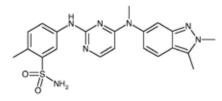




Background: Pazopanib is a multikinase inhibitor that potently targets VEGFR1 (IC₅₀ = 10 nM), VEGFR2 (IC₅₀ = 30 nM), VEGFR3 (IC₅₀ = 47 nM), PDGFR α (IC₅₀ = 71 nM), PDGFR β (IC₅₀ = 84 nM), and c-Kit (IC₅₀ = 74 nM) tyrosine kinases involved in tumor progression and angiogenesis, and can also inhibit many other tyrosine kinases at nanomolar concentrations (1). Research studies have demonstrated that pazopanib effectively blocks ligand-induced autophosphorylation of VEGFR2, PDGFRB, and c-Kit in vitro (1,2), and selectively inhibits VEGF-induced HUVE cell proliferation over FGF (IC₅₀ = ~21 nM vs ~720 nM). Investigators have demonstrated that pazopanib inhibits the growth, survival, and migration of multiple myeloma (MM) cell types (3).

Molecular Formula: C₂₁H₂₂N₇O₂S



Molecular Weight: 437.52 g/mol

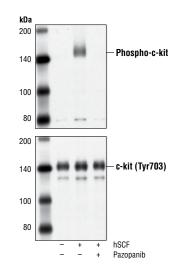
Solubility: Soluble in DMSO at 8 mg/mL with slight warming; very poorly soluble in ethanol and water with maximum in water ~10-20 µM.

Purity: >99%

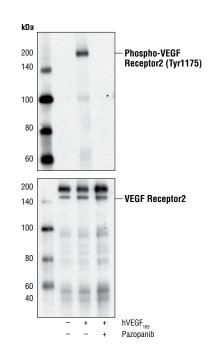
Directions for Use: Pazopanib is supplied as a lyophilized powder. For a 10 mM stock, reconstitute the 10 mg in 2.29 ml DMSO. Working concentrations and length of treatment can vary depending on the desired effect, but it is typically used as a pretreatment at 0.1-10 µM for 0.5-2 hr prior to treating with a stimulator. It can also be used alone, with varying treatment times lasting up to 24 hr.

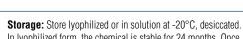
Western blot analysis of extracts from HUVE cells, serum-starved overnight and untreated (-) or treated with Human Vascular Endothelial Growth Factor (hVEGF165) #8065 (50 ng/ml, 5 min; +) either with our without pazopanib pre-treatment (1 μ M, 2 hr; +), using Phospho-VEGF Receptor 2 (Tyr1175) (19A10) Rabbit mAb #2478 (upper) or VEGF Receptor 2 (55B11) Rabbit mAb #2479 (lower).

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Western blot analysis of extracts from NCI-H526 cells, serumstarved overnight and untreated (-) or treated with Human Stem Cell Factor (hSCF) #8925 (100 ng/ml, 5 min; +) either with our without pazopanib pre-treatment (1 µM, 2 hr; +), using Phospho-c-Kit (Tyr703) (D12E12) Rabbit mAb #3073 (upper) or c-Kit (D13A2) XP® Rabbit mAb #3074 (lower).





In lyophilized form, the chemical is stable for 24 months. Once in solution, use within 3 months to prevent loss of potency. Aliquot to avoid multiple freeze/thaw cycles.

Background References:

- (1) Kumar, R. et al. (2007) Mol Cancer Ther 6, 2012-21.
- (2) Kumar, R. et al. (2009) Br J Cancer 101, 1717-23.
- (3) Podar, K. et al. (2006) Proc Natl Acad Sci USA 103, 19478-83.

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Cell Signaling TECHNOLOGY SAFETY DATA SHEET (SDS): According to the OSHA Hazard Communication Standard 29 CFR 1910.1200 Issuing Date: 2014-03-13 Revision Date: 2014-03-13 Version: 1 SECTION 1. Identification Product identifier Product No. Product name Other means of identification 12466 Pazopanib 12466S Recommended use of the chemical and restrictions on use This product is intended for research purposes only. This product is not intended for use in diagnostic procedures or therapeutics. This product is not intended for use in humans or animals. Identified uses Uses advised against Manufacturer, importer, supplier Cell Signaling Technology, Inc. 3 Trask Lane Danvers, MA 01923 TEL: +1 978 867 2300 FAX: +1 978 867 2400 nufacturer address Website Email address Company phone number Emergency telephone number PA. +1 5ro Gor support@cellsignal.com 978-867-2300 In case of emergency call CHEMTREC 1-800-424-9300 SECTION 2. Hazard(s) identification Classification This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200) Category 1B Reproductive toxicity Specific target organ toxicity - repeated exposure (STOT RE) Category 1 GHS Label elements, including precautionary statements Signal Word

