# **PRODUCT** INFORMATION GW 311616A



Item No. 27957

CAS Registry No.:	197890-44-1	
Formal Name:	(3S,3aS,6aR)-hexahydro-3-(1-methylethyl)-	
	1-(methylsulfonyl)-4-[(2E)-1-oxo-4-(1- piperidinyl)-2-buten-1-yl]-pyrrolo[3,2-b] pyrrol-2(1H)-one, monohydrochloride	
MF:	$C_{19}H_{31}N_3O_4S \bullet HCI$	
FW:	434.0	0 1 0
Purity:	≥95%	•HCI
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

GW 311616A is supplied as a crystalline solid. A stock solution may be made by dissolving the GW 311616A in the solvent of choice, which should be purged with an inert gas. GW 311616A is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of GW 311616A in ethanol is approximately 10 mg/ml and approximately 30 mg/ml in DMSO and DMF.

GW 311616A is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, GW 311616A should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. GW 311616A has a solubility of approximately 0.25 mg/ml in a 1:4 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

### Description

GW 311616A is an inhibitor of neutrophil elastase ( $IC_{50}$  = 100 nM).<sup>1</sup> It is selective for neutrophil elastase (IC<sub>50</sub> = 22 nM for the human enzyme) over trypsin, cathepsin G, and plasmin (IC<sub>50</sub>s = >100  $\mu$ M for all), as well as chymotrypsin and tissue plasminogen activator (IC<sub>50</sub>s = >3  $\mu$ M for both), in cell-free assays. GW 311616A (20 μM) inhibits the formation of neutrophil extracellular traps (NETs) induced by phorbol 12-myristate 13-acetate (PMA; Item No. 10008014) in isolated human neutrophils.<sup>2</sup> It inhibits intraneutrophil elastase activity in isolated dog blood six hours after administration of a 0.22 mg/kg dose.<sup>3</sup> GW 311616A also inhibits neutrophil elastase in the liver in a mouse model of liver ischemia-reperfusion injury when administered at a dose of 2 mg/kg.<sup>4</sup>

### References

- 1. Benedek, B., Kopp, B., and Melzig, M.F. Achillea millefolium L. s.l. is the anti-inflammatory activity mediated by protease inhibition? J. Ethnopharmacol. 113(2), 312-317 (2007).
- 2. Nakabo, S., Ohmura, K., Akizuki, S., et al. Activated neutrophil carbamylates albumin via the release of myeloperoxidase and reactive oxygen species regardless of NETosis. Mod. Rheumatol. 30(2), 345-349 (2019)
- 3. Macdonald, S.J.F., Dowle, M.D., Harrison, L.A., et al. The discovery of a potent, intracellular, orally bioavailable, long duration inhibitor of human neutrophil elastase-GW311616A a development candidate. Bioorg. Med. Chem. Lett. 11(7), 895-898 (2001).
- 4. Uchida, Y., Freitas, M.C., Zhao, D., et al. The inhibition of neutrophil elastase ameliorates mouse liver damage due to ischemia and reperfusion. Liver Transpl. 15(8), 939-947 (2009).

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

### SAFFTY 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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