Print Date: Nov 8th 2016

Certificate of Analysis

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Product Name: **XMD 8-92** **Catalog No.: 4132** **Batch No.: 2**

CAS Number: 1234480-50-2

IUPAC Name: 2-[[2-Ethoxy-4-(4-hydroxy-1-piperidinyl)phenyl]amino]-5,11-dihydro-5,11-dimethyl-6*H*-pyrimido[4,5-b][1,4] benzodiazepin-6-one

1. PHYSICAL AND CHEMICAL PROPERTIES

Batch Molecular Formula: $C_{26}H_{30}N_6O_3.¼H_2O$

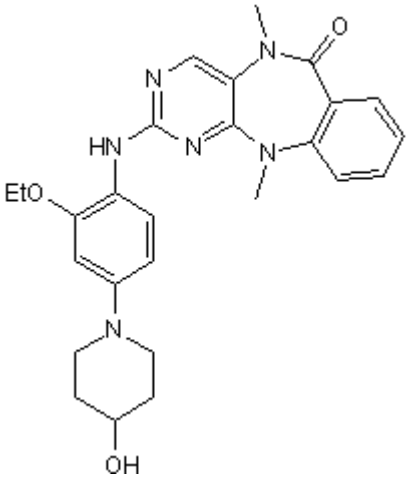
Batch Molecular Weight: 479.05

Physical Appearance: Light Beige solid

Solubility: DMSO to 40 mM

Storage: Store at RT

Batch Molecular Structure:



2. ANALYTICAL DATA

TLC: R_f = 0.22 (Chloroform:Methanol [95:5])

HPLC: Shows 99.5% purity

^{1}H NMR: Consistent with structure

Mass Spectrum: Consistent with structure

Microanalysis:

	Carbon	Hydrogen	Nitrogen
Theoretical	65.19	6.42	17.54
Found	65.19	6.45	17.23

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Product Information

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Description:

ERK5 (BMK1) and BRD4 inhibitor (K_d values are 80 and 190 nM, respectively). Also inhibits DCAMKL2, PLK4 and TNK1 (K_d values are 190, 600 and 890 nM). Blocks growth factor-induced activation of cellular BMK1 and reduces BMK1 activity in in vitro kinase assays. Also reduces BMK1-dependent transactivating activity of MEF2C. Inhibits proliferation in a variety of cancer cell lines; blocks tumor cell proliferation and tumor-associated angiogenesis.

Physical and Chemical Properties:

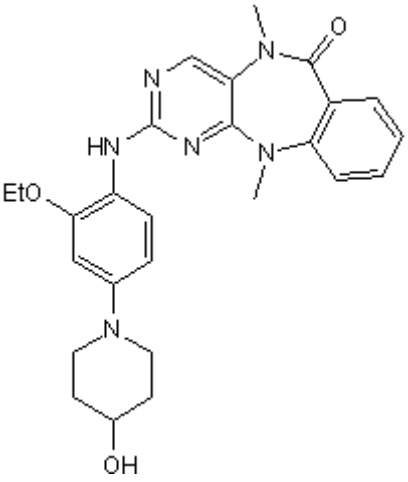
Batch Molecular Formula: $C_{26}H_{30}N_6O_3.¼H_2O$

Batch Molecular Weight: 479.05

Physical Appearance: Light Beige solid

Minimum Purity: >98%

Batch Molecular Structure:



Storage: Store at RT

Solubility & Usage Info:

DMSO to 40 mM

Stability and Solubility Advice:

Some solutions can be difficult to obtain and can be encouraged by rapid stirring, sonication or gentle warming (in a 45-60°C water bath).

Information concerning product stability, particularly in solution, has rarely been reported and in most cases we can only offer a general guide. Our standard recommendations are:

SOLIDS: Provided storage is as stated on the product label and the vial is kept tightly sealed, the product can be stored for up to 6 months from date of receipt.

SOLUTIONS: We recommend that stock solutions, once prepared, are stored aliquoted in tightly sealed vials at -20°C or below and used within 1 month. Wherever possible solutions should be made up and used on the same day.

Licensing Information:

Sold under license from the Dana-Farber Cancer Institute.

References:

Lin *et al* (2016) ERK5 kinase activity is dispensable for cellular immune response and proliferation. Proc.Natl.Acad.Sci.U.S.A. ***113*** 11865. PMID: 27679845.

Erazo *et al* (2013) Canonical and kinase activity-independent mechanisms for extracellular signal-regulated kinase 5 (ERK5) nuclear translocation require dissociation of Hsp90 from the ERK5-Cdc37 complex. Mol.Cell Biol. ***33*** 1671. PMID: 23428871.

Deng *et al* (2011) Discovery of a benzo[*e*]pyrimido-[5,4-*b*][1,4]diazepin-6(11*H*)-one as a potent and selective inhibitor of big MAP kinase 1. ACS Med.Chem.Lett. ***2*** 195. PMID: 21412406.

Yang and Lee (2011) Targeting the BMK1 MAP kinase pathway in cancer therapy. Clin.Cancer Res. ***17*** 3527. PMID: 21385929.

Yang *et al* (2010) Pharmacological inhibition of BMK1 suppresses tumor growth through promyelocytic leukemia protein. Cancer Cell ***18*** 258. PMID: 20832753.