

Sorafenib & Cancer Treatment

Kidney, Liver and Thyroid Cancer in South Africa

The most recent South African National Cancer Registry Report records 409 new cases of kidney cancer, 405 new cases of liver cancer, and 307 new cases of thyroid cancer¹. Worldwide, primary liver cancer is the third leading cause of cancer death² in a single year, while kidney cancers account for about 2% of all cancers diagnosed globally³.

Risk groups for liver, kidney, thyroid cancers

The most common risk factor for liver cancer is chronic infection with the hepatitis B virus (HBV),⁴ which affects an estimated 3 million people in South Africa. Additional factors that increase the risk of liver cancer include a family history of liver cancer, persistence of high HBV DNA levels, co-infection with HIV or hepatitis C virus (HCV), and lifestyle choices such as excessive alcohol use and smoking.⁵ Kidney cancer risk factors can include smoking, obesity, high blood pressure, long-term dialysis or occupational exposure⁶. Risk factors for thyroid cancer are largely uncertain.

Where does sorafenib fit into cancer treatment?

Sorafenib is an oral multikinase inhibitor indicated for the treatment of advanced kidney, liver and thyroid cancer. Sorafenib has been shown to have a predictable and manageable safety profile, as well as important survival benefits.⁷ The recommended daily dosage of sorafenib is 400 mg (2x200 mg tablets), taken twice daily, until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs⁸

How available is brand name sorafenib in South Africa, and how much does it cost?

Only the original manufacturer, Bayer, is registered to market its product in South Africa. Sorafenib is not procured for the public sector. While liver and kidney cancers are both prescribed minimum benefits (PMB) conditions⁹, medical aid schemes can exclude coverage of expensive treatments like sorafenib, due to the

high cost.¹⁰ Bayer's sorafenib is sold through the private sector at a cost of R203.5 per 200mg tablet, meaning that a year of individual treatment at the recommended dosage amounts to R297,110¹¹. This price is far beyond the average annual earnings in South Africa, estimated at R81,672.¹² Generic sorafenib is available in India, however, for approximately 94% less—around R15,000 per year¹³.



What would be the impact of having more affordable sorafenib be available in South Africa?

In 2007 in South Africa, a total of 1,121 people were diagnosed with a cancer that could potentially be treated using sorafenib, depending on characteristics and stage of disease.

How do patents block access to generic sorafenib?

There are no generic versions of sorafenib available in South Africa because the manufacturer, Bayer, holds multiple patents that give it a market monopoly. Sorafenib is a relatively new drug, and Bayer's global patenting strategy¹⁴ has assisted the company in earning over €771 million (over R10.8 billion) on sales of sorafenib in 2013¹⁵.

Bayer's initial patent on the compound used to make sorafenib was filed in 2001 in South Africa, and expires

¹ http://www.nioh.ac.za/assets/files/NCR_Final_Tables_2007.pdf

² http://www.hepb.org/professionals/hepb_and_liver_cancer.htm

³ Lindblad, P. and Adami H.O, Kidney Cancer, in Textbook of Cancer.

⁴ http://www.hepb.org/professionals/hepb_and_liver_cancer.htm

⁵ <http://www.cancer.org/cancer/livercancer/detailedguide/liver-cancer-risk-factors>

⁶ http://www.medicinenet.com/kidney_cancer/article.htm

⁷ Medscape. Retrieved from <http://reference.medscape.com/drug/nexavar-sorafenib-342260>

⁸ Nexavar label. Retrieved from

http://labeling.bayerhealthcare.com/html/products/pi/Nexavar_PI.pdf

⁹ [http://www.semdsa.org.za/images/The_270_PMB_Conditions_\(non-chronic\).pdf](http://www.semdsa.org.za/images/The_270_PMB_Conditions_(non-chronic).pdf)

¹⁰ <http://www.ioi.co.za/business/personal-finance/med-schemes-can-say-no-to-super-drugs-1.1227179#.UanIMEBTAXA>

¹¹ Database of Medicine Prices.South African Medicine Price Registry. Prices retrieved on 29 July 2014.

¹² Quarterly Employment Statistics, March 2014. Statistics South Africa. Retrieved from http://beta2.statssa.gov.za/?page_id=593

¹³ This price is based on the October 2014 exchange rates of the \$113 per month Cipla price, though prices may have fluctuated since Cipla announced this price in May 2012.

