



SAFETY DATA SHEET according to Regulation (EC) No.
1907/2006

122000004975

Angeliq® (Drospirenone + Estradiol coated Tablets)

Version 2.0

Revision Date 17.03.2014

Print Date 18.03.2014

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

1.1 Product identifier

Angeliq® (Drospirenone + Estradiol coated Tablets)

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

Use of the : unfinished drug mixture
Substance/Mixture

1.3 Details of the supplier of the safety data sheet

Company

Bayer Pharma AG
Müllerstr. 178
D-13353 BERLIN
Tel.: +49 (0) 214 30 46440
Mail: msds@bayerhealthcare.com

1.4 Emergency telephone number

In case of emergency: +49 (0) 214 30 99300 (Sicherheitszentrale Bayer)

2. HAZARDS IDENTIFICATION

2.1 Classification of the substance or mixture

GHS-Classification (according to EC 1272/2008):

||| Carcinogenicity, Category 2 (H351)
||| Reproductive toxicity, Category 1A (H360FD)
||| Effects on or via lactation (H362)
||| Hazardous to the aquatic environment, Category 3 (H412)

Classification (67/548/EEC, 1999/45/EC):

Carcinogenic Category 3
Toxic to Reproduction Category 1
Toxic to Reproduction Category 2
Dangerous for the environment
Limited evidence of a carcinogenic effect.
May impair fertility.
May cause harm to the unborn child.
May cause harm to breastfed babies.
Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

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2.2 Label elements

GHS-Labeling (according to EC 1272/2008):



Danger

Hazard statements:

H351 Suspected of causing cancer.
H360FD May damage fertility. May damage the unborn child.
H362 May cause harm to breast-fed children.
H412 Harmful to aquatic life with long lasting effects.

Precautionary statements:

Prevention:

P260 Do not breathe dust or mist.
P263 Avoid contact during pregnancy/ while nursing.
P273 Avoid release to the environment.
P281 Use personal protective equipment as required.

Response:

P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Hazardous components which must be listed on the label:

67392-87-4	Drospirenon
35380-71-3	Estradiol-Hemihydrate

Labelling according to EC Directives:

Labelling in accordance with directive 1999/45/EC (preparations) and its amendments and adaptations



R-phrases)

R60	May impair fertility.
R61	May cause harm to the unborn child.
R40	Limited evidence of a carcinogenic effect.
R52/53	Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R64	May cause harm to breastfed babies.

S-phrases)

S53	Avoid exposure - obtain special instructions before use.
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S22	Do not breathe dust.
S35	This material and its container must be disposed of in a safe way.
S36/37	Wear suitable protective clothing and gloves.
S61	Avoid release to the environment. Refer to special instructions/ Safety data sheets.

Hazardous components which must be listed on the label:

67392-87-4	Drospirenon
35380-71-3	Estradiol-Hemihydrate

2.3 Other hazards

Other hazards which do not result in classification:

None known.

3. COMPOSITION/INFORMATION ON INGREDIENTS

This product is a mixture within the meaning of Regulation (EC) No. 1907/2006.

Hazardous components

Drospirenon

Concentration [Weight percent] ≥ 0.5 - < 10

CAS-No.: 67392-87-4

CAS name: Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-<(>,<)>(2'S,6R,7R,8R,9S,10R,13S,14S,15S,16S)-

EINECS-No.: 266-679-2

Synonyms: Spirogeston

EU - Classification:



Harmful R22



Carcinogenic Category 3 R40



Toxic to Reproduction Category 1 R60



Toxic to Reproduction Category 2 R61

R64



Dangerous for the environment R51/53

GHS Classification:



Acute Tox. 4 H302

Carc. 2 H351

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Repr. 1A H360FD
Lact. H362
Aquatic Chronic 2 H411

Estradiol-Hemihydrate

Concentration [Weight percent] $\geq 1 - < 5$

CAS-No.: 35380-71-3

CAS name: Estra-1,3,5(10)-triene-3,17-diol (17.β)-, hydrate (2:1)

Synonyms: Estradiol(17β) hemihydrate

EU - Classification:



Carcinogenic Category 3 R40



Toxic to Reproduction Category 1 R60



Toxic to Reproduction Category 3 R63

R64

GHS Classification:



Carc. 2 H351

Repr. 1A H360Fd

Lact. H362

contains

Laktose Monohydrat

Concentration [Weight percent] $\geq 55 - \leq 65$

CAS-No.: 64044-51-5

CAS name: D-Glucose, 4-O-β-D-galactopyranosyl-, monohydrate

EINECS-No.: 613-418-9

Synonyms: 4-O-beta-Galactopyranosyl-D-glucose

For the full text of the H+R-phrases mentioned in this Section, see Section 16.

