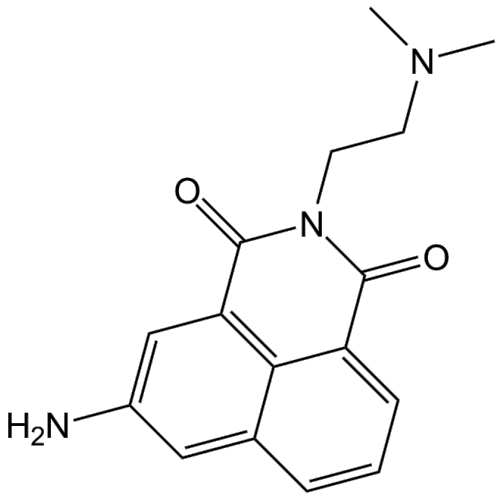
Product Data Sheet

Product Name: Amonafide
Cat. No.: GC11019

Chemical Properties

Cas. No.	69408-81-7		
Chemical Name	5-amino-2-[2-(dimethylamino)ethyl]benzo[de]isoquinoline-1,3-dione		
SMILES	CN(C)CCN1C(=O)C2=CC=CC3=CC(=CC(=C32)C1=O)N		
Formula	$C_{16}H_{17}N_3O_2$	M.Wt	283.33
Solubility	≥ 14.2mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.
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Cell experiment: In experiments measuring survival following 1 h drug treatments, 2 × 106cells are resuspended in 2 mL warm (37°C) HBSS with 5% PCS; the appropriate drug (Amonafide) level is attained with the addition of less than 50 μL. Cells are incubated for 60 min at 37°C after which 10 mL ice cold PBS is added. The cells are then centrifuged at 200 × g for 10 min at 4°C. The wash is repeated once and the cells are resuspended in HBSS with 5% PCS and added to the agar-medium mixture for assessment of surviving clonogenic cells[2].

References:

[1]. Allen SL, et al. Amonafide: a potential role in treating acute myeloid leukemia. Expert Opin Investig Drugs. 2011 Jul;20(7):995-1003.
[2]. Andersson BS, et al. In vitro toxicity and DNA cleaving capacity of benzisoquinolinedione (nafidimide; NSC 308847) in human leukemia. Cancer Res. 1987 Feb 15;47(4):1040-4.
[3]. Ajani JA, et al. In vitro activity of amonafide against primary human tumors compared with the activity of standard agents. Invest New Drugs. 1988 Jun;6(2):79-85.

Background

IC50: 4.67, 2.73, and 6.38 for HT-29, HeLa, and PC3 cells, respectively

Amonafide is a novel topoisomerase II inhibitor. Topoisomerase II plays critical roles including DNA transcription, replication and chromosome segregation. Though the biological functions of topoisomerase II are important for insuring genomic integrity, the ability to interfere with topoisomerase II and generate enzyme mediated DNA damage is an effective strategy for cancer chemotherapy.

In vitro: Amonafide intercalated with DNA and disrupted the loading of topoisomerases. In contrast to the classic agents, amonafide was found to induce higher molecular weight fragmentation, resulting in the apoptosis without DNA cleavage. Amonafide was found to act in an ATP-independent manner and seemed unlikely to induce the chromosome translocations associated with treatmentinduced leukemia [1].

In vivo: Amonafide was found to be able to inhibit IP L1210 leukemia, with optimal increased life

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spans (ILS) of 61% to 106% following single 16 mg/kg dosing on days 1 to 9. Similar efficacy was noted against IP P388 murine leukemia and the SC implanted L1210 leukemia. Additionally, amonafide demonstrated activity against two nonleukemic IP implanted murine tumors, the M5076 sarcoma and the B16 melanoma [2].

Clinical trial: A multicenter, open-label, combination Phase II study was conducted for patients with sAML, evaluating the efficacy of cytarabine and amonafide administered as a continuous iv. Infusion of cytarabine on days 1-7 combined with 600 mg/m2/day for days 1-5[1].

References:

[1] Freeman CL,Swords R,Giles FJ. Amonafide: a future in treatment of resistant and secondary acute myeloid leukemia Expert Rev Hematol.2012 Feb;5(1):17-26.
[2] Saez R,Craig JB,Kuhn JG,Weiss GR,Koeller J,Phillips J,Havlin K,Harman G,Hardy J,Melink TJ, et al. Phase I clinical investigation of amonafide. J Clin Oncol.1989 Sep;7(9):1351-8.

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