# Product Introduction

## Sorafenib Tosylate

Sorafenib Tosylate (Bay 43-9006) is a multikinase inhibitor of **Raf-1**, **B-Raf** and VEGFR-2 with **IC50** of 6 nM, 22 nM and 90 nM, respectively.

### Technical Data:

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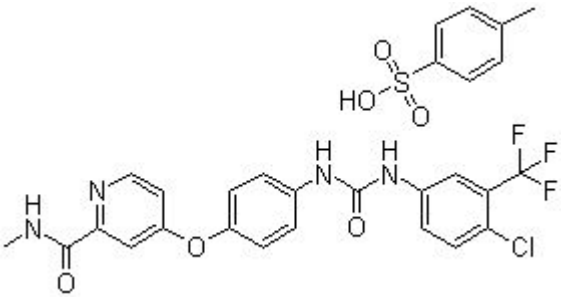
|---|---|---|
| **Molecular Weight (MW):** | 637.03 |  |
| **Formula:** | $C_{21}H_{16}ClF_3N_4O_3.C_7H_8O_3S$ | |
| **Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:** | DMSO 127 mg/mL | |
| | Water 0.01 mg/mL | |
| | Ethanol <1 mg/mL | |
| **Purity:** | >98% | |
| **Storage:** | 3 years -20℃Powder | |
| | 6 months-80℃in DMSO | |
| **CAS No.:** | 475207-59-1 | |

### Biological Activity

Sorafenib tosylate inhibits both wild-type and V599E mutant B-Raf activity with IC50 of 22 nM and 38 nM, respectively. Sorafenib tosylate also potently inhibits mVEGFR2 (Flk-1), mVEGFR3, mPDGFRβ, Flt3, and c-Kit with IC50 of 15 nM, 20 nM, 57 nM, 58 nM, and 68 nM, respectively. Sorafenib tosylate weakly inhibits FGFR-1 with IC50 of 580 nM. Sorafenib tosylate is not active against ERK-1, MEK-1, EGFR, HER-2, IGFR-1, c-Met, PKB, PKA, cdk1/cyclinB, PKCα, PKCγ, and pim-1. Sorafenib tosylate markedly inhibits VEGFR2 phosphorylation in NIH 3T3 cells with IC50 of 30 nM, and Flt-3 phosphorylation in HEK-293 cells with IC50 of 20 nM. Sorafenib tosylate potently blocks MEK 1/2 and ERK 1/2 phosphorylation in most cell lines but not in A549 or H460 cells, while having no effect on inhibition of the PKB pathway. Sorafenib tosylate

inhibits the proliferation of HAoSMC and MDA-MB-231 cells with IC50 of 0.28 μM and 2.6 μM, respectively. [1] In addition to inhibition of the RAF/MEK/ERK signaling pathway, Sorafenib tosylate significantly inhibits the phosphorylation of eIF4E and down-regulates Mcl-1 levels in hepatocellular carcinoma (HCC) cells in a MEK/ERK-independent manner. Sorafenib tosylate inhibits the proliferation of PLC/PRF/5 and HepG2 cells with IC50 of 6.3 μM and 4.5 μM, respectively, and leads to the significant induction of apoptosis. [2]

Oral administration of Sorafenib tosylate (~60 mg/kg) demonstrates broad spectrum, dose-dependent anti-tumor activity against a variety of human tumor xenograft models including MDA-MB-231, Colo-205, HT-29, DLD-1, NCI-H460, and A549, with no evidence of toxicity. In association with the anti-tumor efficacy, Sorafenib tosylatetreatment potently inhibits MEK 1/2 phosphorylation and pERK 1/2 levels in HT-29 and MDA-MB-231 xenografts but not in Colo-205 xenografts, and significantly suppresses tumor microvessel area (MVA) and microvessel density (MVD) in MDA MB-231, HT-29 and Colo-205 tumor xenografts. [1] Sorafenib tosylate treatment produces dose-dependent growth inhibition of PLC/PRF/5 tumor xenografts in SCID mice with TGIs of 49% and 78% at 10 mg/kg and 30 mg/kg, respectively, consistent with the inhibition of ERK and eIF4E phosphorylation, reduction of the microvessel area, and induction of tumor cell apoptosis. [2]

## References

[1] Wilhelm SM, et al. Cancer Res, 2004, 64(19), 7099-7109.
[2] Liu L, et al. Cancer Res, 2006, 66(24), 11851-11858.
[3] Ricci MS, et al. Cancer Cell, 2007, 12(1), 66-80.

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