

## Sorafenib PK Fact Sheet

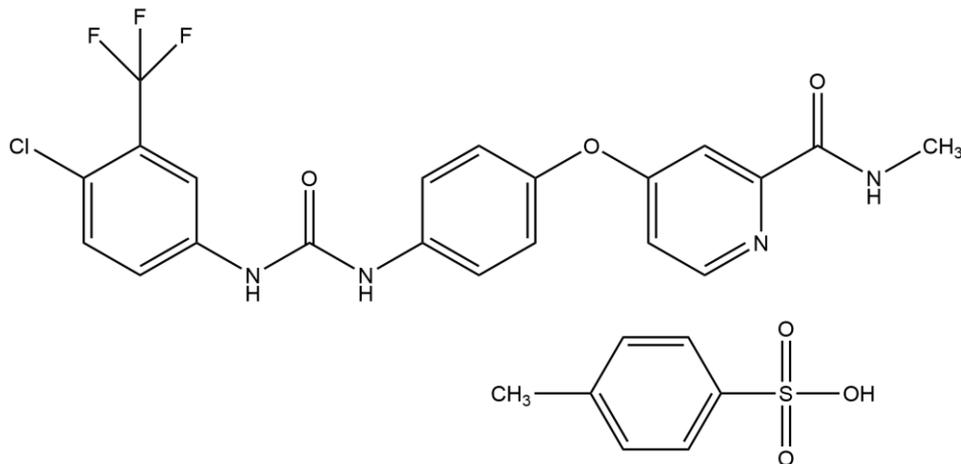
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## Details

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 <sub>max</sub> 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 <sub>max</sub>	3.32 mg/L (400 mg BID, steady state) <sup>1</sup> .
C <sub>24</sub>	No data
AUC	28.91 mg*h/L (400 mg BID, steady state) <sup>1</sup> .
T <sub>max</sub>	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) <sup>2</sup> .
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.

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<b>Inhibitor of</b>	P-gp, UGT1A9, UGT1A9 ( <i>in vitro</i> ), OATP1B1 <sup>3</sup> .
<b>Transported by</b>	OATPB1/B3 ( <i>in vitro</i> ) <sup>4</sup> .

## 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.