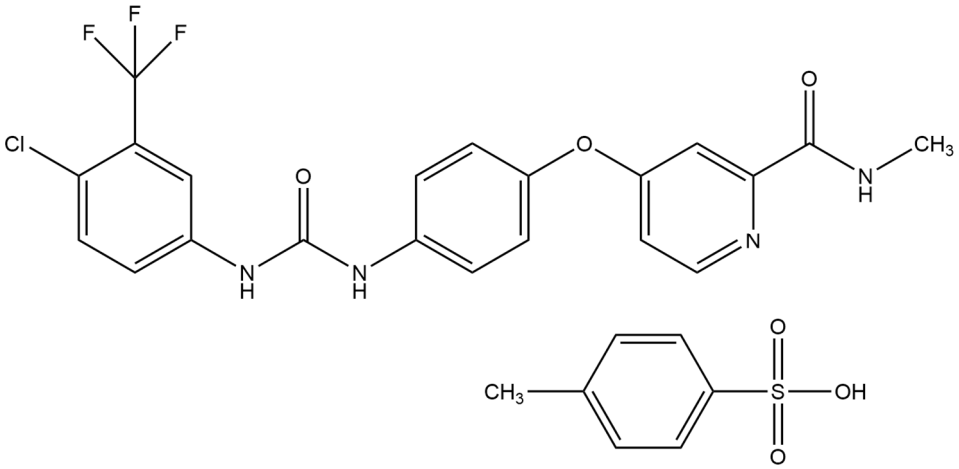
Sorafenib PK Fact Sheet

Details

Generic Name	Sorafenib
Trade Name	Nexavar®
Class	HCC protein kinase inhibitor
Molecular Weight	637
Structure	

Summary of Key Pharmacokinetic Parameters

Linearity/non-linearity	Mean C_{max} and AUC increase less than proportionally beyond doses of 400 mg twice daily.
Steady state	Achieved after 7 days of twice-daily dosing.
Elimination half-life	25-48 h
C_{max}	3.32 mg/L (400 mg BID, steady state)[1].
C_{24}	No data
AUC	28.91 mg*h/L (400 mg BID, steady state)[1].
Tmax	3 h
Bioavailability	Absolute bioavailability is unknown. The mean relative bioavailability of the tablets is 38-49%, as compared to the oral solution.
Absorption	Absorption with a moderate-fat meal does not alter absorption. Absorption with a high-fat meal decreases by 29%, as compared to fasted administration.
Protein Binding	99.5%
Volume of Distribution	213 L (estimated from PPK study)[2].
CSF:Plasma ratio	No data
Renal Clearance	19% of the dose excreted in urine as glucuronidated metabolites.
Renal Impairment	No dosage adjustment required in mild-severe renal impairment.
Hepatic Impairment	No dosage adjustment required in mild-moderate hepatic impairment. No data are available for patients with severe hepatic impairment (Child-Pugh C). Sorafenib exposure may be increased in these patients.

Metabolism and Distribution

Metabolised by	CYP3A4, UGT1A9.
Inducer of	None expected.

Inhibitor of	P-gp, UGT1A9, UGT1A9 (*in vitro*), OATP1B1[3].
Transported by	OATPB1/B3 (*in vitro*)[4].

References

Unless otherwise stated (see below), information is from:
Nexavar Summary of Product Characteristics, Bayer plc, September 2019.
Nexavar Prescribing Information, Bayer HealthCare, June 2020.

1. Furuse, J., Ishii, H., Nakachi, K., et al. 2008. Phase I study of sorafenib in Japanese patients with hepatocellular carcinoma. Cancer Science, 99(1):159-65.
2. Jain, L., Woo, S., Gardner, E.R., Dahut et al. 2011. Population pharmacokinetic analysis of sorafenib in patients with solid tumours. British Journal of Clinical Pharmacology 72(2):294–305.
3. Hu, S., Mathijssen, R.H.J., De Bruijn, P. et al. 2014. Inhibition of OATP1B1 by tyrosine kinase inhibitors: in vitro–in vivo correlations. British Journal of Cancer 110:894–898.
4. Zimmerman, E.I., Hu, S., Roberts, J.L. et al. 2013. Contribution of OATP1B1 and OATP1B3 to the Disposition of Sorafenib and Sorafenib-Glucuronide. Clinical Cancer Research 19(6):1458–1466.