

SAFETY DATA SHEET

SECTION 1. IDENTIFICATION

Product identifier used on the label

: **Vagifem® (estradiol vaginal inserts)**

Other means of identification : Not available.

Recommended use of the chemical and restrictions on use

: Drug product
Recommended restrictions: None known.

Chemical family : Mixture

Name, address, and telephone number of the supplier:

Novo Nordisk Inc.

800 Scudders Mill Road
Plainsboro, NJ, USA
08536

Supplier's Telephone # : 1-800-727-6500

24 Hr. Emergency Tel # : +1-800-727-6500

Name, address, and telephone number of the manufacturer:

Refer to supplier

SECTION 2. HAZARDS IDENTIFICATION

Classification of the chemical

Small, white film-coated tablets.

This material is not classified as hazardous under U.S. OSHA regulations (29CFR 1910.1200) (Hazcom 2012) and Canadian WHMIS regulations (Hazardous Products Regulations) (WHMIS 2015).

This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. Your needs may vary depending upon the potential for exposure in your workplace. The precautionary statements, warnings and hazards included herein may not apply in all cases, such as when the product or device is in its final form and being used to treat the approved medical condition(s) while under the care of a licensed medical professional and in accordance with the FDA-approved Prescribing Information. Refer to FDA-approved Prescribing Information for final marketed products with regard to special storage, handling and administration requirements in the clinical setting.

Label elements

Hazard pictogram(s)

None required under U.S. OSHA Hazcom 2012 and Canadian WHMIS 2015 regulations.

Signal Word

Not required

Hazard statement(s)

Not required

Precautionary statement(s)

Not required

Other hazards

Other hazards which do not result in classification:

Vagifem® may be absorbed through the skin, by inhalation and if swallowed. Exposure to Vagifem® may cause irregular menstruation.

SAFETY DATA SHEET

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Mixture

<u>Chemical name</u>	<u>Common name and synonyms</u>	<u>CAS #</u>	<u>Concentration (% by weight)</u>
Estradiol	3,17β-Dihydroxy-1,3,5(10)-estra- triene 1,3,5-Estratriene-3,17β-diol Dihydrofolliculin 17β-Estradiol	50-28-2	0.06

Estradiol 10 or 25 micrograms (active ingredient)

SECTION 4. FIRST-AID MEASURES

Description of first aid measures

- Ingestion* : Do NOT induce vomiting. Have victim rinse mouth with water, then give one to two glasses of water to drink. Never give anything by mouth to an unconscious person. Seek medical attention if discomfort occurs.
- Inhalation* : If inhaled, move to fresh air. If breathing is difficult, give oxygen by qualified medical personnel only. If breathing has stopped, give artificial respiration. Obtain medical attention if symptoms develop and persist.
- Skin contact* : Wash with water and soap as a precaution. If irritation or symptoms develop, seek medical attention.
- Eye contact* : If in eyes, rinse with water for 15 minutes. Remove contact lenses if present and easy to do. Continue rinsing. If irritation persists, seek prompt medical attention.

Most important symptoms and effects, both acute and delayed

- : None known or reported by the manufacturer.

Indication of any immediate medical attention and special treatment needed

- : Treat symptomatically. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves.

SECTION 5. FIRE-FIGHTING MEASURES

Extinguishing media

Suitable extinguishing media

- : Use media suitable to the surrounding fire such as water fog or fine spray, alcohol foams, carbon dioxide and dry chemical.

Unsuitable extinguishing media

- : Do not use a solid water stream as it may scatter and spread fire.

Special hazards arising from the substance or mixture / Conditions of flammability

- : None known or reported by the manufacturer.

Flammability classification (OSHA 29 CFR 1910.106)

- : Not flammable.

Hazardous combustion products

- : irritating fumes and smoke

Special protective equipment and precautions for firefighters

Protective equipment for fire-fighters

- : Firefighters must use standard protective equipment including flame retardant coat, helmet with face shield, gloves, rubber boots, and in enclosed spaces, SCBA.

Special fire-fighting procedures

- : Move containers from fire area if safe to do so. Water spray may be useful in cooling equipment exposed to heat and flame.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

- : Restrict access to area until completion of clean-up. Ensure clean-up is conducted by trained personnel only. Wear suitable protective equipment. Refer to protective measures listed in sections 7 and 8. Restrict access to area until completion of clean-up.

