

PRODUCT INFORMATION



ONX 0914

Item No. 16271

CAS Registry No.: 960374-59-8
Formal Name: N-[2-(4-morpholinyl)acetyl]-L-alanyl-O-methyl-N-[(1S)-2-[(2R)-2-methyl-2-oxiranyl]-2-oxo-1-(phenylmethyl)ethyl]-L-tyrosinamide

Synonym: PR-957

MF: C₃₁H₄₀N₄O₇

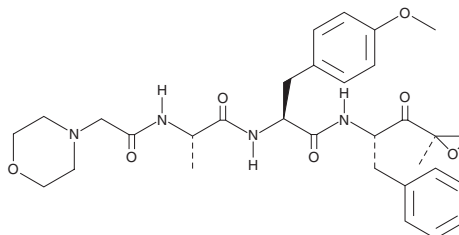
FW: 580.7

Purity: ≥98%

Supplied as: A crystalline solid

Storage: -20°C

Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

ONX 0914 is supplied as a crystalline solid. A stock solution may be made by dissolving the ONX 0914 in the solvent of choice, which should be purged with an inert gas. ONX 0914 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of ONX 0914 in ethanol is approximately 15 mg/ml and approximately 2 mg/ml in DMSO and DMF.

ONX 0914 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ONX 0914 should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. ONX 0914 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The immunoproteasome is a specialized, inducible proteasome that generates peptides presented on major histocompatibility complex (MHC) class I molecules to cytotoxic T cells. Stimulation of cells with inflammatory cytokines such as IFN- γ leads to the replacement of constitutive catalytic proteasome β subunits with inducible β subunits (β 1i (LMP2), β 2i (MECL1), and β 5i (LMP7)), which are required for the production of certain MHC class I-restricted T cell epitopes. ONX 0914 is a selective inhibitor of the β 5i (LMP7) subunit of the immunoproteasome (IC_{50} s = 65 and 73 nM for mouse and human, respectively) and demonstrates significantly weaker activity at the β 5 subunit of the constitutive proteasome (IC_{50} s = 0.92 and 1.04 μ M for mouse and human, respectively).^{1,2} It can block the production of IL-23 by activated monocytes and the production of IFN- γ and IL-2 by T cells.¹ ONX 0914 can also inhibit IL-17-producing T cells under T_H17-polarizing conditions *in vitro* and reduce T_H1 and T_H17 cell differentiation *in vivo*.³ This compound has been shown to attenuate disease progression in several experimental models of autoimmune disorders as well as in some hematologic malignancies.^{1,4-6}

References

1. Muchamuel, T., Basler, M., Aujay, M.A., *et al.* *Nat. Med.* **15**(7), 781-787 (2009).
2. Huber, E.M., Basler, M., Schwab, R., *et al.* *Cell* **148**(4), 727-738 (2012).
3. Kalim, K.W., Basler, M., Kirk, C.J., *et al.* *J. Immunol.* **189**(8), 4182-4193 (2012).
4. Basler, M., Daiee, M., Moll, C., *et al.* *J. Immunol.* **185**(1), 634-641 (2010).
5. Niewerth, D., Franke, N.E., Jansen, G., *et al.* *Haematologica* **98**(12), 1896-1904 (2013).
6. Niewerth, D., Kaspers, G.J., Assaraf, Y.G., *et al.* *J. Hematol. Oncol.* **7**(1), 1-15 (2014).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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