety Data Sheet
STEL: Short-term exposure limit
TWA: Time-weighted average
U.S.: United States

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First version.