

---

**SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING**


---

<b>Exelixis, Inc.</b> <b>210 East Grand Avenue</b> <b>South San Francisco, CA 94080-0511</b> <b>E-mail: SDS@exelixis.com</b>	<b>Emergency telephone</b> <b>number: Chemtrec</b>	<b>+1 (800) 424-9300 (USA</b> <b>and Canada)</b> <b>+1 (703) 527-3887 (Collect</b> <b>calls accepted)</b>
---	---	--

---

**Product identifier** Cabozantinib Malate - Capsule formulation

**Synonyms** XL184, EXEL-7184, EXEL-02977184, BMS-907351

**Trade names** Cometriq™

**Chemical family** Quinoline

**Relevant identified uses of the substance or mixture and uses advised against** Cabozantinib malate drug product is approved for the treatment of patients with progressive, metastatic medullary thyroid cancer.

**Note** The pharmacological, toxicological and ecological properties of this product/mixture have not been fully characterized. This SDS for cabozantinib malate - capsule formulation is written to address potential worker health and safety issues associated with the handling of the formulated product/mixture. Workers manufacturing this product/mixture should consult the SDS for each ingredient for hazard information and handling recommendations.

**Issue Date** 22 May 2013

---

**SECTION 2 - HAZARDS IDENTIFICATION**


---

**Classification of the substance or mixture**

**Regulation (EC) 1272/2008 [GHS]** Reproductive Toxicity - Category 1B. Target organ systemic toxicity (repeat exposure) - Category 2. Mixture not yet fully tested

**Directive 67/548/EEC or 1999/45/EC** T - R60 (Repr. Cat 2), R48/22. Mixture not yet fully tested

**Label elements**

**CLP/GHS hazard pictogram**



---

**SECTION 2 - HAZARDS IDENTIFICATION ...continued**

---

<b>CLP/GHS signal word</b>	Danger
<b>CLP/GHS hazard statements</b>	H360F - May damage fertility. H373 - May cause damage to kidneys through prolonged or repeated exposure.
<b>CLP/GHS precautionary statements</b>	P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. P260 - Do not breathe dust. P281 - Use personal protective equipment as required. P308 + P313 - If exposed or concerned: get medical advice/attention. P314 - Get medical advice/attention if you feel unwell. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.
<b>Other hazards</b>	The most commonly reported adverse drug reactions ( $\geq 25\%$ ) are: diarrhea, stomatitis, palmar-plantar erythrodysesthesia syndrome (PPES), decreased weight, decreased appetite, nausea, fatigue, oral pain, hair color changes, dysgeusia (distortion in sense of taste), hypertension, abdominal pain, and constipation.
<b>US Signal word</b>	Warning
<b>US Hazard overview</b>	If capsules are crushed or broken, may cause adverse reproductive effects and kidney damage (based on animal data). Product/mixture not yet fully tested.
<b>Note</b>	This mixture should be considered hazardous according to Directive 67/548/EEC, Regulation (EC) No 1272/2008 (EU CLP) and applicable US regulations. The pharmacological, toxicological, and ecological properties of this mixture have not been fully characterized. See Section 16 for full text of EU and GHS classifications. The GHS classifications are based on Regulation (EC) 1272/2008.

---

**SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS**

---

<u>Ingredient</u>	<u>CAS #</u>	<u>EINECS/ELIN</u> <u>CS#</u>	<u>Amount</u>	<u>EU</u> <u>Classification</u>	<u>GHS</u> <u>Classification</u>
Cellulose	9004-34-6	232-674-9	75-84%	Not classified	Not classified
Cabozantinib Malate	1140909-48-3	N/A	7-13%	Toxic - T: R60, R22, R48/22	RT1B-H360F; STOT-RE2- H373; ATO4-H302
Stearic acid	57-11-4	200-313-4	1-3%	Not classified	Not classified

**Note** The ingredients listed above are considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of EU and EU/CLP or GHS classifications. The pharmacological, toxicological, and ecological properties of this mixture have not been fully characterized. The EU classification is based on Directive 67/548/EEC and the GHS classification is based on Regulation (EC) 1272/2008.

---

**SECTION 4 - FIRST AID MEASURES**

---

**Description of first aid measures**

<b>Immediate Medical Attention Needed</b>	Yes
<b>Eye Contact</b>	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.
<b>Skin Contact</b>	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
<b>Inhalation</b>	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
<b>Ingestion</b>	If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
<b>Protection of first aid responders</b>	See Section 8 for Exposure Controls/Personal Protection recommendations.
<b>Most important symptoms and effects, both acute and delayed</b>	See Sections 2 and 11
<b>Indication of immediate medical attention and special treatment needed, if necessary</b>	Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions.

