

SAFETY DATA SHEET

CombiPatch™

Section 1: Identification Of the Substance/Mixture And Of The Supplier

Supplier Noven Pharmaceuticals, Inc. 11960 SW 144 St. Miami, FL 33186 Telephone Number: 800-455-8070 Web Site: www.noven.com	Manufacturer Noven Pharmaceuticals, Inc. 11960 SW 144 St. Miami, FL 33186 Telephone Number: 800-455-8070 Web Site: www.noven.com
Supplier Emergency Contacts & Phone Number CHEMTREC: 1-800-424-9300	Manufacturer Emergency Contacts & Phone Number CHEMTREC: 1-800-424-9300

Issue Date: 07/02/2014

Product Name: CombiPatch™

CAS Number: Not Established

Chemical Family: hormone replacement therapy

Product/Material Uses

CombiPatch™ (estradiol/norethindrone acetate transdermal system) is an adhesive-based matrix transdermal patch, designed to release both estradiol and norethindrone acetate (NETA), a progestational agent, continuously upon application to the skin, as a hormone replacement therapy.

Read all package inserts and information before using the product. Discuss the use of the product with your physician.

Section 2: Hazards Identification



Hazard Classification(s)

HAZARD CLASSIFICATION(S):

Reproductive Toxicity: Category 1

Carcinogenicity - Category 1B

Specific Target Organ Toxicity, Repeated Exposure: Category 1

Acute Aquatic Hazard - Category 1

Skin Sensitization: Category 1B

Reproductive Toxicity: Effects on or via Lactation

Specific Target Organ Toxicity, Single Exposure: Category 3

Eye Damage/Irritation: Category 2

Skin Corrosion/Irritation: Category 3

Acute (Oral) Toxicity - Category 4

SIGNAL WORD: DANGER

HAZARD STATEMENTS:

May damage fertility or the unborn child. (H360)

May cause cancer. (H350)

Very toxic to aquatic life (H400)

May cause harm to breast-fed children (H362)

Causes damage to the nervous system, liver and reproductive system through prolonged or repeated exposure. (H372)

May cause drowsiness or dizziness (H336)

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Section 2: Hazards Identification - Continued

Hazard Classification(s) - Continued

Causes eye irritation (H320)
Causes mild skin irritation (H316)
Harmful if swallowed (H302)

PRECAUTIONARY STATEMENTS:

P201 - Obtain special instructions before use.
P202 - Do not handle until all safety precautions have been read and understood.
P263 - Avoid contact during pregnancy/while nursing.
P264 - Wash thoroughly after handling.
P280 - Wear protective gloves when handling.
P301+P310 - IF SWALLOWED: Immediately call a Poison Center or physician.
P302+P352 - IF ON SKIN: wash with plenty of soap and water.
P304+P340 - IF INHALED: remove person to fresh air and keep comfortable for breathing.
P305+P351+P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention.
P337+P313 - If eye irritation persists: Get medical attention/advice.
P332+P313 - If skin irritation occurs: Get medical attention/advice.
P308+P313 - If exposed or concerned: Get medical advice/attention.
P403+P233 - Store in a well-ventilated place. Keep container tightly closed.
P405 - Store locked up.
P501 - Dispose of contents/container in accordance with local, state, federal and international regulation.

Primary Routes(s) Of Entry

Skin

Section 3: Composition/Information On Ingredients

Ingredient Name	CAS Number		Percent Of Total Weight
17b-estradiol	50-28-2	<	1
dipropylene glycol	25265-71-8		3 - 5
norethindrone acetate	51-98-9		1 - 2
oleic acid	112-80-1		3 - 5
povidone	9003-39-8		3 - 5

Section 4: First Aid Measures

Eye

Eye contact is considered unlikely due to the physical form of the product. However, eye contact may occur with contaminated hands. In case of contact with the eyes rinse cautiously with water for 15 minutes with eyelids open. Remove contact lenses, if present and easy to do. Continue rinsing. Seek medical attention if irritation or redness persists.

Skin

This product is intended to be applied to the skin. In case of accidental or unwanted contact, wash the affected area under tepid running water using a mild soap. Avoid abrading the skin, which may increase the degree of skin absorption. Seek medical attention if irritation, redness or other symptoms occur.

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Section 4: First Aid Measures - Continued

Ingestion

Immediately call a Poison Center or doctor/physician. If swallowed, induce vomiting only if directed to do so by medical personnel. Never give anything by mouth to an unconscious victim or person having convulsions.

Inhalation

Inhalation is considered very unlikely due to the physical form of the product. Inhalation of chemicals contained in the product is expected to be negligible from normal clinical use. Contact a physician if a person feels unwell after handling the product.

Note To Physician

Ensure that medical personnel take precautions to protect themselves. Wash hands and skin thoroughly. Wash contaminated clothing before reuse.

