



SAFETY DATA SHEET

Revision date: 07-Oct-2013

Version: 1.1

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

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International CHEMTREC (24 hours): +1-703-527-3887

Material Name: Aprela

Trade Name:	DUAVEE
Synonyms:	APRELA; DUAVIVE; Bazedoxifene, Conjugated Estrogen Tablets
Chemical Family:	Not determined
Intended Use:	Pharmaceutical product used for osteoporosis

2. HAZARDS IDENTIFICATION

Appearance: Pink or Brown tablets
Signal Word: DANGER

Statement of Hazard: May cause cancer.
May cause allergic skin reaction.
Suspected of damaging fertility.
Very toxic to aquatic life with long lasting effects.

Additional Hazard Information:
Long Term:

Repeat-dose studies in animals have shown a potential to cause adverse effects on fertility, reproductive system, and the developing fetus. Occupational studies have shown that males working with estrogen-like compounds have shown clinical signs of hyperestrogenism including enlarged breasts and milk secretion. Loss of libido, breast tenderness, and changes in sex hormone levels have also occurred. Occupational exposure in females has resulted in menstrual irregularities (breakthrough bleeding, menstrual flow changes, spotting and amenorrhea).

Known Clinical Effects: Clinical use of estrogens has resulted in breast changes (enlargement, tenderness, and secretion), along with effects on the genitourinary (changes in vaginal bleeding), and GI systems. Effects on the skin, eyes, and CNS have also been reported. Ingestion of this material may cause effects similar to those seen in clinical use including back pain, decreased red blood cell count (anemia), headache, pain, respiratory infection, bronchial tube inflammation (bronchitis), urinary tract infection, allergic reaction, hives, redness and swelling of the skin (urticaria), insomnia, depression palpitations, hot flashes, diarrhea, difficult digestion (dyspepsia), constipation, acid reflux, dry mouth, and flatulence.

EU Classification
EU Indication of danger: Carcinogenic: Category 1
Toxic to Reproduction: Category 3
Dangerous for the Environment
Irritant

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2. HAZARDS IDENTIFICATION

EU Hazard Symbols:



EU Risk Phrases:

R43 - May cause sensitization by skin contact.
R45 - May cause cancer.
R62 - Possible risk of impaired fertility.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Hazardous Substance. Dangerous Goods.

Australian Hazard Classification (NOHSC):

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Bazedoxifene Acetate	198481-33-3	Not Listed	N;R50/53 Repr.Cat.3;R62 Xi,R43	5-10
Polyethylene glycol	25322-68-3	Not Listed	Not Listed	*
Magnesium Stearate	557-04-0	209-150-3	Not Listed	*
Sucrose	57-50-1	200-334-9	Not Listed	*
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Conjugated estrogens	12126-59-9	235-199-5	Carc.Cat.1;R45 Repr.Cat.1;R60 Repr.Cat.1;R61	0.2

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Pharmaceutical ink	Not assigned	Not Listed	Not Listed	*
Calcium phosphate, tribasic	7758-87-4	231-840-8	Not Listed	*
Ascorbic acid (Vitamin C)	50-81-7	200-066-2	Not Listed	*
Lactose NF, monohydrate	64044-51-5	Not Listed	Not Listed	*
Water, purified	7732-18-5	231-791-2	Not Listed	*
Tablet coating	NOT ASSIGNED	Not Listed	Not Listed	*
Hydroxypropyl cellulose	9004-64-2	Not Listed	Not Listed	*
Hydroxyethyl cellulose	9004-62-0	Not Listed	Not Listed	*
Sucrose Palmitate	26446-38-8	247-706-7	Not Listed	*

Additional Information: Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

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For the full text of the R phrases mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Eye Contact:	Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.
Skin Contact:	Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
Ingestion:	Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.
Inhalation:	Remove to fresh air and keep patient at rest. Seek medical attention immediately.
Symptoms and Effects of Exposure:	For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

5. FIRE FIGHTING MEASURES

Extinguishing Media:	Use carbon dioxide, dry chemical, or water spray.
Hazardous Combustion Products:	Formation of toxic gases is possible during heating or fire. May include oxides of carbon and nitrogen
Fire Fighting Procedures:	During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.
Fire / Explosion Hazards:	Fine particles (such as dust and mists) may fuel fires/explosions.