---

**SECTION 5 - FIREFIGHTING MEASURES**

---

<b>Extinguishing media</b>	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
<b>Specific hazards arising from the substance or mixture</b>	No information identified. May emit toxic fumes of carbon monoxide, carbon dioxide, oxides of nitrogen, and fluorine-containing compounds.
<b>Flammability/Explosivity</b>	No explosivity or flammability data identified. High concentrations of finely divided airborne organic particles can potentially explode if ignited.
<b>Advice for firefighters</b>	Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use.

---

**SECTION 6 - ACCIDENTAL RELEASE MEASURES**

---

<b>Personal precautions, protective equipment and emergency procedures</b>	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated.
<b>Environmental precautions</b>	Do not empty into drains. Avoid release to the environment.
<b>Methods and material for containment and cleaning up</b>	For small spills (such as in a laboratory), soak up material with absorbent, e.g., damp paper towel, and wash spill area thoroughly with soap and water. For large spills in manufacturing, use an industrial vacuum cleaner equipped with a high efficiency particulate (HEPA) filter if available. Alternatively if in solid or dried form, do not raise dust. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize powder from entering the air. Add excess liquid to allow for the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.
<b>Reference to other sections</b>	See Sections 8 and 13 for more information.

---

**SECTION 7 - HANDLING AND STORAGE**

---

<b>Precautions for safe handling</b>	Avoid contact with eyes, skin and other mucous membranes. Avoid breathing dust. Wash thoroughly after handling. Use only in a well-ventilated area.
<b>Conditions for safe storage including any incompatibilities</b>	Store at room temperature away from incompatible materials. Keep out of reach of children. Avoid extreme temperatures. Protect from light and heat.
<b>Specific end use(s)</b>	No information identified.

---

**SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION**

---

**Control  
Parameters/Occupational  
Exposure Limit Values**

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>
Cellulose	ACGIH, Australia, Belgium, Estonia, France, Portugal, Romania, Singapore, Spain	TWA-8 HR	10 mg/m <sup>3</sup>

---

**SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued**


---

**Control  
Parameters/Occupational  
Exposure Limit Values  
...continued**

<u>Compound</u>	<u>Issuer</u>	<u>Type</u>	<u>OEL</u>	
	Ireland, United Kingdom	TWA-8 HR	10 mg/m <sup>3</sup> (inhalable dust); 4 mg/m <sup>3</sup> (respirable dust)	
	Ireland	STEL	20 mg/m <sup>3</sup> (total inhalable dust)	
	Latvia	TWA-8 HR	2 mg/m <sup>3</sup>	
	Mexico	TWA-8 HR/STEL	10/20 mg/m <sup>3</sup>	
	NIOSH	TWA-8 HR	10 mg/m <sup>3</sup> (total dust); 5 mg/m <sup>3</sup> (respirable dust)	
	OSHA	TWA-8 HR	15 mg/m <sup>3</sup> (total dust); 5 mg/m <sup>3</sup> (respirable fraction)	
	United Kingdom	STEL	20 mg/m <sup>3</sup> (inhalable dust); 12 mg/m <sup>3</sup> (respirable dust)	
	Cabozantinib Malate	BMS	OEL-TWA	3 µg/m <sup>3</sup>
	Stearic acid	ACGIH	TWA-8 HR	10 mg/m <sup>3</sup> (stearates)

**DNELs/PNECs** None identified.

**Exposure/Engineering controls** None required for normal handling of packaged product. If handling bulk capsules, avoid breakage to limit dust generation. If capsules are crushed, chipped or broken: selection and use of engineering controls, containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Capsule transfers should be done utilizing closed systems and/or with local exhaust ventilation in place to limit the potential for dust emissions. Open handling should not be performed when handling potent substances, or substances of unknown toxicity. Capsules should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

**Respiratory protection** None required for normal handling of packaged product. If capsules are crushed or broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine handling tasks, an approved and properly fitted air-purifying respirator with appropriate HEPA filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a powered air-purifying respirator equipped with appropriate HEPA filters or combination filters or a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where a lower level of respiratory protection may not provide adequate protection.