Environmental precautions : Ensure spilled product does not enter drains, sewers, waterways, or confined spaces.

SAFETY DATA SHEET

Methods and material for containment and cleaning up

- : Ventilate area of release. Stop spill or leak at source if safely possible. Dike for water control. Contain and absorb spilled liquid with non-combustible, inert absorbent material (e.g. sand), then place absorbent material into a container for later disposal (see Section 13).

Special spill response procedures

- : If a spill/release in excess of the EPA reportable quantity is made into the environment, immediately notify the national response center in the United States (phone: 1-800-424-8802).
 US CERCLA Reportable quantity (RQ): See section 15.

SECTION 7. HANDLING AND STORAGE

Precautions for safe handling

- : Avoid contact with eyes, skin and clothing. Wash thoroughly after handling. Do not ingest.

- Storage temperature: 25°C. Do not refrigerate.
- Conditions for safe storage** : Keep only in original packaging.

- Incompatible materials** : Strong acids, bases and oxidizing or reducing agents.

SECTION 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

<u>Exposure Limits:</u>				
<u>Chemical Name</u>	<u>ACGIH TLV</u>		<u>OSHA PEL</u>	
	<u>TWA</u>	<u>STEL</u>	<u>PEL</u>	<u>STEL</u>
Estradiol	N/Av	N/Av	N/Av	N/Av

Exposure controls

Ventilation and engineering measures

- : Use in a well-ventilated area. Use general or local exhaust ventilation to maintain air concentrations below recommended exposure limits.

Respiratory protection

- : Use the indicated respiratory protection if the occupational exposure limit is exceeded and/or in case of product release (dust and/or fumes). Advice should be sought from respiratory protection specialists.

Skin protection

- : Wear protective gloves. Advice should be sought from glove suppliers.

Eye / face protection

- : Wear eye/face protection. Wear safety glasses with side shields (or goggles).

Other protective equipment

- : Wear sufficient clothing to prevent skin contact. Depending on conditions of use, an impervious apron should be worn. An eyewash station and safety shower should be made available in the immediate working area.

General hygiene considerations

- : Avoid contact with skin, eyes and clothing. Upon completion of work, wash hands before eating, drinking, smoking or use of toilet facilities. Handle in accordance with good industrial hygiene and safety practice. Contaminated work clothing must not be allowed out of the workplace.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- Appearance** : Small, white film-coated tablets
- Odour** : None.
- Odour threshold** : Not available.
- pH** : Not available.
- Melting Point/Freezing point** : 173-179°C
- Initial boiling point and boiling range**
- : Not available.
- Flash point** : Not available.

SAFETY DATA SHEET

Flashpoint (Method) : Not available.
Evaporation rate (BuAe = 1) : Not available.
Flammability (solid, gas) : Not applicable.
Lower flammable limit (% by vol.)
: Not applicable.
Upper flammable limit (% by vol.)
: Not applicable.
Oxidizing properties : Not applicable
Explosive properties : Not explosive
Vapour pressure : Not available.
Vapour density : Not available.
Relative density / Specific gravity
: Not available.
Solubility in water : Insoluble.
Other solubility(ies) : Not available.
Partition coefficient: n-octanol/water or Coefficient of water/oil distribution
: Not available.
Auto-ignition temperature : Not applicable.
Decomposition temperature : Not available.
Viscosity : Not available.
Volatiles (% by weight) : Not available.
Volatile organic Compounds (VOC's)
: Not available.
Absolute pressure of container
: Not applicable.
Flame projection length : Not applicable.
Other physical/chemical comments
: None reported by the manufacturer.

SECTION 10. STABILITY AND REACTIVITY

Reactivity : This product is not reactive.
Chemical stability : Material is stable under normal conditions.
Possibility of hazardous reactions
: Under normal conditions of handling and storage, hazardous reactions will not occur.
Conditions to avoid : Avoid contact with incompatible materials. Do not freeze.
Incompatible materials : Strong acids, bases and oxidizing or reducing agents.
Hazardous decomposition products
: None known, refer to hazardous combustion products in Section 5.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:

Routes of entry inhalation : YES
Routes of entry skin & eye : YES
Routes of entry Ingestion : YES
Routes of exposure skin absorption
: NO

Potential Health Effects:

Signs and symptoms of short-term (acute) exposure

Sign and symptoms Inhalation

: May cause mild transient irritation.