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions:	Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.
Measures for Cleaning / Collecting:	Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.
Measures for Environmental Protections:	Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.
Additional Consideration for Large Spills:	Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

General Handling:	Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls. Refer to Section 12 - Ecological Information, for information on potential effects on the environment.
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7. HANDLING AND STORAGE

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Refer to available public information for specific member state Occupational Exposure Limits.

Bazedoxifene Acetate

Pfizer OEL TWA-8 Hr: 1µg/m³, Sensitizer

Polyethylene glycol

Austria OEL - MAKs 1000 mg/m³
Germany - TRGS 900 - TWAs 1000 mg/m³
Germany (DFG) - MAK 1000 mg/m³ average molecular weight 200-600
Slovakia OEL - TWA 1000 mg/m³
Slovenia OEL - TWA 1000 mg/m³

Magnesium Stearate

ACGIH Threshold Limit Value (TWA) 10 mg/m³
Lithuania OEL - TWA 5 mg/m³
Sweden OEL - TWAs 5 mg/m³

Sucrose

ACGIH Threshold Limit Value (TWA) 10 mg/m³
Australia TWA 10 mg/m³
Belgium OEL - TWA 10 mg/m³
Bulgaria OEL - TWA 10.0 mg/m³
Estonia OEL - TWA 10 mg/m³
France OEL - TWA 10 mg/m³
Ireland OEL - TWAs 10 mg/m³
Latvia OEL - TWA 5 mg/m³
Lithuania OEL - TWA 10 mg/m³
OSHA - Final PELs - TWAs: 15 mg/m³
Portugal OEL - TWA 10 mg/m³
Slovakia OEL - TWA 6 mg/m³
Spain OEL - TWA 10 mg/m³

Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA) 10 mg/m³
Australia TWA 10 mg/m³
Belgium OEL - TWA 10 mg/m³
Estonia OEL - TWA 10 mg/m³
France OEL - TWA 10 mg/m³
Ireland OEL - TWAs 10 mg/m³
Latvia OEL - TWA 4 mg/m³
Latvia OEL - TWA 2 mg/m³
OSHA - Final PELs - TWAs: 15 mg/m³
Portugal OEL - TWA 10 mg/m³
Spain OEL - TWA 10 mg/m³

Conjugated estrogens

Pfizer OEL TWA-8 Hr: 0.15µg/m³

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8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls: Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Environmental Exposure Controls: Refer to specific Member State legislation for requirements under Community environmental legislation.

Personal Protective Equipment: Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

Hands: Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.

Eyes: Wear safety glasses or goggles if eye contact is possible.

Skin: Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

Respiratory protection: If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Tablets	Color:	Brown or Pink
Molecular Formula:	Mixture	Molecular Weight:	Mixture

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.

Conditions to Avoid: Fine particles (such as dust and mists) may fuel fires/explosions.

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients.

Acute Toxicity: (Species, Route, End Point, Dose)

Bazedoxifene Acetate

Rat Oral LD 50 > 4000 mg/kg
Mouse Oral LD 50 > 4000 mg/kg

Microcrystalline cellulose

Rat Oral LD50 > 5000 mg/kg
Rabbit Dermal LD50 > 2000 mg/kg

Ascorbic acid (Vitamin C)

Rat Oral LD 50 11.9 g/kg

Conjugated estrogens

Rat IP LD50 325 mg/kg
Mouse IV LD50 1740 mg/kg

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11. TOXICOLOGICAL INFORMATION