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Hazard statement(s) May damage fertility or the unborn child Causes damage to organs through prolonged or repeated exposure

Precautionary Statement(s)

Precationary statistication (1) Obtain special instructions before use Do not handle until all safety precautions have been read and understood Use personal prodective equipment as required Do not breathe dust/tume/gas/mist/vapors/spray Wash face, hands and any exposed skin thoroughly after handling IF exposed or concerned: Get medical advice/attention

Supplementary Hazard Information

Hazards not otherwise classified (HNOC) No information available Unknown Acute Toxicity 100% of the mixture consists of ingredient(s) of unknown toxicity.

SECTION 3. Composition/information on ingredients			
Formula	C21H23N7O2S		
Molecular Weight	437.52		
Common name	Pazopanib		
Synonyms	Pazopanib; Votrier	nt; GW786034; UNII-7RN5DR86CH	K
Chemical N	Name	CAS No.	Weight %
5-[[4-[(2,3-Dimethyl-2H-indaz -pyrimidinyl]amino]-2-meth		444731-52-6	60-100
		4. First-aid measures	
Eye contact	Rinse thoroughly v	vith plenty of water for at least 15 n	ninutes, lifting lower and upper eyelids
	Rinse thoroughly v Consult a physicia	vith plenty of water for at least 15 n n.	ninutes, lifting lower and upper eyelid
Eye contact Skin contact Inhalation	Rinse thoroughly v	vith plenty of water for at least 15 n n.	ninutes, lifting lower and upper eyelid
Skin contact	Rinse thoroughly v Consult a physicia Wash skin with so Move to fresh air.	vith plenty of water for at least 15 n n.	
Skin contact Inhalation Ingestion	Rinse thoroughly v Consult a physicia Wash skin with so Move to fresh air. Clean mouth with	with plenty of water for at least 15 n n. ap and water. water and afterwards drink plenty o	
Skin contact Inhalation	Rinse thoroughly v Consult a physicia Wash skin with so Move to fresh air. Clean mouth with and effects, both acute and	with plenty of water for at least 15 n n. ap and water. water and afterwards drink plenty c I delayed	

Hepatoxicity manifested as increases in serum transaminases (ALT, AST) and bilirubin; can be severe and fatal. Hemorrhagic events have been reported. Notes to physiciar

Advice for emergency responders

For further assistance, contact your local Poison Control Center.
Ensure that medical personnel are aware of the material(s) invol-

nedical personnel are aware of the material(s) involved, and take precautions to protect themselves

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SECTION 5. Fire-fighting measures

Extinguishing media

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Suitable Extinguishing Media Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Unsuitable Extinguishing Media CAUTION: Use of water spray when fighting fire may be inefficient. Specific hazards arising from the chemical No information available. Explosion Data Sensitivity to Mechanical Impact None. Sensitivity to Static Discharge None. Protective Equipment and Precautions for Firefighters As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear. SECTION 6. Accidental release measures Personal precautions, protective equipment and emergency procedures For non-emergency personnel Ensure adequate ventilation. Other information No information available. Environmental precautions Do not flush into surface water or sanitary sewer system Methods and material for containment and cleaning up Prevent further leakage or spillage if safe to do so. Use personal protective equipment. Cover powder spill with plastic sheet or tarp to minimize spreading and keep powder dry. Take up mechanically and collect in suitable container for disposal. Avoid dust formation. Clean containminated surface thoroughly. Methods for containment Methods for cleaning up SECTION 7. Handling and storage Precautions for safe handling Handle in accordance with good industrial hygiene and safety practice Conditions for safe storage, including any incompatibilities Technical measures/Storage Keep containers tightly closed in a dry, cool and well-ventilated place conditions Packaging material Incompatible products No information available. None known based on information supplied. SECTION 8. Exposure controls/personal protection

Control parameters

12466 - Pazopanib

This product, as supplied, does not contain any hazardous materials with occupational exposure limits established by the region specific regulatory bodies.

Appropriate engineering controls

Showers, evewash stations, and ventilation systems.

Individual protection measures, such as personal protective equipment

Personal protective equipment (PPE) needs to be selected depending on the implemented engineering controls,

frequency/duration of work activitie	s and the concentrations of the hazardous substance.
Eye/face protection	Safety glasses with side-shields.
Skin and body protection	Wear protective gloves/clothing.
Respiratory protection	If exposure limits are exceeded or irritation is experienced, NIOSH/MSHA approved respiratory protection should be worn. Positive-pressure supplied air respirators may be required for high airborne contaminant concentrations. Respiratory cortection must be
	provided in accordance with current local regulations.

