

# Clarithromycin related compound Z, EvoPure® PRODUCT DATA SHEET

issue date 01/06/2020

<b>Product Name:</b>	Clarithromycin related compound Z, EvoPure®
<b>Product Number:</b>	E022
<b>CAS Number:</b>	N/A
<b>Molecular Formula:</b>	$C_{37}H_{68}N_2O_{13}$
<b>Molecular Weight:</b>	748.94
<b>Storage Conditions:</b>	-20°C
<b>Description:</b>	<p>Clarithromycin related compound Z, EvoPure® (Erythromycin A (Z) 9-oxime) is a highly purified impurity found in Clarithromycin that can be used as a reference standard.</p> <p>For all Clarithromycin products, <a href="#">click here</a>.</p>
<b>Mechanism of Action:</b>	<p>Macrolide antibiotics inhibit bacterial growth by targeting the 50S ribosomal subunit preventing peptide bond formation and translocation during protein synthesis. Resistance to Clarithromycin is commonly attributed to mutations in 50S rRNA preventing Clarithromycin binding allowing the cell to synthesize error-free proteins.</p> <p>Anti-cancer mechanisms include reduction of cytokines, inhibition of autophagy, and anti-angiogenesis. The compound can act on signal transduction pathways, transcription factors, drug pharmacokinetics, growth signals, and metastasis. These features can be exploited to make tumor cells more prone to apoptosis and reduce escape mechanisms. The mechanism used depend on the type of cancer.</p>
<b>Spectrum:</b>	<p>Clarithromycin is a broad-spectrum antibiotic with bacteriostatic action wide range of Gram- positive and Gram-negative bacteria including anaerobes. It is also effective for <i>Mycoplasma</i> and <i>Mycobacteria</i>.</p>

**Microbiology Applications** Clarithromycin is commonly used in clinical *in vitro* microbiological antimicrobial susceptibility tests (panels, discs, and MIC strips) against Gram-positive and Gram-negative bacteria. Medical microbiologists use AST results to recommend antibiotic treatment options for infected patients. Representative MIC values include:

- *Haemophilus influenza* 2 µg/mL - 32 µg/mL
- *Streptococcus pneumoniae* 0.12 µg/mL – 64 µg/mL
- For a complete list of Clarithromycin MIC values, [click here](#).

TOKU-E's Clarithromycin used in methacrylate-based copolymer films that released the compound (along with doxycycline and rifampicin) for up to 21 days were found to prevent biofilm formation when in an *in vitro* bioreactor model (Rose et al, 2015).

### **Cancer Applications**

Clarithromycin is involved in autophagy-lysosome pathway. It can inhibit autophagy in myeloma and myeloid leukaemia cells. It inhibits lysosomal function after fusion of the autophagosomes with the lysosomes. Thus, it could be a potential adjuvant where autophagy is used by the tumor as an escape mechanism. (Nakamura *et al*, 2010)

The combined treatment of clarithromycin with the proteasome inhibitor bortezomib enhances cytotoxicity in the breast cancer cell lines MDA-MB-231 and MDA-MB-468. A wild-type murine embryonic fibroblast (MEF) cell line also exhibited enhanced cytotoxicity (Komatsu et al, 2012).

Direct antineoplastic effects of CAM may depend on the tumor type. Researchers found a direct anti-tumor activity of CAM on lymphoma cells (Ochi et al, 2006) and it directly induced apoptosis in a murine B cell lymphoma cell line (Ohara et al, 2004).

### **Technical Data:**

HPLC, NMR, FTIR, and MS analysis may be available. For more info, please email [info@toku-e.com](mailto:info@toku-e.com).

## References:

- Goldman RC, Zakula D, Flamm R, Beyer J, Capobianco J (1994) Tight binding of clarithromycin, its 14-(R)-hydroxy metabolite, and erythromycin to *Helicobacter pylori* ribosomes. *Antimicrob. Agents Chemother.* 38(7):1496-500. PMID 7979278
- Komatsu S et al (2012) Clarithromycin enhances bortezomib-induced cytotoxicity via endoplasmic reticulum stress-mediated CHOP (GADD153) induction and autophagy in breast cancer cells. *Int. J. Oncol.* 40(4):1029-1039 PMID 22200786
- Tenson T, Lovmar M and Ehrenberg M (2003) The mechanism of action of macrolides, lincosamides and streptogramin B reveals the nascent peptide exit path in the ribosome. *J. Mol. Biol.* 330(5):1005-1014 PMID 12860123
- Morikawa K, Watabe H, Araake M and Morikawa S (1996) Modulatory effect of antibiotics on cytokine production by human monocytes *in vitro*. *Antimicrob. Agents. Chemother.* 40(6):1366-1370 PMID 8726002
- Nakamura M et al (2010) Clarithromycin attenuates autophagy in myeloma cells *Int J Oncol* 37:815–320 PMID 20811702
- Niemi M, Neuvonen PJ, and Kivisto KT (2001) The cytochrome P4503A4 inhibitor clarithromycin increases the plasma concentrations and effects of repaglinide. 70(1):58-65 PMID 11452245
- Ochi M et al (2006) Regression of primary low-grade mucosa-associated lymphoid tissue lymphoma of duodenum after long-term treatment with clarithromycin. *Scand J Gastroenterol* 41:365–369 DOI: PMID: 16497629
- Ohara T et al (2004) Antibiotics directly induce apoptosis in B cell lymphoma cells derived from BALB/c mice *Anticancer Res* 24(6) pp 3723–30
- Rose, WE et al (2015) Prevention of biofilm formation by methacrylate-based copolymer films loaded with rifampin, clarithromycin, doxycycline alone or in combination. *Pharm. Res.* 32(1): 61-73 PMID 24934663
- Ichiyama T et al (2001) Clarithromycin Inhibits NF- $\kappa$ B Activation in Human Peripheral Blood Mononuclear Cells and Pulmonary Epithelial Cells. *Antimicrob. Agents. Chemother.* 45 (1): 44-47 PMID 11120942
- Van Nuffel AMT et al 2015 Repurposing drugs in oncology (ReDO)- Clarithromycin as an anti-cancer agent. *Ecancer* 9:513
- Vermeer LMM, Isringhausen CD, Ogilvie BW and Buckley DB (2016) Evaluation of ketoconazole and its alternative clinical CYP3A4/5 inhibitors as inhibitors of drug transporters: The *in vitro* effects of ketoconazole, ritonavir, clarithromycin, and itraconazole on 13 clinically-relevant drug transporters. *Drug Metab. Disp.* 44 (3) 453-459 PMID 26668209