SAFETY DATA SHEET

Revision Date 16-Jul-2019 **Version** 1

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING

Product identifier
Product Name Alora

Other means of identification
Product Code RM00008
Synonyms Estradiol Transdermal System

Recommended use of the chemical and restrictions on use
Recommended Use Treatment of moderate to severe vasomotor symptoms associated with the menopause.• Treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with the menopause. When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered.• Treatment of hypoestrogenism due to hypogonadism, castration or primary ovarian failure.• Prevention of postmenopausal osteoporosis. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and non estrogen medications should be carefully considered.

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to medicinal use of the product. In this instance patients should consult prescribing information/package insert/product label or consult their pharmacist or physician. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate safety data sheet for each ingredient.

Details of the supplier of the safety data sheet
Manufacturer
Allergan plc
5 Giralda Farms
Madison, NJ USA 07940
+1-800-272-5525
E-mail address SDS@Allergan.com

Emergency telephone number
Emergency Telephone Call CHEMTREC Day or Night
Within USA or Canada: 1-800-424-9300
Outside USA and Canada: +1-703-741-5970 (collect calls accepted)

2. HAZARDS IDENTIFICATION

Classification

OSHA Regulatory Status
This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Serious eye damage/eye irritation	Category 1
Carcinogenicity	Category 1A
Reproductive toxicity	Category 1A
Effects on or via lactation	Yes

Label elements

Emergency Overview

Danger

Hazard statements

H318 - Causes serious eye damage
H350 - May cause cancer
H360 - May damage fertility or the unborn child
H362 - May cause harm to breast-fed children

Appearance Patch **Physical state** Solid **Odor** No information available

Chemical Name	**Symptoms**
ESTRADIOL USP	1. Genitourinary systemChanges in vaginal bleeding pattern and abnormal withdrawal bleeding or flow; breakthrough bleeding, spotting, dysmenorrhea; increase in size of uterine leiomyomata; vaginitis, including vaginal candidiasis; change in amount of cervical secretion; changes in cervical ectropion; ovarian cancer; endometrial hyperplasia; endometrial cancer.2. BreastsTenderness, enlargement, pain, nipple discharge, galactorrhea; fibrocystic breast changes; breast cancer.3. CardiovascularDeep and superficial venous thrombosis; pulmonary embolism; thrombophlebitis; myocardial infarction; stroke; increase in blood pressure.4. GastrointestinalNausea, vomiting; abdominal cramps, bloating; cholestatic jaundice; increased incidence of gallbladder disease; pancreatitis; enlargement of hepatic hemangiomas.5. SkinChloasma or melasma that may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; pruritus, rash.6. EyesRetinal vascular thrombosis, steepening of corneal curvature, intolerance to contact lenses.7. Central Nervous SystemHeadache, migraine, dizziness; mental depression; chorea; nervousness, mood disturbances, irritability; exacerbation of epilepsy; dementia.8. MiscellaneousIncrease or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; arthralgias; leg cramps; changes in libido; urticaria, angioedema, anaphylactoid/anaphylactic reactions; hypocalcemia; exacerbation of asthma; increased triglycerides.OVERDOSAGESerious ill effects have not been reported following acute ingestion of large doses of estrogen-containing oral contraceptives by young children. Overdosage of estrogen may cause nausea and vomiting, and withdrawal bleeding may occur in females.

Chemical Name	**Medical Conditions Aggravated by Exposure**
ESTRADIOL USP	BOXED WARNINGESTROGENS INCREASE THE RISK OF ENDOMETRIAL CANCERClose clinical surveillance of all women taking estrogens is important. Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. There is no evidence that the use of “natural” estrogens results in a different endometrial risk profile than “synthetic” estrogens at equivalent estrogen doses. (See WARNINGS, Malignant neoplasms, Endometrial cancer.)CARDIOVASCULAR AND OTHER RISKSEstrogens with or without progestins should not be used for the prevention of cardiovascular disease. (See WARNINGS, Cardiovascular disorders.)The Women’s Health Initiative (WHI) study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50 to 79 years of age) during 5 years of treatment with oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) relative to placebo. (See CLINICAL PHARMACOLOGY, Clinical Studies.)The Women’s Health Initiative Memory Study (WHIMS), a substudy of WHI, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with oral conjugated estrogens plus medroxyprogesterone acetate relative to placebo. It is unknown whether this finding applies to younger postmenopausal women or to women taking estrogen alone therapy. (See CLINICAL PHARMACOLOGY, Clinical