Section 5: Fire Fighting Measures

Fire And Explosion Hazards

Thermal decomposition ("burning") may evolve toxic and irritating combustion byproducts.

Extinguishing Media

Small fires may be extinguished with carbon dioxide or dry chemical powder. Large fires may be extinguished with water spray or firefighting foam.

Fire Fighting Instructions

Evacuate personnel to a safe area. Avoid breathing vapors, gases and fumes. Firefighters should wear self-contained breathing apparatus and full protective gear. Do not allow runoff to enter sewers or waterways.

Section 6: Accidental Release Measures

Avoid release to the environment. Avoid contamination of sewers and waterways. Use appropriate personal protective equipment (PPE) for spill cleanup. Pick up released product with appropriate implements and return to original container if packages are undamaged and reusable. Contact manufacturer for special instructions.

Section 7: Handling And Storage

Handling Precautions

Consult a physician before use. Medical personnel should wear gloves when handling. Apply immediately upon removal from pouch. Wash thoroughly after handling, and before eating, drinking, smoking and using toilet facilities. Avoid contact with eyes and skin except for the site of administration. Do not taste or swallow.

Storage Precautions

Store in original unopened pouch until it is ready to be used. Do not store unpouched. Pharmacists - store refrigerated (36 °F to 46 °F). Patients - store in a cool, dry area, away from heat and out of direct sunlight. Do not store above 30 °C (86 °F). Keep product in a safe place away from children and pets.

Shelf life = 6 months.

Work/Hygienic Practices

Use good personal hygiene. Wash thoroughly with soap and water after handling.

Section 8: Exposure Controls/Personal Protection

Engineering Controls

None required under normal conditions of therapeutic administration and use.

Eye/Face Protection

None normally required. Safety glasses are recommended as minimum industrial eye protection when handling bulk product or performing spill cleanup.

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Section 8: Exposure Controls/Personal Protection - Continued

Skin Protection

Lab coat or other work clothing. The use of chemical-resistant gloves, such as nitrile, are recommended as minimum industrial skin protection when handling product or performing spill cleanup.

Respiratory Protection

None required under normal conditions of therapeutic administration and use. General room ventilation is normally adequate. Firefighters and emergency responders should wear positive pressure demand self-contained breathing apparatus.

Other/General Protection

Wash thoroughly after handling.

Ingredient(s) - Exposure Limits

17b-estradiol

Recommended Ceiling Limit: 0.1 ug/m³

dipropylene glycol

DFG MAK-TWA: 200 mg/m³

norethindrone acetate

Recommended 8-hr TWA: 0.7 ug/m³

Section 9: Physical And Chemical Properties

Appearance

A transparent patch system.

Odor

odorless

Chemical Type: Mixture

Physical State: Solid

Melting Point: NA °F

Boiling Point: NA °F

Solubility: insoluble

Section 10: Stability And Reactivity

Stability: Stable under normal conditions.

Hazardous Polymerization: will not occur

Conditions To Avoid (Stability)

Heating or storage at elevated temperatures (>77 deg F). Avoid exposure to heat, spark, open flame and other sources of ignition.

Incompatible Materials

Incompatible with strong oxidizing agents, such as chlorine, nitric acid, sulfuric acid, hydrogen peroxide, nitrates, perchlorates and permanganates - may increase risk of fire and explosion.

Hazardous Decomposition Products

Burning may produce hazardous, toxic or irritating decomposition fumes.

Section 11: Toxicological Information

Acute Studies

There is insufficient information is available to determine the acute dermal and inhalation toxicity.

Eye Effects

Eye contact with the product is considered unlikely due to the physical form, although handling of the product may allow for transfer of materials from the hands to the eyes. May cause eye irritation.

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Section 11: Toxicological Information - Continued

Skin Effects

This product is intended for application to the skin. Some individuals may experience skin irritation and redness. Some ingredients of the patch adhesive are considered to be skin sensitizers - may cause an allergic skin reaction in sensitive individuals.

Possible side effects from use of the product include: heart attack, stroke, blood clots, dementia, breast cancer, cancer of the lining of the uterus, cancer of the ovary, high blood pressure, high blood sugar, gall bladder disease, liver problems, changes in thyroid hormone levels, enlargement of benign tumors of the uterus ("fibroids") and depression. Call your health provider if you experience lumps in/on the breast, unusual vaginal bleeding, changes in vision or speech, sudden severe headaches, or severe pain in your chest or legs with or without shortness of breath, weakness and fatigue.

Less serious, but common side effects include: headache, breast tenderness, irregular vaginal bleeding or spotting, stomach or abdominal cramps, bloating, drowsiness/fatigue, nausea and vomiting, hair loss, fluid retention, vaginal yeast infection.

The above does not include all possible side effects from using the product. Consult with your healthcare provider or pharmacist.

Acute Oral Effects

Ingestion is considered unlikely due to the physical form of the product. Do not taste or swallow. Accidental or intentional ingestion may cause effects similar to those noted from skin administration. May be harmful or fatal if swallowed. Seek immediate medical attention.