---

**SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued**

---

<b>Hand protection</b>	Should not be needed for normal handling of packaged product. Impervious gloves are recommended if skin contact with product is possible and for bulk processing operations. Base the choice of hand protection on the job activity and potential for hand contact.
<b>Skin protection</b>	None required for normal handling of packaged product. Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.
<b>Eye/face protection</b>	Should not be needed during normal handling of packaged product. Wear safety glasses with side shields if eye contact is likely, e.g., during clean-up of large spill. Base the choice of protection on the job activity and potential for contact with eyes and face.
<b>Environmental Exposure Controls</b>	Should not be required during normal handling of packaged product. In case of spill, do not release to drains. Avoid release to the environment.
<b>Other protective measures</b>	Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors). Decontaminate all protective equipment following use.

---

**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES**

---

**Information on basic physical and chemical properties**

<b>Appearance</b>	Capsule
<b>Color</b>	Gray/opaque (20 mg) or Swedish orange/opaque (80 mg)
<b>Odor</b>	No information identified.
<b>Odor threshold</b>	No information identified.
<b>pH</b>	Not applicable.
<b>Melting point/freezing point</b>	No information identified.
<b>Initial boiling point and boiling range</b>	Not applicable
<b>Flash point</b>	No information identified.
<b>Evaporation rate</b>	No information identified.
<b>Flammability (solid, gas)</b>	No information identified.

---

**SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES ...continued**

---

<b>Upper/lower flammability or explosive limits</b>	No information identified.
<b>Vapor pressure</b>	No information identified
<b>Vapor density</b>	No information identified.
<b>Relative density</b>	No information identified.
<b>Water solubility</b>	No information identified.
<b>Solvent solubility</b>	No information identified.
<b>Partition coefficient (n-octanol/water)</b>	No information identified.
<b>Auto-ignition temperature</b>	No information identified.
<b>Decomposition temperature</b>	No information identified.
<b>Viscosity</b>	No information identified.
<b>Explosive properties</b>	No information identified.
<b>Oxidizing properties</b>	No information identified.
<b>Other information</b>	
<b>Molecular weight</b>	635.6 (cabozantinib malate)
<b>Molecular formula</b>	C <sub>28</sub> H <sub>24</sub> FN <sub>3</sub> O <sub>5</sub> ·C <sub>4</sub> H <sub>6</sub> O <sub>5</sub> (cabozantinib malate)
<b>Other</b>	<i>Ignitability</i> : Minimum Ignition Energy - between 10-30 mJ (Mike 3 apparatus) - (cabozantinib malate)

---

**SECTION 10 - STABILITY AND REACTIVITY**

---

<b>Reactivity</b>	Avoid strong acids, bases and oxidizers.
<b>Chemical stability</b>	Stable under normal handling and storage conditions.
<b>Possibility of hazardous reactions</b>	Not expected to occur.
<b>Conditions to avoid</b>	Avoid direct sunlight and conditions that might generate heat.
<b>Incompatible materials</b>	No information identified.
<b>Hazardous decomposition products</b>	No information identified.

---

**SECTION 11 - TOXICOLOGICAL INFORMATION**

---

**Information on toxicological effects**

**Route of entry** May be absorbed by inhalation, skin contact and ingestion.

**Acute toxicity**

<u>Compound</u>	<u>Type</u>	<u>Route</u>	<u>Species</u>	<u>Dose</u>
Cellulose	LC <sub>50</sub>	Inhalation	Rat	>5800 mg/m <sup>3</sup> /4h
	LD <sub>50</sub>	Oral	Rat	>5000 mg/kg
	LD <sub>50</sub>	Dermal	Rabbit	>2000 mg/kg
Cabozantinib Malate	LD <sub>50</sub>	Oral	Rat	300 mg/kg
	NOAEL	Oral	Rat	<100 mg/kg
	NOAEL	Oral	Dog	2000 mg/kg
Stearic acid	LD <sub>50</sub>	Oral	Rat	>4640 mg/kg
	LC <sub>50</sub>	Inhalation	Rat	>2000 mg/m <sup>3</sup>
	LD <sub>50</sub>	Dermal	Rabbit	>5000 mg/kg

**Irritation/Corrosion** No data available.

**Sensitization** No data available.

**STOT-single exposure** No information identified.

**STOT-repeated exposure/Repeat-dose toxicity** Repeated dose studies with cabozantinib malate in rodents produced dose-dependent renal toxicity. In 26-week oral studies in rats, the LOAEL was 1 mg/kg/day, with a NOAEL of 0.3 mg/kg/day. Repeated dose studies in dogs produced changes in reproductive tissues (e.g., moderate to severe bilateral hypospermatogenesis in testes, and lack corpora lutea in ovaries), and were correlated with decreased testicular and ovarian weights. In 26-week oral studies in dogs, the NOAEL was 5 mg/kg/day, with a maximum tolerated dose (MTD) of 20 mg/kg/day.