	Studies.)Other doses of oral conjugated estrogens with medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestins were not studied in the WHI clinical trials and, in the absence of comparable data, these risks should be assumed to be similar. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman. Estrogens should not be used in individuals with any of the following conditions:Undiagnosed abnormal genital bleeding.Known, suspected, or history of cancer of the breast except in appropriately selected patients being treated for metastatic disease.Known or suspected estrogen-dependent neoplasia.Active deep vein thrombosis, pulmonary embolism or history of these conditions.Active or recent (e.g., within the past year) arterial thromboembolic disease (e.g., stroke, myocardial infarction).Liver dysfunction or disease.Estradiol tablets should not be used in patients with known hypersensitivity to its ingredients.Known or suspected pregnancy. There is no indication for estradiol in pregnancy. There appears to be little or no increased risk of birth defects in children born to women who have used estrogens and progestins from oral contraceptives inadvertently during early pregnancy.

Precautionary statements
P280 - Wear eye protection/ face protection
P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
P310 - Immediately call a POISON CENTER or doctor/physician
P202 - Do not handle until all safety precautions have been read and understood
P281 - Use personal protective equipment as required
P405 - Store locked up
P501 - Dispose of contents/ container to an approved waste disposal plant
P201 - Obtain special instructions before use
P260 - Do not breathe dusts or mists
P263 - Avoid contact during pregnancy/while nursing
P264 - Wash face, hands and any exposed skin thoroughly after handling
P270 - Do not eat, drink or smoke when using this product
P308 + P313 - IF exposed or concerned: Get medical advice/attention

Other Information

Unknown Acute Toxicity 80% of the mixture consists of ingredient(s) of unknown toxicity

Over the counter drugs in their solid form are considered exempt under the criteria of the Federal OSHA Hazard Communication Standard 20 CFR 1910.1200. However, in an industrial setting where a component's occupational exposure limit may be surpassed, than can be considered hazardous

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS No.	EINECS	Weight-%
SORBITAN MONOOLEATE NF	1338-43-8	215-665-4	10 - 30*
Siliconized Polyester Film	25038-59-9	N/A	10 - 30*
ESTRADIOL USP	50-28-2	200-023-8	10 - 30*
Polyethylene film	9002-88-4	N/A	3 - 7*
ETHYL ACETATE	141-78-6	205-500-4	<0.1*

*The exact percentage (concentration) of composition has been withheld as a trade secret.

4. FIRST AID MEASURES

First aid measures

Eye contact Rinse immediately with plenty of water and seek medical advice.

Skin Contact Wash off immediately with soap and plenty of water while removing all contaminated clothes and shoes.

Inhalation Remove to fresh air.

Ingestion Consult a physician if necessary.

Chemical Name
ESTRADIOL USP

Note to physicians
This product should only be given to patients by persons experienced in management of patients receiving the type of therapy intended for this product. Treat symptoms and eliminate exposure.

5. FIRE-FIGHTING MEASURES

Suitable extinguishing media
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media
None known.

Specific hazards arising from the chemical
Fire may produce irritating, corrosive and/or toxic gases.

Explosion data
Sensitivity to Mechanical Impact Not impact sensitive.
Sensitivity to Static Discharge Fine dust dispersed in air, in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.

Protective equipment and precautions for firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions Use personal protection recommended in Section 8. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing.

Environmental precautions See Section 12 for additional ecological information.

Methods for containment Prevent further leakage or spillage if safe to do so.

Methods for cleaning up Use personal protective equipment as required. Cover powder spill with plastic sheet or tarp to minimize spreading and keep powder dry. Take up mechanically, placing in appropriate containers for disposal. Avoid creating dust. Clean contaminated surface thoroughly.

7. HANDLING AND STORAGE

Advice on safe handling Avoid contact with skin, eyes or clothing. Avoid generation of dust. Do not eat, drink or smoke when using this product.

Storage Conditions Keep containers tightly closed in a dry, cool and well-ventilated place. Store away from incompatible materials.

Incompatible materials None known based on information supplied.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

Exposure Guidelines .