Acute Inhalation Effects

Inhalation is considered unlikely due to the physical form. No effects are known or expected from normal therapeutic use.

Excessive inhalation of certain ingredients of the product have been associated with respiratory irritation, dizziness, drowsiness, incoordination, and mental confusion.

Subchronic (Target Organ Effects)

Prolonged or repeated exposure may damage the gall bladder, increase the risk of thromboembolic vascular disease and cause cancer of the breast, cervix, uterus, vagina endometrium, testes and liver. May have effects on blood sugar levels and cholesterol levels. May have effects on both female and male fertility.

Chronic/Carcinogenicity

There is sufficient evidence in humans for the carcinogenicity of post-menopausal estrogen therapy. An increased risk of endometrial and ovarian cancers has been reported with the use of estrogen therapy; although most studies do not show significant increased risk when used for less than 1 year. There is an increased risk of endometrial carcinoma for up to 15 years following discontinuation of estrogen therapy.

Prolonged or repeated exposure to other ingredients of this product have been associated with damage to the nervous system, kidneys and liver.

The International Agency for Research on Cancer (IARC) classifies 17B-estradiol as being carcinogenic to humans (Group 1). The National Toxicology Program (NTP) also classifies estradiol as a known human carcinogen. IARC classifies norethindrone acetate as being possibly carcinogenic to humans (Group 2B).

Teratogenicity (Birth Defects)

The use of estrogens or estrogens/progestins during pregnancy may cause increased risk of congenital defects in the reproductive organs of the fetus, and possibly other birth defects. Avoid handling product during pregnancy.

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Section 11: Toxicological Information - Continued

Reproductive Effects

Estrogens are excreted in breast milk, and may decrease the quantity and quality of milk. Nursing and pregnant women should avoid exposure.

Men exposed to estrogens may experience a decrease in testicular size accompanied by a decline in testosterone production. May impair fertility and decrease libido. In severe cases, gynecomastia (i.e., breast tenderness and enlargement) may occur. These symptoms may persist for a prolonged period of time.

Mutagenicity (Genetic Effects)

17 β -Estradiol has been associated with chromosomal aberrations in the germ cells of laboratory test animals. Norethindrone acetate was negative in a battery of in vitro and in vivo mutagenicity tests.

Conditions Aggravated By Exposure

Estrogens should not be used by individuals with any of the following conditions: abnormal genital bleeding, known or suspected history of cancer of the breast, active deep vein thrombosis, pulmonary embolism, history of stroke or myocardial infarction, or liver disease.

Ingredient(s) - Carcinogenicity

17 β -estradiol

NTP - Listed On The National Toxicology Program

Listed In The IARC Monographs

Ingredient(s) - Toxicological Data

dipropylene glycol

LD50 (oral, rat): 14850 mg/kg

LD50 (oral, rabbit): >20 mL/kg

LD50 (oral, unspecified mammal): 15 gm/kg

LD50 (dermal, rabbit): >20500 mg/kg

oleic acid

LD50 (oral, rat): 25,000 mg/kg

LD50 (oral, mouse): 28,000 mg/kg

povidone

LD50 (oral, rat): 100 gm/kg

LD50 (oral, mouse): 12 gm/kg

Section 12: Ecological Information

Ecotoxicological Information

Harmful to aquatic organisms. Do not allow to enter sewers and waterways.

Section 13: Disposal Considerations

Individual patches used by consumers may be disposed of in normal household trash. Fold adhesive sides together before disposing.

Dispose of large quantities or bulk amounts in an environmentally responsible manner in accordance with applicable federal, state and local government regulations. Avoid/prevent release to the environment. This product is suitable for disposal by incineration or in an approved landfill.

RCRA Information

Waste material is not considered a "hazardous waste" as defined by U.S. EPA RCRA regulations.

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Section 14: Transport Information

Proper Shipping Name

Not regulated for transportation

Section 15: Regulatory Information

SARA Hazard Classes

Acute Health Hazard
Chronic Health Hazard

State Regulations

The following statement is made in order to comply with the California Safe Drinking Water and Toxic Enforcement Act of 1986. *This product contains 17b-estradiol a chemical known to the State of California to cause cancer, and norethindrone acetate, a chemical known by the State of California to cause reproductive toxicity.*

Ingredient(s) - State Regulations

17b-estradiol
New Jersey - Workplace Hazard
New Jersey - Special Hazard
Pennsylvania - Workplace Hazard
Pennsylvania - Special Hazard
California - Proposition 65
Massachusetts - Hazardous Substance
New York City - Hazardous Substance
norethindrone acetate
California - Proposition 65

Section 16: Other Information

NFPA Rating

Health: 1

Fire: 0

Reactivity: 0

HMIS Rating

Health: *3

Fire: 0

Reactivity: 0

Disclaimer

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