Activella® 1.0 mg/0.5 mg, Activella 0.5 mg/0.1mg

Safety Data Sheet

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

Date of issue: 1/23/2015 Version: 1.0

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

1.1. Product identifier

Product form : Tablet

Product name : Activella® 1.0 mg/0.5 mg, Activella 0.5 mg/0.1mg

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

Use of the substance/mixture : Drug Product

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: Hazards identification

2.1. Classification of the substance or mixture

Classification (GHS-US)

Skin Sens. 1 H317
Carc. 2 H351
Repr. 1A H360

2.2. Label elements

GHS-US labeling

Hazard pictograms (GHS-US) :

GHS07 GHS08

Signal word (GHS-US) : Danger

Hazard statements (GHS-US) :
H317 - May cause an allergic skin reaction
H351 - Suspected of causing cancer (Dermal, Inhalation, oral)
H360 - May damage fertility or the unborn child. May cause gynecomastia in exposed males.

Precautionary statements (GHS-US) :
P201 - Obtain special instructions before use
P202 - Do not handle until all safety precautions have been read and understood
P261 - Avoid breathing mist
P272 - Contaminated work clothing should not be allowed out of the workplace
P280 - Wear appropriate PPE
P302+P352 - IF ON SKIN: Wash with plenty of soap and water
P308+P313 - IF exposed or concerned: Get medical advice/attention
P321 - Specific treatment (see See Section 4 on this label)
P333+P313 - If skin irritation or rash occurs: Get medical advice/attention
P362+P364 - Take off contaminated clothing and wash it before reuse
P405 - Store locked up
P501 - Dispose of contents/container to comply with local/regional/national/international regulations

2.3. Other hazards

Other hazards not contributing to the classification : Inactive ingredients include: copovidone K25-3, 1hypromellose, lactose monohydrate, starch, talc, triacetin, and magnesium stearate. The film coating contains hypromellose and polyethylene glycol.

2.4. Unknown acute toxicity (GHS-US)

No data available

SECTION 3: Composition/information on ingredients

3.1. Substance

Not applicable

Full text of H-phrases: see section 16

3.2. Mixture

Name	Product identifier	%	Classification (GHS-US)
0.5 mg Estradiol and 0.1 mg Norethisterone acetate (active ingredient)	(CAS No) 50-28-2	0.5 - 1	Skin Sens. 1, H317 Carc. 2, H351 Repr. 1A, H360
1 mg Estradiol and 0.5 mg Norethisterone acetate (active ingredient)	(CAS No) 51-98-9	0.5 - 1	Skin Sens. 1, H317 Carc. 2, H351 Repr. 1A, H360

SECTION 4: First aid measures

4.1. Description of first aid measures

First-aid measures general : Ensure that medical personnel are aware of the material(s) involved and take precautions to protect themselves.

First-aid measures after inhalation : Not an anticipated route of entry. If inhaled, remove person to fresh air.

First-aid measures after skin contact : Remove affected clothing and wash all exposed skin area with mild soap and water, followed by warm water rinse. Wash contaminated clothing before reuse.

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 inadvertant ingestion : Rinse mouth thoroughly and then drink plenty of water. Do not induce vomiting. Seek medical advice in case of persistent discomfort.

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

Symptoms/injuries after inhalation : Inhalation of dust may cause irritation to the upper airways. Activella® tablets contain very potent steroid that can be absorbed by the inhalation as well as orally.

Symptoms/injuries after skin contact : May cause irritation by the active substance or any of the excipients. Estrogen-induced hypocalcemia may occur. May cause diarrhea, CNS depression, and migraines.

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

Symptoms/injuries after ingestion : Activella® tablets are intended for oral administration. The warnings, precautions, and adverse reactions associated with the use of systemic estrogen therapy should be taken into account.

Chronic symptoms : Activella® tablets contain potent steroidal estrogens, which are known according to the International Agency for Research on Cancer (IARC). Estrogen therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas.

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

No additional information available

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media : Any. Use media appropriate for surrounding fire.

5.2. Special hazards arising from the substance or mixture

Fire hazard : Not flammable.