Rat Oral LD50 > 5000 mg/kg

Sucrose

Rat Oral LD50 29.7 g/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Bazedoxifene Acetate

Skin Irritation Rabbit Non-irritating
Skin Sensitization - LLNA Mouse Positive
Eye Irritation (*In vitro*, REET) Rabbit Minimal
Eye Irritation Rabbit Minimal

Microcrystalline cellulose

Skin Irritation Rabbit Non-irritating
Eye Irritation Rabbit Non-irritating

Conjugated estrogens

Eye Irritation Rabbit Severe

Polyethylene glycol

Eye Irritation Rabbit Mild
Skin Irritation Rabbit Mild

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Bazedoxifene Acetate

30 Day(s) Rat Oral (F) 5 mg/kg/day LOAEL Female reproductive system
30 Day(s) Non-human Primate Oral (M) 200 mg/kg/day NOAEL None identified
30 Day(s) Non-human Primate Oral (F) 10 mg/kg/day LOAEL Female reproductive system
26 Week(s) Rat Oral 10 mg/kg/day LOAEL Skin, Female reproductive system, Mammary gland, Kidney
27 Week(s) Non-human Primate Oral 1 mg/kg/day LOAEL Female reproductive system

Magnesium Stearate

13 Week(s) Rat Oral 1092 g/kg LOAEL Liver

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Bazedoxifene Acetate

Reproductive & Fertility-Males Rat Oral 300 mg/kg/day NOAEL Fertility
Reproductive & Fertility - Females Rat Oral 0.3 mg/kg/day LOAEL Fertility, Reproductive toxicity, Maternal Toxicity
Embryo / Fetal Development Rabbit Oral 0.5 mg/kg/day LOAEL Developmental toxicity, Maternal Toxicity
Embryo / Fetal Development Rat Oral 1 mg/kg/day LOAEL Maternal Toxicity, Fetotoxicity

Conjugated estrogens

Embryo / Fetal Development Rat Subcutaneous 7 mg/kg/day LOAEL Embryotoxicity, Fetotoxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Bazedoxifene Acetate

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11. TOXICOLOGICAL INFORMATION

Bacterial Mutagenicity (Ames) *Salmonella*, *E. coli* Negative
In Vitro Micronucleus Chinese Hamster Ovary (CHO) cells Negative
In Vivo Micronucleus Mouse Bone Marrow Negative
Mammalian Cell Mutagenicity Mouse Lymphoma Negative

Sucrose

Bacterial Mutagenicity (Ames) *Salmonella* Negative

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Bazedoxifene Acetate

2 Year(s) Rat Oral, in feed Benign tumors

Carcinogen Status:

None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

Conjugated estrogens

IARC: Group 1
NTP: Listed

12. ECOLOGICAL INFORMATION

Environmental Overview: Very toxic to aquatic life with long lasting effects. Releases to the environment should be avoided. Environmental properties have not been thoroughly investigated.

Mobility, Persistence and Degradability: Not readily biodegradable (0 % after 28 days).

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Bazedoxifene Acetate

Selenastrum capricornutum (Green Alga) OECD EC50 72 Hours 0.46 mg/L
Pseudokirchneriella subcapitata (Green Alga) OECD ErC50 72 Hours 0.095 mg/L
Pimephales promelas (Fathead Minnow) OECD LC50 96 Hours 1.77 mg/L
Daphnia magna (Water Flea) OECD LC50 48 Hours 6.28 mg/L

Bacterial Inhibition: (Inoculum, Method, End Point, Result)

Bazedoxifene Acetate

Activated sludge OECD EC50 3 Hours > 8.0 mg/L

Chronic Aquatic Toxicity: (Species, Method, Duration, Endpoint, Result, Adverse Endpoint)

Bazedoxifene Acetate

Pimephales promelas (Fathead Minnow) OECD 33 Day(s) NOEC 0.86 mg/L Survival
Daphnia magna (Water Flea) OECD 21 Day(s) NOEC 1.1 mg/L Reproduction
Daphnia magna (Water Flea) OECD 21 Day(s) EC50 1.8 mg/L Survival

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13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

This material is regulated for transportation as a hazardous material/dangerous good.