Chemical Name	ACGIH TLV	OSHA PEL	NIOSH IDLH	Allergan OEL (ug/m³)
ESTRADIOL USP 50-28-2	N/A	N/A	N/A	0.02 ug/m^3

ETHYL ACETATE 141-78-6	TWA: 400 ppm	TWA: 400 ppm TWA: 1400 mg/m^3 (vacated) TWA: 400 ppm (vacated) TWA: 1400 mg/m^3	IDLH: 2000 ppm TWA: 400 ppm TWA: 1400 mg/m^3	N/A

NIOSH IDLH Immediately Dangerous to Life or Health

Other Information Vacated limits revoked by the Court of Appeals decision in AFL-CIO v. OSHA, 965 F.2d 962 (11th Cir., 1992).

Appropriate engineering controls

Engineering Controls The health hazard risks of handling this material are dependent on factors, such as physical form and quantity. Site specific risk assessments should be conducted to determine the appropriate exposure control measures. Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels as low as reasonably achievable.

Individual protection measures, such as personal protective equipment

Eye/face protection No eye protection is normally needed during medical administration of this product. During operations in which dusts of the product may be generated, safety glasses should be considered.

Skin and body protection During medical administration of this product, medical latex or nitrile gloves should be worn to avoid absorption of the product. Use appropriate protective clothing for the task (e.g., lab coat, etc.).

Respiratory protection Respiratory protection is generally not needed during routine conditions of use of this product. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

9. PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical state	Solid	**Appearance**	Patch
Color	No information available	**Odor**	No information available
Odor threshold	No information available		

Property	**Values**
pH	No information available
Melting point/freezing point	No information available
Boiling point / boiling range	No information available
Flash point	No information available
Evaporation rate	No information available
Flammability (solid, gas)	No information available
Flammability Limit in Air	
Upper flammability limit:	No information available
Lower flammability limit:	No information available
Vapor pressure	No information available
Vapor density	No information available
Specific Gravity	No information available
Water solubility	No information available
Solubility in other solvents	No information available
Partition coefficient	No information available
Autoignition temperature	No information available
Decomposition temperature	No information available
Explosive properties	No information available
Oxidizing properties	No information available

Other Information

Molecular weight	No information available
VOC Content (%)	No information available
Density	No information available
Bulk density	No information available

10. STABILITY AND REACTIVITY

Reactivity
Not defined As Reactive substance

Chemical stability
Stable under normal conditions.

Possibility of Hazardous Reactions
None under normal processing.

Conditions to avoid
Aerosol formation.

Incompatible materials
None known based on information supplied.

Hazardous Decomposition Products
None known based on information supplied.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Acute toxicity

Chemical Name	Inhalation	Eye contact	Skin Contact	Ingestion
ESTRADIOL USP	Inhalation of airborne dusts generated by this product may slightly irritate the nose, throat, and lungs. Symptoms are generally alleviated upon breathing fresh air.	Irritating to eyes.	May cause skin irritation and/or dermatitis.	Ingestion is not a significant route of occupational overexposure. Acute ingestion of large quantities of this product or chronic ingestion caused by poor hygiene practices may cause adverse symptoms. Symptoms of ingestion overexposure may include nausea, vomiting, and diarrhea.

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50
SORBITAN MONOOLEATE NF	> 39800 mg/kg (Rat)	N/A	N/A
Polyethylene film	= 8 g/kg (Rat) > 2000 mg/kg (Rat)	N/A	N/A
ETHYL ACETATE	= 5620 mg/kg (Rat)	> 18000 mg/kg (Rabbit) > 20 mL/kg (Rabbit)	N/A

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Chemical Name	Germ cell mutagenicity	Carcinogenicity	Reproductive toxicity	Effects on or via lactation
ESTRADIOL USP	Not Suspected of being a Mutagen.	Confirmed human carcinogen.	Presumed to produce significant toxicity to specific target organ(s).	Detectable amounts of this compound have been identified in the milk of nursing women receiving this drug. Caution should be exercised when taking this compound is administered to

				nursing women.

Chemical Name	STOT - single exposure	STOT - repeated exposure
ESTRADIOL USP	No information available.	Presumed to produce significant toxicity to specific target organ(s).

Chronic toxicity May cause adverse liver effects. Contains a known or suspected reproductive toxin.
Target Organ Effects Bladder, Central nervous system, Eyes, Gastrointestinal tract (GI), liver, Pancreas, Reproductive System, Skin, Urinary Tract.

