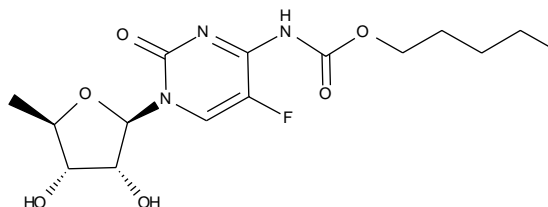


1. Product and Company Identification

Product name	Capecitabine	
Product code	04 4111 2	
Company information	Manufacturer: F. Hoffmann-La Roche AG Postfach CH-4070 Basel Switzerland	Local representation:
	Phone	+41-61/688 54 80
	Fax	+41-61/681 72 76

2. Composition/Information on ingredients

Characterization	pharmaceutical active substance in the group of fluorinated cytosines
Chemical name	- 5'-Deoxy-5-fluoro-N4-pentyloxycarbonyl-cytidine
Synonyms	- XELODA - NeoFurtulon successor - N-[1-(5-Deoxy-β-D-ribofuranosyl)-5-fluoro-1,2-dihydro-2-oxo-4-pyrimidinyl]-n-pentyl carbamate
CAS number	154361-50-9
UN number	3077
Roche number	Ro0091978-000
Empirical formula	C ₁₅ H ₂₂ FN ₃ O ₆
Molecular mass	359.34 g/mol



Capecitabine

3. Hazards identification

Most important hazards	<ul style="list-style-type: none">- Irritating to eyes and skin.- May cause cancer.- Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.- May cause harm to the unborn child.
Note	<ul style="list-style-type: none">- Cytostatics in general have to be classified as potentially carcinogenic, teratogenic and mutagenic. During handling any occupational exposure as well as environmental contamination have to be avoided.

4. First-aid measures

Eye contact	<ul style="list-style-type: none">- rinse immediately with tap water for 10 minutes - open eyelids forcibly- consult a physician if irritation persists
Skin contact	<ul style="list-style-type: none">- remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents- consult a physician if skin irritation persists
Inhalation	<ul style="list-style-type: none">- remove the casualty to fresh air and keep him/her calm- consult physician
Ingestion	<ul style="list-style-type: none">- summon a physician immediately- let drink repeatedly plenty of water and induce vomiting (only if conscious), repeat several times
Note to physician	<ul style="list-style-type: none">- treat symptomatically- in case of accidental exposure, keep a sample of urine in order to determine the content of fluoro-β-alanine

5. Fire-fighting measures

Suitable extinguishing media	<ul style="list-style-type: none">- water spray jet, dry powder, foam, carbon dioxide
Specific hazards	<ul style="list-style-type: none">- formation of toxic and corrosive combustion gases (hydrogen fluoride, nitrogen oxides) possible- consider danger for the environment: dike spilled liquid- consider dust explosion hazard
Protection of fire-fighters	<ul style="list-style-type: none">- precipitate gases/vapours/mists with water spray- use self-contained breathing apparatus- avoid skin contact

Capecitabine

6. Accidental release measures

- | | |
|--------------------------|--|
| Personal precautions | <ul style="list-style-type: none">- evacuate area, remove sources of ignition, ventilate- keep people away and stay on the upwind side |
| Environmental protection | <ul style="list-style-type: none">- avoid release to the environment |
| Methods for cleaning up | <ul style="list-style-type: none">- collect spilled material (avoid dust formation) and hand over to waste removal in sealed containers- clean floors and contaminated objects with plenty of water- collect spilled solutions with inert adsorbent and hand over to waste removal |

7. Handling and storage

Handling

- | | |
|--------------------|--|
| Technical measures | <ul style="list-style-type: none">- processing in closed systems, if possible superposed by inert gas (e.g. nitrogen)- local exhaust ventilation necessary- avoid dust formation; very high dust explosion hazard- take precautionary measures against electrostatic charging |
|--------------------|--|

Storage

- | | |
|---------------------|---|
| Storage conditions | <ul style="list-style-type: none">- room temperature- store in a dry place |
| Validity | <ul style="list-style-type: none">- 24 months, at room temperature- see expiry date on the label |
| Packaging materials | <ul style="list-style-type: none">- tightly closing; material: stainless steel, aluminium, enamel, glass, plastic |

8. Exposure controls/Personal protection

- | | |
|----------------------|--|
| Engineering Measures | <ul style="list-style-type: none">- see 7. |
|----------------------|--|

Monitoring

- | | |
|-----------------------------|--|
| Threshold value (Roche) air | <ul style="list-style-type: none">- IOEL (Internal Occupational Exposure Limit): 0.01 mg/m³ (defined as 8-hour time-weighted average) |
|-----------------------------|--|

Personal protective equipment

- | | |
|------------------------|---|
| Respiratory protection | <ul style="list-style-type: none">- in case of open handling or accidental release: particle mask or respirator with independent air supply |
| Hand protection | <ul style="list-style-type: none">- protective gloves (eg made of neoprene, nitrile or butyl rubber) |
| Eye protection | <ul style="list-style-type: none">- safety glasses |
| Body protection | <ul style="list-style-type: none">- protective clothing |