¹⁴ Bayer annual report 2013, pg. 282

¹⁵ Bayer annual report 2013, pg. 158

only in 2021¹⁶. At least four additional patents on sorafenib have been filed in South Africa by Bayer and two other manufacturers (Sanofi and Ranbaxy), the latest of which expires in 2032¹⁷. These patents cover modified formulations of sorafenib, methods of preparing and using the drug, and combinations of sorafenib with other compounds. Such modifications to existing products—which are common practice in the pharmaceutical industry—are not considered innovative in all countries, and in India and Ukraine, these same patents have been opposed, are still under examination, or have been rejected outright. In South Africa, however, no examination of patent applications occurs and there is no opportunity for patent opposition, so many patents are granted, even those that do not necessarily meet national standards.

How have other countries accessed more affordable sorafenib?

In March of 2012, the Indian government issued a compulsory license (CL) on sorafenib, allowing generic manufacturers to produce and sell cheaper versions of the drug. Prior to the CL, Bayer had set the price of sorafenib in India at US \$69,000 per year—41 times the projected average annual income in India¹⁸. The CL introduced competition into the national market, lowering the price of sorafenib from US \$5,500 for Bayer's product to US \$175 a month for a generic from Natco—a staggering 97% price reduction¹⁹. The CL also allowed for other generic manufacturers to offer even cheaper versions of sorafenib in India. Only two months after Natco was allowed to sell generic sorafenib, the generic manufacturer, Cipla cut its price of generic sorafenib by 75% to \$113 a month²⁰. The CL was challenged by Bayer, but an Indian court upheld the CL in 2013, citing the unaffordability of Bayer's product.²¹

Compulsory licensing is a legal flexibility permissible under the World Trade Organisation's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). It can be used by a government in many circumstances, including when a patent holder charges excessive prices that undermine public health. Patent holders receive a set royalty on sales of the generic products until the patent expires, while the availability of more affordable products broadens access. South

Africa has never issued a CL on a medicine, in part because the procedures for doing so require a decision by a High Court, and are expensive and time-consuming.

How can access to sorafenib be improved in South Africa?

The Department of Health or other party could consider filing a compulsory license on sorafenib, in order to facilitate access to more affordable generics while Bayer's primary patent is still valid. Parallel importation is another legal flexibility that could be utilised to import Bayer's sorafenib from another country where the product is sold at a lower price than in South Africa.

Bayer should lower the price of sorafenib in South Africa, and allow secondary patents to lapse.

Generic manufacturers should file registration dossiers in South Africa for permission to bring more affordable quality-approved sorafenib products to market. This could facilitate the ability of the Department of Health to file a compulsory license and/or procure sorafenib for the public sector. Generic manufacturers should not file any further secondary patents on sorafenib, and allow existing patents to lapse.

The Patents Office should not reinstate any patents that lapse on sorafenib, and reject any new patents filed on sorafenib.

The Department of Trade and Industry must finalise a national intellectual property policy and amend the country's patent laws, in order to limit patent evergreening, and establish easier procedures for issuing compulsory licenses or conducting parallel importation. These reforms will promote access to more affordable medicines.

¹⁶ CIPC online public patent search-Patent Application No.: 2007/07638

¹⁷ CIPC online public patent search-Patent Application No.: 2011/08110 and 2012/02721

¹⁸ Knowledge Ecology International. KEI Statement on India's granting of compulsory license to patents on cancer drug sorafenib (NATCO Vs. BAYER). Retrieved from <http://keionline.org/node/1384>

¹⁹ Intellectual Property Watch. 2013: India Battles For Right To Use Compulsory Licences To Make Medicines Affordable. January 22 2013. Retrieved from

<http://www.ip-watch.org/2013/01/22/2013-india-battles-for-right-to-use-compulsory-licences-to-make-medicines-affordable/>

²⁰ The Hindu. Cipla slashes generic price of Bayer's cancer drug Nexavar. May 3 2012. Retrieved from <http://www.thehindu.com/business/companies/cipla-slashes-generic-price-of-bayers-cancer-drug-nexavar/article3381049.ece>

²¹ Wharton School of the University of Pennsylvania. Sparring Over Sorafenib: How Will Natco's Move against Bayer Affect Pharma Licensing? April 19 2012. Retrieved from <http://knowledge.wharton.upenn.edu/article/sparring-over-sorafenib-how-will-natcos-move-against-bayer-affect-pharma-licensing/>