SAFETY DATA SHEET

Sign and symptoms ingestion

: Ingestion may cause gastrointestinal irritation, nausea, vomiting and diarrhea.

Sign and symptoms skin

: Direct skin contact may cause slight or mild, transient irritation.

Sign and symptoms eyes

: Direct eye contact may cause slight or mild, transient irritation.

Potential Chronic Health Effects

: Frequent or prolonged contact may dry the skin, leading to discomfort and dermatitis.

Mutagenicity

: Not expected to be mutagenic in humans.

Carcinogenicity

: No components are listed as carcinogens by ACGIH, IARC, OSHA or NTP. Contains material which can cause cancer.

Reproductive effects & Teratogenicity

: Not expected to cause reproductive effects. Causes effects on or via lactation.

Sensitization to material

: May cause an allergic skin reaction (e.g. hives, rash) in some hypersensitive individuals.

Specific target organ effects

: According to the classification criteria of U.S. OSHA regulations (29CFR 1910.1200) (Hazcom 2012) and Canadian WHMIS regulations (Hazardous Products Regulations) (WHMIS 2015), this product is not expected to cause target organ toxicity through single or repeated exposures.

Medical conditions aggravated by overexposure

: None known.

Synergistic materials

: Not available.

Toxicological data

: There is no available data for the product itself, only for the ingredients. See below for individual ingredient acute toxicity data.

<u>Chemical name</u>	<u>LC₅₀(4hr)</u>	<u>LD₅₀</u>	
	<u>inh, rat</u>	<u>(Oral, rat)</u>	<u>(Rabbit, dermal)</u>
Estradiol	N/Av	N/Av	N/Av

Other important toxicological hazards

: None known or reported by the manufacturer.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

: Not classified for hazards to the environment. However, this does not exclude the possibility that large or frequent spills can have a harmful or damaging effect on the environment.

Ecotoxicity data:

<u>Ingredients</u>	<u>CAS #</u>	<u>Toxicity to Fish</u>		
		<u>LC50 / 96h</u>	<u>NOEC / 21 day</u>	<u>M Factor</u>
Estradiol	50-28-2	N/Av	N/Av	None.

<u>Ingredients</u>	<u>CAS #</u>	<u>Toxicity to Daphnia</u>		
		<u>EC50 / 48h</u>	<u>NOEC / 21 day</u>	<u>M Factor</u>
Estradiol	50-28-2	N/Av	N/Av	None.

SAFETY DATA SHEET

<u>Ingredients</u>	<u>CAS #</u>	<u>Toxicity to Algae</u>		
		<u>EC50 / 96h or 72h</u>	<u>NOEC / 96h or 72h</u>	<u>M Factor</u>
Estradiol	50-28-2	N/Av	N/Av	None.

Persistence and degradability

: No data is available on the product itself.

Bioaccumulation potential

: No data is available on the product itself.

<u>Components</u>	<u>Partition coefficient n-octanol/water (log Kow)</u>	<u>Bioconcentration factor (BCF)</u>
Estradiol (CAS 50-28-2)	N/Av	N/Av

Mobility in soil

: No data is available on the product itself.

Other Adverse Environmental effects

: No other adverse environmental effects (e.g. ozone depletion, photochemical ozone creation potential, endocrine disruption, global warming potential) are expected from this component.

SECTION 13. DISPOSAL CONSIDERATIONS

Handling for Disposal

: 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.

Methods of Disposal





: Dispose in accordance with all applicable federal, state, provincial and local regulations.

RCRA

: If this product, as supplied, becomes a waste in the United States, it may meet the criteria of a hazardous waste as defined under RCRA, Title 40 CFR 261. It is the responsibility of the waste generator to determine the proper waste identification and disposal method. For disposal of unused or waste material, check with local, state and federal environmental agencies.

SAFETY DATA SHEET

SECTION 14. TRANSPORT INFORMATION

Regulatory Information	UN Number	UN proper shipping name	Transport hazard class(es)	Packing Group	Label
49CFR/DOT	None.	Not regulated.	not regulated	none	
49CFR/DOT Additional information	None.				
IMDG	None.	Not regulated.	not regulated	none	
IMDG Additional information	None.				
ICAO/IATA	None.	Not regulated.	not regulated	none	
ICAO/IATA Additional information	None.				
TDG	None.	Not regulated.	not regulated	none	
TDG Additional information	None.				