Capecitabine

- General protective and hygiene measures
- instruction of employees mandatory
 - shower after work recommended

9. Physical and chemical properties

Colour	white to light yellow
Form	powder
Odour	odourless
Bulk density	~ 0.2 g/cm ³
Solubility	26'000 mg/l, water (20 °C) 207'000 mg/l, ethanol (20 °C) > 40 %, methanol 11.8 %, acetonitrile > 59 %, dimethyl formamide 2.5 %, ethyl acetate
Partition coefficient	log P _{ow} ~ 4.5 (n-octanol/water) pH 7.4
Dissociation constant	pK ₁ = 8.8 (acidic group(s))
Melting temperature	116 to 117 °C

10. Stability and reactivity

- Stability
- stable under the conditions mentioned in chapter 7
- Conditions to avoid
- temperatures above 100 °C (decomposition)
- Materials to avoid
- strong acids (hydrolysis)

11. Toxicological information

- Acute toxicity
- LD₅₀ > 2'000 mg/kg (oral, rat)
- Sensitization
- slightly sensitizing (several species)
- Subchronic toxicity
- high doses may damage proliferating cells (e.g., bone marrow, leukocytes)
- Mutagenicity
- may cause mutations in vitro (clastogenic effect in lymphocytes)
 - lymphocyte test; evidence of clastogenicity
- Reproduction toxicity
- suspected to be teratogenic and to lower parental fertility
 - decreased weight of testis and epididymis, decrease and degeneration of spermatocytes and spermatids (760 mg/kg/d; oral, mouse, male)
 - reduced mating ability and fertility rate (760 mg/kg/d; oral, mouse, female)

Capecitabine

- Note
- may cause diarrhoea, nausea, vomiting, loss of appetite, irritation of mucous membranes and alteration of the haemopoietic system (leukopenia) in dependence of the dose
 - cytostatics are potentially carcinogenic

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)
- Abiotic degradation
- slow degradation, probably ester hydrolysis (30 mg/l; HPLC)
 $t_{1/2} \sim 21$ d, ~ 22 °C, pH ~ 7
 - rapid degradation only at very acidic pH (1000 mg/l, water; HPLC)
 $t_{1/2} \geq 60$ h, ~ 22 °C, pH 2
 $t_{1/2} \sim 6$ h, ~ 22 °C, pH 1
 $t_{1/2} < 2$ h, ~ 22 °C, pH 0.5
 $t_{1/2} \sim 1$ h, 30 °C, pH 0.5
- Ecotoxicity
- strongly toxic for algae (*Selenastrum capricornutum*)
EbC₅₀ (72 h) 0.58 mg/l
ErC₅₀ (72 h) 2.0 mg/l
NOEC (72 h) 0.14 mg/l
(OECD No. 201)
 - barely toxic for planktonic crustaceans (*Daphnia magna*)
EC₅₀ (48 h) > 850 mg/l
NOEC (48 h) 500 mg/l
 - barely toxic for fish (rainbow trout)
LC₅₀ (96 h) > 867 mg/l
NOEC (96 h) 867 mg/l
 - barely inhibitory on aerobic bacterial respiration
EC₅₀ > 1000 mg/l
(Activated Sludge Respir. Inhib. Test, OECD No. 209)
- Mobility
- medium adsorption to activated sludge, medium mobility (water-activated sludge, 3 h)
 $K_d = 272$ l/kg (activated sludge)
(Adsorption to activated sludge in biodegradability test)
- Note
- strictly avoid contamination of the environment

13. Disposal considerations

- Waste from residues
- observe local/national regulations regarding waste disposal
 - incinerate in qualified installation with flue gas scrubbing

Capecitabine

14. Transport information

IATA	Class	UN/ID	PG		PI	Label	
	9	3077	III		911/911	9	
IMDG	Class	UN	PG	EmS	PI	Label	Mark
	9	3077	III	F-A S-F	P002/IBC08	9	
RID/ADR	Class	UN	PG	Haz.no	PI	Label	Classif.code
	9	3077	III	90	P002/IBC08	9	M7

Proper shipping name ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

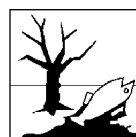
Technical name Capecitabine

15. Regulatory information

Classification and labelling according to EU directives



T



N

R36/38	Irritating to eyes and skin.
R45	May cause cancer.
R51/53	Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R61	May cause harm to the unborn child.
S22	Do not breathe dust.
S45	In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).
S36/37/39	Wear suitable protective clothing, gloves and eye/face protection.
S53	Avoid exposure --- obtain special instructions before use.
S61	Avoid release to the environment. Refer to special instructions/Safety data sheets.

Emission limit (Switzerland) 1 mg/m³ at mass-flux ≥ 5 g/h (carcinogenic, class 2)

Water hazard class (Germany) 3: strongly hazardous for water (own classification according to directive VwVwS of 17.05.1999)

Capecitabine

16. Other information

- | | |
|-----------------------|--|
| Use | - pharmaceutical active substance (cytostatic) |
| Edition documentation | - changes from previous version in sections 11 |

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