**Reproductive toxicity** In rats given oral doses of 0, 1, 2.5, or 5 mg/kg/day cabozantinib malate prior to mating, the NOAEL for reproductive performance and fertility was 1 mg/kg/day in males and <1 mg/kg/day in females.

**Developmental toxicity** In rats given an oral dose of 0.6 mg/kg/day cabozantinib malate during organogenesis, teratogenic effects noted included: edema, cleft palate/lip, dermal aplasia and kinked/rudimentary tail. Increased post-implantation losses were noted at 0.03 mg/kg/day, but not at 0.01 mg/kg/day. In rabbits given oral doses of 0, 0.3, 1, or 3 mg/kg/day during organogenesis, the LOAEL and NOAEL for birth defects was 3 mg/kg/day (reduced spleen size) and 1 mg/kg/day, respectively.

**Genotoxicity** Cabozantinib malate was negative in an Ames bacterial cell mutagenicity assay, a chromosomal aberration assay in human peripheral lymphocytes, and in an *in vivo* mouse bone marrow micronucleus assay.

**Carcinogenicity** No studies identified. This substance is not listed by NTP, IARC, ACGIH or OSHA as a carcinogen.

**Aspiration hazard** No data available.



---

**SECTION 11 - TOXICOLOGICAL INFORMATION ...continued**

---

**Human health data** See "Section 2 - Other Hazards"

---

**SECTION 12 - ECOLOGICAL INFORMATION**

---

**Toxicity**

<u>Compound</u>	<u>Type</u>	<u>Species</u>	<u>Concentration</u>
Cellulose	--	--	--
Cabozantinib Malate	--	--	--
Stearic acid	--	--	--

**Additional toxicity information** No data available.

**Persistence and Degradability** No data available.

**Bioaccumulative potential** No data available.

**Mobility in soil** No data available.

**Results of PBT and vPvB assessment** No data available.

**Other adverse effects** No data available.

**Note** The environmental characteristics of this product/mixture have not been fully investigated. Releases to the environment should be avoided.

---

**SECTION 13 - DISPOSAL CONSIDERATIONS**

---

**Waste treatment methods** Used product should be disposed of according to local, state, and federal regulations. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

---

**SECTION 14 - TRANSPORT INFORMATION**

---

**Transport** Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.

**UN number** None assigned.

---

**SECTION 14 - TRANSPORT INFORMATION ...continued**

---

<b>UN proper shipping name</b>	None assigned.
<b>Transport hazard classes and packing group</b>	None assigned.
<b>Environmental hazards</b>	Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant.
<b>Special precautions for users</b>	Mixture not fully tested - avoid exposure.
<b>Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code</b>	Not applicable.

---

**SECTION 15 - REGULATORY INFORMATION**

---

<b>Safety, health and environmental regulations/legislation specific for the substance or mixture</b>	This SDS complies with the requirements under US, EU and GHS (EU CLP - Regulation EC No 1272/2008) guidelines.
<b>Chemical safety assessment</b>	Not conducted.
<b>OSHA Hazardous</b>	Yes. May cause adverse reproductive effects (based on animal data). May cause kidney damage (based on animal data). Mixture not fully tested.
<b>WHMIS classification</b>	Not required. Drugs and cosmetics are not subject to WHMIS. This SDS is compliant with the hazard criteria of the Controlled Products Regulations and the SDS contains all of the information required by those regulations.
<b>TSCA status</b>	Not listed
<b>SARA section 313</b>	Not listed.
<b>California proposition 65</b>	Not listed.

---

**SECTION 16 - OTHER INFORMATION**

---

<b>Full text of R phrases and EU Classifications</b>	T - Toxic. R60 - May impair fertility. R48/22 - Danger of serious damage to health by prolonged exposure if swallowed.
<b>Full text of H phrases, P phrases and GHS classification</b>	RT1B - Reproductive toxicity Category 1B. H360F - May damage fertility. STOT-RE2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H373 - May cause damage to kidneys through prolonged or repeated exposure.

---

**SECTION 16 - OTHER INFORMATION ...continued**

---

<b>Sources of data</b>	Information from published literature and internal company data.
<b>Abbreviations</b>	ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System
<b>Revisions</b>	This is the first version of this SDS.
<b>Disclaimer</b>	The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions. No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.