Reactivity : Not reactive under normal use and conditions.

5.3. Advice for firefighters

Protection during firefighting : Positive pressure self-contained breathing apparatus (SCBA) and structural firefighters' protective clothing will provide adequate protection.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

General measures : Seek fresh air.

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

For containment	:	Do not touch or walk through spilled material.
Methods for cleaning up	:	HEPA Vacuum or wet methods and place in a disposal container.

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. Use personal protective equipment as required.
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 temperature	:	Store in a dry place protected from light at 20 to 25°C (77 °F). Excursions permitted to 15ºC to 30ºC (59ºF to 86ºF). Do not refrigerate.

7.3. Specific end use(s)

Drug Product

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

8.2. Exposure controls

Appropriate engineering controls	:	Work must be done with effective mechanical ventilation. 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.
Respiratory protection	:	Not normally required. If the tablets crushed and dust is released personal pretection (breathing protection (filtertype P3) must be used.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state	:	Solid
Appearance	:	Small, white, film-coated tablets.
Molecular mass	:	281.4 g/mol
Color	:	White.
Odor	:	No data available
Odor threshold	:	No data available
pH	:	No data available
pH solution	:	No data available
Relative evaporation rate (butyl acetate=1)	:	No data available
Melting point	:	173 - 179 °C
Freezing point	:	No data available
Boiling point	:	No data available
Flash point	:	No data available
Auto-ignition temperature	:	No data available
Decomposition temperature	:	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	:	Insoluble
Log Pow	:	No data available
Log Kow	:	No data available
Viscosity, kinematic	:	No data available
Viscosity, dynamic	:	No data available
Explosive properties	:	No data available
Oxidizing properties	:	No data available
Explosive limits	:	No data available

SECTION 10: Stability and reactivity

10.1. Reactivity

Not reactive under normal use and conditions.

10.2. Chemical stability

Product is stable.

10.3. Possibility of hazardous reactions

Hazardous polymerization will not occur.

10.4. Conditions to avoid

None under recommended storage and handling conditions (see section 7).

10.5. Incompatible materials

No known incompatibilities.

10.6. Hazardous decomposition products

No known hazardous decomposition products.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity : Not classified

Activella® 1.0 mg/0.5 mg, Activella 0.5 mg/0.1mg	
Additional information	Hypersensitivity to the active substance or to any of the excipients. Postmarketing studies have indicated the following adverse skin reactions: Urticaria, erythematous or pruritic rash, genital pruritus.

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

(Proteins are not expected to have any genotoxic potential. None of the excipients in Novolog® posses any genotoxic potential.)

Carcinogenicity : Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, uterus, cervix, vagina, testis, and liver

Activella® 1.0 mg/0.5 mg, Activella 0.5 mg/0.1mg	
Additional information	Long-term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, uterus, cervix, vagina, testis, and liver.

Reproductive toxicity : May damage fertility or the unborn child. May cause gynecomastia in exposed males.

Specific target organ toxicity (single exposure) : Not classified

Specific target organ toxicity (repeated exposure) : Not classified

Activella® 1.0 mg/0.5 mg, Activella 0.5 mg/0.1mg	
Additional information	An increased risk of stroke and deep vein thrombosis (DVT) has been reported with estrogen-alone therapy. An increased risk of probable dememtia, DVT, stroke, and myocardial infarction has been reported with estrogen plus progestin therapy.

Aspiration hazard	: Not classified
Symptoms/injuries after inhalation	: Inhalation of dust may cause irritation to the upper airways. Activella® tablets contain very potent steroid that can be absorbed by the inhalation as well as orally.
Symptoms/injuries after skin contact	: May cause irritation by the active substance or any of the excipients. Estrogen-induced hypocalcemia may occur. May cause diarrhea, CNS depression, and migraines.
Symptoms/injuries after eye contact	: May cause irritation. Avoid contact with the eyes.
Symptoms/injuries after ingestion	: Activella® tablets are intended for oral administration. The warnings, precautions, and adverse reactions associated with the use of systemic estrogen therapy should be taken into account.
Chronic symptoms	: Activella® tablets contain potent steroidal estrogens, which are known according to the International Agency for Research on Cancer (IARC). Estrogen therapy may cause an exacerbation of asthma, diabetes mellitus, epilepsy, migraine, porphyria, systemic lupus erythematosus, and hepatic hemangiomas.