Do not eat, drink or smoke when using this product Hygiene measures SECTION 9. Physical and chemical properties

Information on basic physical and chemical properties

Physical state	Solid
Appearance	Crystalline powder
Odor	No information available
Color	White to off-white
Odor Threshold	No information available
pH	No information available
Melting point/freezing point	301-303 °C
Initial boiling point and boiling	No information available
range	
Flash point	No information available
Evaporation rate	No information available
Flammability (solid, gas)	No information available
Upper flammability limit	No information available
Lower flammability limit	No information available
Vapor pressure	No information available
Vapor density	No information available
Relative density	No information available
Solubility	Practically insoluble
Solubility in other solvents	8.3 mg/mL in Dimethyl sulfoxide (DMSO) with slight warming; very poorly soluble in Ethanol (EtOH).
Partition coefficient: n-octanol/wa	aterNo information available
Autoignition temperature	No information available
Decomposition temperature	No information available
Explosive properties	No information available
Oxidizing properties	No information available
Molecular Weight	437.52
VOC content	No information available
Viscosity	No information available
Density	No information available
-	
	SECTION 10. Stability and reactivity

Reactivity

No information available

Chemical stability

Stable under recommended storage conditions

12466 - Pazopanib		Revision Date: 2014-03-13
Possibility of hazardous reaction	ns	
Hazardous reactions Hazardous polymerization	None under normal processing. None under normal processing.	
Conditions to Avoid		
No information available.		
Incompatible Materials		
None known based on information	supplied.	
Hazardous Decomposition Prod	ucts	
None known based on information	supplied.	
	SECTION 11. Toxicological information	
Information on likely routes of e	xposure	
Inhalation	There is no data available for this product.	
Eye contact	There is no data available for this product.	
Skin contact	There is no data available for this product.	
Ingestion	May cause adverse liver effects.	
Information on toxicological effe	ects	
This product is for experimental us known. Please use caution while h	es only. The product has not been completely analyzed and all andling this product.	of the hazards may not be

Symptoms	Symptoms of overexposure may be headache, dizziness, tiredness, nausea and vomiting
Corrosivity	No information available.
Sensitization	No information available.
Mutagenic effects	Not mutagenic in AMES Test.
Carcinogenicity	No component of this product present at levels greater than or equal to 0.1% is identifiab as probable, possible or confirmed carcinogen by IARC, ACGIH, NTP, or OSHA.
Reproductive toxicity	This material is classified as a Pregnancy Category D: Positive evidence of risk.
STOT - single exposure	No information available.
STOT - repeated exposure	Causes damage to organs through prolonged or repeated exposure if swallowed. May cause disorder and damage to the: Liver.
Target Organ Effects	Liver, Reproductive system, Digestive System.
Neurological effects	No information available.
Aspiration Hazard	No information available.

Ecotoxicity

100% of the mixture consists of components(s) of unknown hazards to the aquatic environment

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12466 - Pazopanib CERCLA

This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) 40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material.

California Proposition 65

This product does not contain any Proposition 65 chemicals.

U.S. State Right-to-Know Regulations

This product does not contain any substances regulated under applicable state right-to-know regulations

U.S. EPA Label Information

This product does not contain any substances regulated as pesticides.

SECTION 16. Other information

Issuing Date: 2014-03-13 Revision Date: 2014-03-13 Disclaimer

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.

End of Safety Data Sheet

12466 - Pazopanib

Mobility

No information available. No information available. No information available Persistence and degradability Bioaccumulation

Other adverse effects

No information available

Waste Disposal Methods

Dispose of in accordance with all applicable national environmental laws and regulations.

Disposal considerations

Do not empty into drains; dispose of this material and its container in a safe way.

SECTOIN 14. Transport information

SECTION 13. Disposal considerations

This material is not subject to regulation as a hazardous material for shipping.

SECTION 15. Regulatory information				
North American Inventory Listing				
Component	TSCA	DSL	NDSL	
5-[[4-[(2,3-Dimethyl-2H-indazol-6-yl)m	Not Listed	Not Listed	Not Listed	
ethylamino]-2-pyrimidinyl]amino]-2-met				
hylbenzolsulfonamide				
444731-52-6 (60-100)				

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372.

Yes Yes No No No

SARA 311/312 Hazard Categories

Acute	Health Haz	ard			
Chroni	c Health H	lazard			
Fire Ha	zard				
Sudde	n Release	of Press	ure Haza	rd	
Reacti	ve Hazard				

Clean Water Act

This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42).

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