4. FIRST AID MEASURES

4.1 Description of first aid measures

General advice: Take off all contaminated clothing immediately.

If inhaled: Remove to fresh air. If symptoms persist, call a physician.

In case of skin contact: After contact with skin, wash immediately with plenty of soap and water. If skin reactions occur, contact a physician.



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In case of eye contact: In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

If swallowed: If swallowed, seek medical advice immediately and show this container or label.

4.2 Most important acute symptoms/effects

Symptoms: No information available.

Risks: No information available.

4.3 Indication of any immediate medical attention and special treatment needed

No information available.

5. FIREFIGHTING MEASURES

5.1 Extinguishing media

Suitable extinguishing media: Any

5.2 Special hazards arising from the substance or mixture

Specific hazards during firefighting: Fire may cause evolution of: Carbon monoxide (CO) Carbon dioxide (CO₂)

Further information: Prevent fire extinguishing water from contaminating surface water or the ground water system.

5.3 Advice for firefighters

Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

6. ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

Use personal protective equipment.

6.2 Environmental precautions

Do not flush into surface water or sanitary sewer system.

6.3 Methods and materials for containment and cleaning up

Methods for cleaning up: Contain spillage, and then collect with an electrically protected vacuum cleaner or by wet-brushing and place in container for disposal according to local regulations (see section 13).



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6.4 Reference to other sections

Additional advice: Avoid dust formation.

7. HANDLING AND STORAGE

7.1. Precautions for safe handling

Handling:

Avoid dust formation. Only handle product with local exhaust ventilation. Avoid contact with skin, eyes and clothing.

|| No special protective measures against fire required.

7.2 Conditions for safe storage, including any incompatibilities

For storage suitable stores with adequate product-reception volume must be used. During handling local official regulations must be observed in order to avert impairment of water by the product.

Storage temperature: 15 - 30 °C

Do not use after expiration date.

7.3 Specific end use(s)

No statements available.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1 Control parameters

Components with workplace control parameters (Europe)

Substance	CAS-No.	Basis	Type:	Value	Ceiling Limit Value	Remarks
Starch	9005-25-8	EH40 WEL	VLA-ED	4 mg/m ³		Respirable.
Starch	9005-25-8	EH40 WEL	VLA-ED	10 mg/m ³		Inhalable

Components with workplace control parameters (internationally)

Substance	CAS-No.	Basis	Type:	Value	Ceiling Limit Value	Remarks
Starch	9005-25-8	EH40 WEL	VLA-ED	4 mg/m ³		Respirable.
Starch	9005-25-8	EH40 WEL	VLA-ED	10 mg/m ³		Inhalable



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Drospirenon	67392-87-4		OEL*	0.01 mg/m ³		
Estradiol- Hemihydrate	35380-71-3		OEL*	0.002 mg/m ³		

*OEL (BHC) = Occupational Exposure Limit, company threshold limit value (TLV)

8.2 Exposure controls

Personal protective measures:

Respiratory protection:

Recommended respiratory protection: full mask with filter ABEK-ST (ABEK-P3)

Hand protection:

Hand protection: protective gloves for chemicals made of Baypren, nitrile rubber or PVC wear
Breakthrough time not tested; dispose of immediately after contamination. Advice: The gloves should not be reused.

Eye protection:

Safety glasses

Hygiene measures:

Cleanliness Guidelines (GMP) for manufacturing of drugs must be observed!

Other protective measures:

No special safety precautions are required during handling of pharmaceuticals in their intended finished form (tablets or liquid formulations) by chemists, the hospital's medical staff or patients. Wear suitable protective equipment.

The personal protective equipment is applicable for the handling of bulk material without packaging and for incidents if an exposure by the active ingredient or hazardous components can be expected.

For the intake of ready for use pharmaceuticals or the external use on the skin please read the label and the package leaflet.

9. PHYSICAL AND CHEMICAL PROPERTIES

9.1 Information on basic physical and chemical properties

Form: solid, tablet
 Colour: Red and Yellow
 Odour: No statements available.



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Melting point/range:	No statements available.
Boiling point/boiling range:	No statements available.
Density:	No statements available.
Bulk density:	No statements available.
Vapour pressure:	No statements available.
Viscosity, dynamic:	No statements available.
Viscosity, kinematic:	No statements available.
Flow time:	No statements available.
Surface tension:	No statements available.
Water solubility:	No statements available.
Solubility(ies):	No statements available.
pH:	No statements available.
Partition coefficient (n-octanol/water):	Estradiol-Hemihydrate log Pow: 3.3
Flash point:	Not applicable
inflammability (solid, gaseous):	No statements available.
Explosion limits:	No statements available.

9.2 Other information

Miscibility with water: Not applicable

10. STABILITY AND REACTIVITY

10.1 Reactivity

No statements available.

reaction with Water / Air

No statements available.

Ignition temperature:

No statements available.

Burning number:

No statements available.

Flammability (solid, gas):

No statements available.

10.2 Chemical stability

No statements available.



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Thermal decomposition:

no data available

Dust explosion characteristic number:

No statements available.

Dust explosion class:

no data available

Explosive properties:

No statements available.

Impact Sensitivity:

no data available

Hazardous reactions:

None known.

10.3 Possibility of hazardous reactions

deflagration ability:

No statements available.

Smoldering combustion:

No statements available.

10.4 Conditions to avoid

no data available

Oxidizing properties:

No statements available.

Minimum ignition energy:

no data available

10.5 Incompatible materials

Materials to avoid:

no data available

10.6 Hazardous decomposition products

Carbon monoxide (CO), Carbon dioxide (CO₂)

Further information:

The following applies in general to flammable organic substances and preparations: in correspondingly fine distribution, when whirled up a dust explosion potential may generally be assumed.



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11. TOXICOLOGICAL INFORMATION

11.1 Information on toxicological effects

Other information on toxicity:

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No data is available on the product itself.

Acute oral toxicity:

Angeliq® (Drospirenone + Estradiol coated Tablets)

Acute toxicity estimate (ATE) > 5,000 mg/kg

Method: Calculation method

Drospirenon

LD50 rat: 500 - 2,000 mg/kg

LD50 mouse: 500 - 2,000 mg/kg

Estradiol-Hemihydrate

LD50 rat: > 4,000 mg/kg

Test substance: data based on the valerate

Acute inhalation toxicity:

No statements available.

Acute dermal toxicity:

No statements available.

Acute toxicity (other routes of administration):

Drospirenon

LD50 intraperitoneal mouse: > 1,000 mg/kg

LD50 intraperitoneal rat: 500 mg/kg

Corrosivity:

No statements available.

Skin irritation:

No statements available.

Eye irritation:

No statements available.

Sensitisation:

No statements available.

Phototoxicity:

No statements available.

Subacute, subchronic and prolonged toxicity:

No statements available.

STOT - single exposure:



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No statements available.

STOT - repeated exposure:

No statements available.

Aspiration toxicity:

No statements available.

Genotoxicity in vitro:

Drospirenon

Result: negative

Method: Mutagenicity (micronucleus test)

Genotoxicity in vivo:

No statements available.

Carcinogenicity:

Drospirenon

Suspected of causing cancer.

Estradiol-Hemihydrate

Sex steroids may stimulate the growth of hormone-dependent tissue and tumors.

Fertility:

Drospirenon

Result: May damage fertility.

Estradiol-Hemihydrate

Result: May damage fertility.

Developmental toxicity:

Drospirenon

Result: May damage the unborn child.

Estradiol-Hemihydrate

Result: Suspected of damaging the unborn child.

May cause harm to breast-fed children.

Human experience:

No statements available.

Neurotoxicity:

No statements available.

Neurological symptoms:

No statements available.



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Pharmaceutic effects:

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Contraceptive

Drospirenon

Steroid hormone

Estradiol-Hemihydrate

Steroid hormone

12. ECOLOGICAL INFORMATION

Ecotoxicology Assessment

No statements available.

12.1 Toxicity

Toxicity to fish:

Drospirenon

LC50 ca. 7 mg/l

Test species: Danio rerio (zebra fish) Duration of test: 3 h

Estradiol-Hemihydrate

LC50 > 0.5 mg/l

Test species: Oncorhynchus mykiss (rainbow trout) Duration of test: 96 h

No mortality in the water-soluble range.

Toxicity to daphnia and other aquatic invertebrates:

Drospirenon

EC50 > 7.8 mg/l

Test species: Daphnia pulex (Water flea) Duration of test: 48 h

Toxicity to algae:

No statements available.

Toxicity to bacteria:

No statements available.

Toxicity to fish (Chronic toxicity):

No statements available.

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):

No statements available.

Toxicity on soil-dwelling organisms:

No statements available.

Toxicity on other terrestrial non-mammal:

No statements available.



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12.2 Persistence and degradability

Biodegradability:

Estradiol-Hemihydrate

not rapidly biodegradable

Not toxic to the microbes of activated sludge.

Biochemical Oxygen Demand (BOD):

No statements available.

Chemical Oxygen Demand (COD):

No statements available.

BSB in proportion to CSB:

No statements available.

Dissolved organic carbon (DOC):

No statements available.

Adsorbed organic bound halogens (AOX):

No statements available.

Theoretical biological oxygen requirement:

No statements available.

BSB in proportion to ThSB:

No statements available.

Total organic carbon (TOC):

No statements available.

Physico-chemical removability:

No statements available.

Stability in water:

No statements available.

Additional degradation pathways:

No statements available.

Photodegradation:

No statements available.

M-Factor:

No statements available.

12.3 Bioaccumulative potential

Bioaccumulation:

No statements available.

Partition coefficient (n-octanol/water):

Estradiol-Hemihydrate

log Pow: 3.3



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12.4 Mobility in soil

Environmental distribution:

No statements available.

Surface tension:

No statements available.

Stability in soil:

No statements available.

12.5 Results of PBT and vPvB assessment

No statements available.

12.6 Other adverse effects

General advice:

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Do not allow to enter surface waters or groundwater.

13. DISPOSAL CONSIDERATIONS

13.1 Waste treatment methods

Transport to suitable incinerator with reduced non-air emission.

Contaminated packaging: Contaminated, empty containers are to be treated in the same way as the contents.

14. TRANSPORT INFORMATION

ADR/RID	--
GGVS/GGVE	--
ADNR	--
IATA	--
IMDG	--



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14.6 Special precautions for user

For personal protection see section 8.

14.7 Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

not applicable

Other information : No dangerous cargo
Keep separated from foodstuffs

15. REGULATORY INFORMATION

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

Guidelines and information sheets issued by the Chemical Industry Employers' Insurance Association:

The recommendations given in the leaflet of the "Berufsgenossenschaft der Chemischen Industrie" (Employers' Liability Insurance Association for the German Chemical Industry) entitled "Fruchtschädigungen - Schutz am Arbeits-platz" (M 039) should be followed.

15.2 Chemical Safety Assessment

No statements available.

16. OTHER INFORMATION

Full text of R-phrases referred to under sections 2 and 3

R22	Harmful if swallowed.
R40	Limited evidence of a carcinogenic effect.
R51/53	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.
R60	May impair fertility.
R61	May cause harm to the unborn child.
R63	Possible risk of harm to the unborn child.
R64	May cause harm to breastfed babies.

Full text of H-Statements mentioned in chapters 2 and 3

H302	Harmful if swallowed.
H351	Suspected of causing cancer.
H360Fd	May damage fertility. Suspected of damaging the unborn child.
H360FD	May damage fertility. May damage the unborn child.
H362	May cause harm to breast-fed children.
H411	Toxic to aquatic life with long lasting effects.



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H412 Harmful to aquatic life with long lasting effects.

Changes since the last version are highlighted in the margin. This version replaces all previous versions.

Further information

The information provided in this 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.