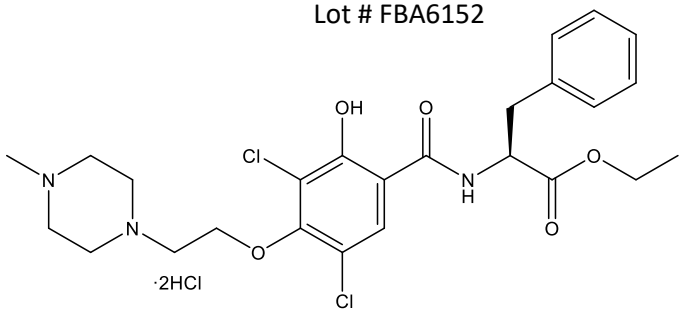
Catalog # 10-4842
JTE-607

CAS# 188791-09-5

Ethyl (2S)-2-[[3,5-Dichloro-2-hydroxy-4-[2-(4-methylpiperazin-1-yl)ethoxy]benzoyl]amino]-3-phenylpropanoate dihydrochloride

Lot # FBA6152



JTE-607 inhibits inflammatory cytokine production in human peripheral blood mononuclear cells (PBMC's) without causing immunosuppression: IC_{50}'s = 11 nM (TNF-α), 5.9 nM (IL-1β), 8.8 nM (IL-6), 7.3 nM (IL-8), and 9.1 nM (IL-10).[1] It displayed efficacy in a mouse model of septic shock.[2] JTE-607 also showed inhibitory activity against acute myelogenous leukemia cell lines.[3,4] Recently, the mechanism of action of JTE-607 (a pro-drug, with the active species being the free acid) has been found to be inhibition of pre-messenger RNA endonuclease Cleavage and Polyadenylation Specificity Factor 3 (CPSF3).[5,6] This prevents release of newly synthesized mRNA's resulting in read-through transcription and the formation of DNA-RNA hybrid R-loop structures. Transcripts down-regulated by JTE-607 were related to DNA damage-based phenotype.

1) Kakutani *et al*. (1999), *JTE-607, a novel inflammatory cytokine synthesis inhibitor without immunosuppression, protects from endotoxin shock in mice;* Inflamm. Res., **48** 461
2) Iwamura *et al*. (2004), *Comparative study of glucocorticoids, cyclosporine A, and JTE-607 [(-)-Ethyl-N{3,5-dichloro-2-hydroxy-4-[2-(4-methylpiperazin-1-yl)ethoxy]benzoyl]-L-phenylalaninate dihydrochloride] in a mouse septic shock model;* J. Pharmacol. Exp. Ther., **311** 1256
3) Uesato *et al*. (2006), *JTE-607, a multiple cytokine production inhibitor, ameliorates disease in a SCID mouse xenograft acute myeloid leukemia model*; Exp. Hematol., **34** 1385
4) Tajima *et al*. (2010), *JTE-607, a multiple cytokine production inhibitor, induces apoptosis accompanied by an increase in p21waf1/cip1 in acute myelogenous leukemia cells;* Cancer Sci., **101** 774
5) Kakegawa *et al*. (2019), *JTE-607, a multiple cytokine production inhibitor, targets CPSF3 and inhibits pre-mRNA;* Biochem. Biophys. Res. Commun., **518** 32
6) Ross *et al*. (2020), *CPSF3-dependent pre-mRNA processing as a druggable node in AML and Ewing's sarcoma;* Nat. Chem. Biol., **16** 50

PHYSICAL DATA

Molecular Weight:	597.36
Molecular Formula:	$C_{25}H_{31}Cl_2N_3O_5 \cdot 2HCl$
Purity:	>98% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (>25 mg/ml)
Physical Description:	Off-white to pale yellow solid
Storage and Stability:	Store as supplied desiccated at -20°C for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 1 month.

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