Numerical measures of toxicity - Product Information

Unknown Acute Toxicity 80% of the mixture consists of ingredient(s) of unknown toxicity
The following values are calculated based on chapter 3.1 of the GHS document .
ATEmix (oral) 53120 mg/kg

12. ECOLOGICAL INFORMATION

Ecotoxicity

Very toxic to aquatic life with long lasting effects

85% of the mixture consists of components(s) of unknown hazards to the aquatic environment

Chemical Name	Algae/aquatic plants	Fish	Crustacea
ESTRADIOL USP 50-28-2	N/A	.002 micrograms/L	2040 micrograms/L
ETHYL ACETATE 141-78-6	3300: 48 h Desmodesmus subspicatus mg/L EC50	220 - 250: 96 h Pimephales promelas mg/L LC50 flow-through 352 - 500: 96 h Oncorhynchus mykiss mg/L LC50 semi-static 484: 96 h Oncorhynchus mykiss mg/L LC50 flow-through	560: 48 h Daphnia magna mg/L EC50 Static

Chemical Name	Persistence and degradability	Bioaccumulation	Mobility	Partition coefficient
ESTRADIOL USP 50-28-2	Slow	N/A	Immobile	4.01
ETHYL ACETATE 141-78-6	N/A	N/A	N/A	0.6

Other adverse effects No information available

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes Disposal should be in accordance with applicable regional, national and local laws and regulations.

Contaminated packaging Do not reuse container. Dispose of contents/containers in accordance with local regulations.

US EPA Waste Number U056 U112

Chemical Name	RCRA	RCRA - Basis for Listing	RCRA - D Series Wastes	RCRA - U Series Wastes
ETHYL ACETATE 141-78-6	-	Included in waste stream: F039	-	U112
CYCLOHEXANE 110-82-7	-	-	-	U056

Chemical Name	California Hazardous Waste Status
ETHYL ACETATE 141-78-6	Toxic Ignitable

14. TRANSPORT INFORMATION

DOT Not regulated

TDG Not regulated

ICAO (air) Not regulated

IATA Not regulated

IMDG Not regulated

ADR Not regulated

ADN Not regulated

15. REGULATORY INFORMATION

International Inventories

TSCA	Not Listed
DSL/NDSL	Listed
EINECS/ELINCS	Not Listed

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances

US Federal Regulations

Carcinogenicity The table below indicates whether each agency has listed any ingredient as a carcinogen This product contains one or more substances which are classified by IARC as carcinogenic to humans (Group I), probably carcinogenic to humans (Group 2A) or possibly carcinogenic to humans (Group 2B)

Chemical Name	ACGIH	IARC	NTP	OSHA
ESTRADIOL USP 50-28-2	-	Group 1	-	X
Polyethylene film 9002-88-4	-	Group 3	-	-

IARC (International Agency for Research on Cancer)
Group 1 - Carcinogenic to Humans
Not classifiable as a human carcinogen
OSHA (Occupational Safety and Health Administration of the US Department of Labor)
X - Present

SARA 313
Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

SARA 311/312 Hazard Categories

Acute health hazard	Yes
Chronic Health Hazard	No
Fire hazard	No
Sudden release of pressure hazard	No
Reactive Hazard	No

CWA (Clean Water Act)
This product contains the following substances which are regulated pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42)

CERCLA
This material, as supplied, contains one or more substances regulated as a hazardous substance under the Comprehensive

Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302)

Chemical Name	Hazardous Substances RQs	CERCLA/SARA RQ	Reportable Quantity (RQ)
ETHYL ACETATE 141-78-6	5000 lb	-	RQ 5000 lb final RQ RQ 2270 kg final RQ

US State Regulations

California Proposition 65

This product contains the following Proposition 65 chemicals

Chemical Name	California Proposition 65
ESTRADIOL USP - 50-28-2	Carcinogen

U.S. State Right-to-Know Regulations

Chemical Name	New Jersey	Massachusetts	Pennsylvania
ESTRADIOL USP 50-28-2	-	X	X
CYCLOHEXANE 110-82-7	X	X	X
ETHYL ACETATE 141-78-6	X	X	X

16. OTHER INFORMATION

Revision Date 16-Jul-2019
Revision Note No information available

Disclaimer

The information provided in this Material Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

End of Safety Data Sheet