UN number: UN 3077
UN proper shipping name: Environmentally Hazardous Substance, Solid, n.o.s (Bazedoxifene acetate)
Transport hazard class(es): 9
Packing group: III
Environmental Hazard(s): Marine Pollutant

15. REGULATORY INFORMATION

EU Symbol: T N
EU Indication of danger: Carcinogenic: Category 1
Toxic to Reproduction: Category 3
Dangerous for the Environment
Irritant

EU Risk Phrases:
R43 - May cause sensitization by skin contact.
R45 - May cause cancer.
R62 - Possible risk of impaired fertility.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

EU Safety Phrases:
S22 - Do not breathe dust.
S29 - Do not empty into drains.
S53 - Avoid exposure - obtain special instructions before use.
S57 - Use appropriate containment to avoid environmental contamination.
S61 - Avoid release to the environment. Refer to special instructions/Safety data sheets.

OSHA Label:
DANGER

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15. REGULATORY INFORMATION

May cause cancer.
May cause allergic skin reaction.
Suspected of damaging fertility.
Very toxic to aquatic life with long lasting effects.

Canada - WHMIS: Classifications

WHMIS hazard class:

D2a very toxic materials

D2b toxic materials



Bazedoxifene Acetate

California Proposition 65

Not Listed

Polyethylene glycol

California Proposition 65

Not Listed

Inventory - United States TSCA - Sect. 8(b)

Present

Australia (AICS):

Present

Standard for the Uniform Scheduling
for Drugs and Poisons:

Schedule 3

Pharmaceutical ink

California Proposition 65

Not Listed

Calcium phosphate, tribasic

California Proposition 65

Not Listed

Inventory - United States TSCA - Sect. 8(b)

Present

Australia (AICS):

Present

EU EINECS/ELINCS List

231-840-8

Magnesium Stearate

California Proposition 65

Not Listed

Inventory - United States TSCA - Sect. 8(b)

Present

Australia (AICS):

Present

EU EINECS/ELINCS List

209-150-3

Ascorbic acid (Vitamin C)

California Proposition 65

Not Listed

Inventory - United States TSCA - Sect. 8(b)

Present

Australia (AICS):

Present

REACH - Annex IV - Exemptions from the
obligations of Register:

Present

EU EINECS/ELINCS List

200-066-2

Sucrose

California Proposition 65

Not Listed

Inventory - United States TSCA - Sect. 8(b)

Present

Australia (AICS):

Present

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15. REGULATORY INFORMATION

REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	200-334-9
Lactose NF, monohydrate	
California Proposition 65	Not Listed
Australia (AICS):	Present
Microcrystalline cellulose	
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	232-674-9
Water, purified	
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
REACH - Annex IV - Exemptions from the obligations of Register:	Present
EU EINECS/ELINCS List	231-791-2
Tablet coating	
California Proposition 65	Not Listed
Hydroxypropyl cellulose	
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Hydroxyethyl cellulose	
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Sucrose Palmitate	
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	247-706-7
Conjugated estrogens	
California Proposition 65	carcinogen, initial date 2/27/87; developmental. initial date 4/1/90
EU EINECS/ELINCS List	235-199-5

16. OTHER INFORMATION

Text of R phrases and GHS Classification abbreviations mentioned in Section 3

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R62 - Possible risk of impaired fertility.
R43 - May cause sensitization by skin contact.
R45 - May cause cancer.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.
R50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Data Sources: Pfizer proprietary drug development information. Safety data sheets for individual ingredients.

Reasons for Revision: Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking.

Prepared by: Product Stewardship Hazard Communication
Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet