

CONTROL OF SUBSTANCES HAZARDOUS TO HEALTH (COSHH) SHEET

SECTION 1 – IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

PRODUCT NAME: Capecitabine Accord Film-coated Tablets 150, 300, 500 mg

PRODUCT USE: Pharmaceutical active substance (cytostatic)

COMPANY INFORMATION:

Accord Healthcare Limited
Sage House
319, Pinner Road
North Harrow
Middlesex, HA1 4HF
United Kingdom
Phone: +44 (0) 208 901 3370
E-Mail: uk@accord-healthcare.com

SYNONYMS:

- Capecitabine Accord Tablets (150, 300, 500 mg)
- Capecitabine Accord F.C. Tablets (150, 300, 500 mg)

SECTION 2 – HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

FORM: oblong, biconvex tablet

COLOR: strength-specific

POTENTIAL HEALTH EFFECTS

- Exposure: Inhalation, Ingestion, Skin contact, Eye contact
- Target Organs: eye, skin, mucous membranes, gastrointestinal system
- Acute Effects: May cause eye irritation. May cause skin irritation. May cause gastrointestinal effects. Signs and symptoms may include nausea, vomiting, diarrhea, constipation, cramps, and loss of appetite.
- Chronic Effects: May cause skin irritation.
- Carcinogenicity: formulation not listed by NTP, IARC or OSHA

GHS CLASSIFICATION

Health Hazards:

- 3.5 Germ cell mutagenicity (Category 2) H341. Suspected of causing genetic defects.
- 3.6 Carcinogenicity (Category 1B) H350. May cause cancer.
- 3.7 D Reproductive toxicity (Category 1B) H360D May damage the unborn child.

- 3.7 F Reproductive toxicity (Category 1B) H360F May damage fertility.

Precautionary statements:

- P201 Obtain special instructions before use.
- P260 Do not breathe dust
- P281 Use personal protective equipment as required.
- P308 + P313 IF exposed or concerned: Get medical advice/attention.

ADDITIONAL HEALTH INFORMATION

- Some components of this product are considered potential reproductive effectors at high dosage. Refer to Section 11 (Toxicological information) for additional information on this product.
- The most common dose-dependent adverse effects associated with therapeutic treatments include diarrhea, nausea, vomiting, sores in mouth and throat, abdominal pain, constipation, loss of appetite, dehydration, rash and dry, itchy or discolored skin.
- Additional effects may include nail problems, hair loss, tiredness, weakness, dizziness, headache, fever, chest, back, joint and muscle pain, trouble sleeping, taste problems and palms of the hands or soles of the feet tingle, become painful or swollen.

NOTE

Cytostatics in general have to be classified as potentially carcinogenic, teratogenic and mutagenic. During handling any occupational exposure as well as environmental contamination has to be avoided.

SECTION 3 – COMPOSITION/INFORMATION ON INGREDIENTS

CHARACTERIZATION: pharmaceutical active substance in the group of fluorinated cytosines

INGREDIENTS

Capecitabine

CAS: 154361-50-9

Microcrystalline cellulose

CAS: 9004-34-6

Magnesium stearate

CAS: 557-04-0

*1~ Capecitabine

SECTION 4 – FIRST AID MEASURES

SKIN EXPOSURE:

- Remove immediately contaminated clothes wash affected skin with water & soap.
- Do not use any solvents.
- Consult a physician if skin irritation persists.

EYE EXPOSURE:

- Rinse immediately with tap water for 10 minutes.
- Open eyelids forcibly.
- Consult a physician if irritation persists.

INHALATION:

- Remove the casualty to fresh air and keep him/her calm.
- Get medical treatment.

INGESTION:

- Summon a physician immediately.
- Let drink repeatedly plenty of water and induce vomiting (only if <conscious), repeat several times.

NOTE TO PHYSICIAN:

- Treat symptomatically
- In case of accidental exposure; keep a sample of urine in order to determine the content of fluoro- β -alanine.

SECTION 5 – FIRE FIGHTING MEASURES

SUITABLE EXTINGUISHING MEDIA: water spray jet, dry powder, foam, carbon dioxide

FLASH POINT (LIQUID): Not applicable

SPECIFIC HAZARDS:

- Very high probability of ignition of dust whirled up
- Formation of toxic and corrosive combustion gases (hydrogen fluoride, nitrogen oxides) possible
- Consider danger for the environment: dike spilled liquid

PROTECTION OF FIRE FIGHTERS:

- Precipitate gases/vapours/mists with water spray
- Use self-contained breathing apparatus
- Avoid skin contact

SECTION 6 – ACCIDENTAL RELEASE MEASURES**PERSONAL PRECAUTIONS:**

- Ensure adequate ventilation
- Keep people away and stay on the upwind side

ENVIRONMENTAL PROTECTION:

- Do not allow to enter drains or waterways
- If the substance reaches waters or the sewer system, inform the competent authority
- The solvent should be held back due to environmental protection

METHODS FOR CLEANING UP

- collect spilled material (avoid dust formation) and hand over to waste removal in sealed containers

SECTION 7 – HANDLING AND STORAGE

STORAGE CONDITIONS:

- Pack specific (Does not required any special storage condition or below 30 °C)
- Protected from light and humidity

VALIDITY: 3 years at specified condition, see "EXP" date stated on the label.

SECTION 8 – EXPOSURE CONTROLS/PERSONAL PROTECTION

ENGINEERING MEASURES: see 7.

MONITORING:

Threshold value (USA) air

- ACGIH-TLV: 10 mg/m³ *2
- OSHA-PEL: 15 mg/m³ (total dust) *2
- OSHA-PEL: 5 mg/m³ (respirable fraction) *2
- NIOSH-REL: 10 mg/m³ (total dust) *2
- NIOSH-REL: 5 mg/m³ (respirable fraction) *2

Threshold value (Roche) air

- IOEL (Internal Occupational Exposure Limit): 0.01 mg/m³ (defined as 8-hour time-weighted average) *1

PERSONAL PROTECTIVE EQUIPMENT:

Hand protection:

- Protective gloves (e.g. made of neoprene, nitrile or butyl rubber)

Eye protection:

- Safety glasses

General protective and hygiene measures:

- Instruction of employees mandatory
- Shower after work recommended

*1 referring to: Capecitabine

*2 referring to: Microcrystalline cellulose

SECTION 9 – PHYSICAL AND CHEMICAL PROPERTIES

COLOR: Strength-specific

FORM: Oblong, biconvex tablet

SOLUBILITY:

- 26'000 mg/l, water (20 °C) *1
- 207'000 mg/l, ethanol (20 °C) *1

PARTITION COEFFICIENT: log P_{ow} ~ 4.5 (n-octanol/water) pH 7.4 *1

MELTING TEMPERATURE: 116 to 117 °C *1

*1 referring to: Capecitabine

SECTION 10 – STABILITY AND REACTIVITY

STABILITY: Stable under the conditions mentioned in chapter 7.

SECTION 11 – TOXICOLOGY INFORMATION

ACUTE TOXICITY:

- LD50 > 2'000 mg/kg (oral, rat) *1
- LD50 > 2'000 mg/kg (oral, rat) *3

SENSITIZATION: Slightly sensitizing (several species) *1

SUBCHRONIC TOXICITY high doses may damage proliferating cells (e.g. bone marrow, leucocytes) *1

MUTAGENICITY:

- May cause mutations in vitro (clastogenic effect in lymphocytes) *1
- Lymphocyte test; evidence of clastogenicity *1

REPRODUCTIVE TOXICITY Suspected to be teratogenic and to lower parental fertility *1

NOTE:

- May cause diarrhea, nausea, vomiting, loss of appetite, irritation of mucous membranes and alteration of the hemopoietic system(leukopenia) in dependance of the dose *1
- Cytostatics are potentially carcinogenic *1

*1 referring to: Capecitabine

*3 referring to: Magnesium stearate

SECTION 12 – ECOLOGICAL INFORMATION

INHERENT BIODEGRADABILITY:

- inherently biodegradable evidence for prior abiotic primary degradation as a rate-limiting process
 - 29 %, 28 d
 - 44 %, 56 d
 - 55 %, 84 d
 - (MITI Test II, OECD No. 302 C) *1

ECOTOXICITY:

- Barely toxic for algae (*Selenastrum capricornutum*)
 - EbC50 (72 h) 58 mg/l
 - ErC50 (72 h) 200 mg/l
 - NOEC (72 h) 14 mg/l
 - (OECD No. 201) *1
- Barely toxic for planktonic crustaceans (*Daphnia magna*)
 - EC50 (48 h) > 850 mg/l
 - NOEC (48 h) 500 mg/l *1
- Barely toxic for fish (rainbow trout)
 - LC50 (96 h) > 867 mg/l
 - NOEC (96 h) 867 mg/l *1
- Barely inhibitory on aerobic bacterial respiration
 - EC50 > 1000 mg/l
 - (Activated Sludge Respir. Inhib. Test, OECD No. 209) *1

MOBILITY:

- Medium adsorption to activated sludge, medium mobility (water activated sludge, 3 h)
 - $K_d = 272 \text{ l/kg}$ (activated sludge)
 - (Adsorption to activated sludge in biodegradability test) *1

*1 referring to: Capecitabine

SECTION 13 – DISPOSAL CONSIDERATIONS**WASTE FROM RESIDUES:**

- Observe local/national regulations regarding waste disposal
- Incinerate in qualified installation with flue gas scrubbing
- DO NOT FLUSH unused medications or POUR them down a sink or drain. If available in your area, use takeback programs run by household hazardous waste collection programs or community pharmacies to dispose of unused and expired medicines. If you don't have access to a takeback program, dispose of these medicines in the household trash by removing them from their original containers and mixing them with an undesirable substance, such as used coffee grounds or kitty litter.

SECTION 14 – TRANSPORTATION INFORMATION**NOTE:** Not classified by transport regulations, proper shipping name non-regulated.**SECTION 15 – REGULATORY INFORMATION****TSCA STATUS:** FDA Exemption - not on inventory**Reporting Requirements**

- The United States Environmental Protection Agency (USEPA) has not established a Reportable Quantity (RQ) for releases of this material.
- In New Jersey, report all releases which are likely to endanger the public health, harm the environment or cause a complaint to the NJDEPE Hotline (1-609-292-5560) and to local officials.
- State and local regulations vary and may impose additional reporting requirements.

SECTION 16 – OTHER INFORMATION**Edition documentation:** NA

The information in this safety data sheet is based on current scientific knowledge and originator product. It should not be taken as expressing or implying any warranty concerning product characteristics.