SECTION 12: Ecological information

12.1. Toxicity

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

12.2. Persistence and degradability

No additional information available

12.3. Bioaccumulative potential

Activella® 1.0 mg/0.5 mg, Activella 0.5 mg/0.1mg	
BCF fish	200 mg/kg
Bioaccumulative potential	Contains constituents with the potential to bioaccumulate.

12.4. Mobility in soil

No additional information available

12.5. Other adverse effects

No additional information available

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste disposal recommendations : The product is not hazardous waste. Dispose in a safe manner in accordance with local/national regulations.

SECTION 14: Transport information

In accordance with DOT

Not regulated for transport

Additional information

Other information : No supplementary information available.

ADR

Transport document description :

Transport by sea

No additional information available

Air transport

No additional information available

SECTION 15: Regulatory information

15.1. US Federal regulations

0.5 mg Estradiol and 0.1 mg Norethisterone acetate (50-28-2)
Not listed on the United States TSCA (Toxic Substances Control Act) inventory

1 mg Estradiol and 0.5 mg Norethisterone acetate (active ingredient) (51-98-9)
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

Classification according to Regulation (EC) No. 1272/2008 [CLP]

Classification according to Directive 67/548/EEC [DSD] or 1999/45/EC [DPD]

Not classified

15.2.2. National regulations

No additional information available

15.3. US State regulations

0.5 mg Estradiol and 0.1 mg Norethisterone acetate (50-28-2)				
U.S. - California - Proposition 65 - Carcinogens List	U.S. - California - Proposition 65 - Developmental Toxicity	U.S. - California - Proposition 65 - Reproductive Toxicity - Female	U.S. - California - Proposition 65 - Reproductive Toxicity - Male	No significance risk level (NSRL)
Yes				

1 mg Estradiol and 0.5 mg Norethisterone acetate (active ingredient) (51-98-9)				
U.S. - California - Proposition 65 - Carcinogens List	U.S. - California - Proposition 65 - Developmental Toxicity	U.S. - California - Proposition 65 - Reproductive Toxicity - Female	U.S. - California - Proposition 65 - Reproductive Toxicity - Male	No significance risk level (NSRL)
Yes	Yes			

0.5 mg Estradiol and 0.1 mg Norethisterone acetate (50-28-2)
U.S. - New York - Reporting of Releases Part 597 - List of Hazardous Substances

1 mg Estradiol and 0.5 mg Norethisterone acetate (active ingredient) (51-98-9)
U.S. - New York - Reporting of Releases Part 597 - List of Hazardous Substances

SECTION 16: Other information

Data sources : Novo Nordisk Medical Information for Health Care Professionals. [http://www.novonordiskmedicalinformation.com/products.aspx].

U.S. National Library of Medicaine: DAILY MED [http://dailymed.nlm.nih.gov/dailymed/index.cfm].

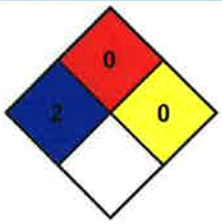
Novo Nordisk. 2013. Activella Prescribing Information. Retireived from http://www.novonordiskmedicalinformation.com/products.aspx

Training advice : No special training is necessary but a thorough knowledge of this safety data sheet is assumed.

Full text of H-phrases: see section 16:

Carc. 2	Carcinogenicity Category 2
Repr. 1A	Reproductive toxicity Category 1A
Skin Sens. 1	Skin sensitization Category 1
H317	May cause an allergic skin reaction
H351	Suspected of causing cancer
H360	May damage fertility or the unborn child

NFPA health hazard	: 2 - Intense or continued exposure could cause temporary incapacitation or possible residual injury unless prompt medical attention is given.
NFPA fire hazard	: 0 - Materials that will not burn.
NFPA reactivity	: 0 - Normally stable, even under fire exposure conditions, and are not reactive with water.



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