Special precautions for user : None known or reported by the manufacturer.

Environmental hazards : This substance does not meet the criteria for an environmentally hazardous substance according to the IMDG Code. See ECOLOGICAL INFORMATION, Section 12.

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
: Not available.

SECTION 15 - REGULATORY INFORMATION

US Federal Information:

Components listed below are present on the following U.S. Federal chemical lists:

<u>Ingredients</u>	CAS #	TSCA Inventory	CERCLA Reportable Quantity(RQ) (40 CFR 117.302):	SARA TITLE III: Sec. 302, Extremely Hazardous Substance, 40 CFR 355:	SARA TITLE III: Sec. 313, 40 CFR 372, Specific Toxic Chemical	
					Toxic Chemical	de minimus Concentration
Estradiol	50-28-2	NL	N/Ap	N/Av	No	N/Ap

SARA TITLE III: Sec. 311 and 312, SDS Requirements, 40 CFR 370 Hazard Classes: None. Under SARA Sections 311 and 312, the EPA has established threshold quantities for the reporting of hazardous chemicals. The current thresholds are 500 pounds or the threshold planning quantity (TPQ), whichever is lower, for extremely hazardous substances and 10,000 pounds for all other hazardous chemicals.

US State Right to Know Laws:

The following chemicals are specifically listed by individual States:

SAFETY DATA SHEET

<u>Ingredients</u>	CAS #	California Proposition 65		State "Right to Know" Lists					
		Listed	Type of Toxicity	CA	MA	MN	NJ	PA	RI
Estradiol	50-28-2	Yes	Carcinogen	Yes	Yes	Yes	No	Yes	Yes

Canadian Information:

WHMIS information: Refer to Section 2 for a WHMIS Classification for this product.

International Information:

Components listed below are present on the following International Inventory list:

<u>Ingredients</u>	CAS #	European EINECS	Australia AICS	Philippines PICCS	Japan ENCS	Korea KECI/KECL	China IECSC	NewZealand IOC
Estradiol	50-28-2	200-023-8	Present	Present	N/Av	N/Av	Present	HSR003871

SECTION 16. OTHER INFORMATION**Legend**

: ACGIH: American Conference of Governmental Industrial Hygienists
 CAS: Chemical Abstract Services
 CERCLA: Comprehensive Environmental Response, Compensation, and Liability Act of 1980
 CFR: Code of Federal Regulations
 CSA: Canadian Standards Association
 DOT: Department of Transportation
 EPA: Environmental Protection Agency
 HSDB: Hazardous Substances Data Bank
 IARC: International Agency for Research on Cancer
 Inh: Inhalation
 LC: Lethal Concentration
 LD: Lethal Dose
 N/Av: Not Applicable
 N/Av: Not Available
 NTP: National Toxicology Program
 OECD: Organisation for Economic Co-operation and Development
 OSHA: Occupational Safety and Health Administration
 PEL: Permissible exposure limit
 RCRA: Resource Conservation and Recovery Act
 RTECS: Registry of Toxic Effects of Chemical Substances
 SARA: Superfund Amendments and Reauthorization Act
 STEL: Short Term Exposure Limit
 TLV: Threshold Limit Values
 TWA: Time Weighted Average
 WHMIS: Workplace Hazardous Materials Identification System

References

: 1. ACGIH, Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices
 2. ECHA - European Chemical Agency
 3. Canadian Centre for Occupational Health and Safety, CCInfoWeb databases, (Chempendium, HSDB and RTECs).
 4. Safety Data Sheets from manufacturer.
 5. US EPA Title III List of Lists
 6. California Proposition 65 List
 7. OECD - The Global Portal to Information on Chemical Substances - eChemPortal

Preparation Date (mm/dd/yyyy)

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Other special considerations for handling

: Provide adequate information, instruction and training for operators.

SAFETY DATA SHEET

<p><u>Prepared for:</u> Novo Nordisk 800 Scudders Mill Road Plainsboro, NJ 08536 1-800-727-6500 www.novonordisk-us.com</p>	
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