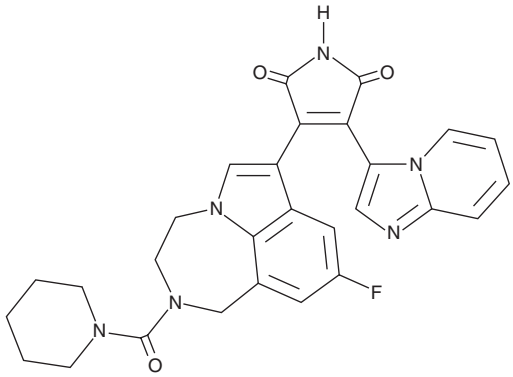
PRODUCT INFORMATION

LY2090314

Item No. 22211

CAS Registry No.:	603288-22-8
Formal Name:	3-[9-fluoro-1,2,3,4-tetrahydro-2-(1-piperidinylcarbonyl)pyrrolo[3,2,1-jk][1,4]benzodiazepin-7-yl]-4-imidazo[1,2-a]pyridin-3-yl-1H-pyrrole-2,5-dione
MF:	$C_{28}H_{25}FN_6O_3$
FW:	512.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 213 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥2 years



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

Laboratory Procedures

LY2090314 is supplied as a crystalline solid. A stock solution may be made by dissolving the LY2090314 in the solvent of choice. LY2090314 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of LY2090314 in ethanols is approximately 0.25 mg/ml and approximately 10 mg/ml in DMSO and DMF.

LY2090314 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, LY2090314 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. LY2090314 has a solubility of approximately 0.16 mg/ml in a 1:5 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

LY2090314 is potent and selective inhibitor of glycogen synthase kinase 3 (GSK3) with IC_{50} values of 1.5 and 0.9 nM for human recombinant GSK3α and GSK3β, respectively.[1] It has >10-fold selectivity for GSK3 over a panel of 40 kinases at a concentration of 20 µM. LY2090314 induces time-dependent stabilization of β-catenin total protein and activates Wnt signaling *in vitro*. It has potent antiproliferative activity in BRAF wild-type/NRAS mutant and BRAF mutant melanoma cell lines (IC_{50}s = 6.0-11.8 nM) but has limited to no activity in non-melanoma cell lines with (IC_{50}s = 430 to >20,000 nM). Knockdown of β-catenin in A375 and M14 melanoma cells induces LY2090314 resistance *in vitro*, indicating that LY2090314-induced cell death is dependent upon Wnt activation. *In vivo*, LY2090314 reduces tumor volume in a murine A375 melanoma xenograft model as a single agent and synergizes with decabarzine for a greater antitumor effect. Formulations containing LY2090314 are under clinical investigation for the treatment of advanced solid tumors.[2]

References

1. Atkinson, J.M., Rank, K.B., Zeng, Y., *et al.* Activating the Wnt/β-catenin pathway for the treatment of melanoma--application of LY2090314, a novel selective inhibitor of glycogen synthase kinase-3. *PLoS One* **10(4)**, e0125028 (2015).
2. Gray, J.E., Infante, J.R., Brail, L.H., *et al.* A first-in-human phase I dose-escalation, pharmacokinetic, and pharmacodynamic evaluation of intravenous LY2090314, a glycogen synthase kinase 3 inhibitor, administered in combination with pemetrexed and carboplatin. *Invest New Drugs* **33(6)**, 1187-1196 (2015).

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.**CAYMANCHEM**.COM