



Health
Canada

Santé
Canada

Health Products
and Food Branch

Direction générale des produits
de santé et des aliments

Marketed Health Products Directorate
A.L. 1906 C
OTTAWA, Ontario
K1A 0K9

May 15, 2024

24-102359-422

To whom it may concern,

Re: Health Canada will publish a summary safety review regarding Nexavar (sorafenib)

As an ongoing commitment to openness and transparency, Health Canada would like to notify you that a summary safety review (SSR) regarding Nexavar (sorafenib) and the potential risk of tumour lysis syndrome will be published (see attached document). The SSR is intended to provide Canadians with a sufficient understanding of the safety review conducted by Health Canada, specifically what was assessed, what was found and what action was taken. The SSR will be posted in subsequent days.¹

This advance notification is being sent for your information only. A broader dissemination to your members would be greatly appreciated.

Any question related to the SSR process or requests for further information on the safety review should be directed to the Marketed Health Products Directorate; e-mail: hc.mhpdssrcoordinator-dpscreicoordonateur.sc@hc-sc.gc.ca

Canada

.../2

¹ <http://www.hc-sc.gc.ca/dhp-mps/medeff/reviews-examens/index-eng.php>

– 2 –

Please feel free to contact us, should you require further information.

Sincerely,

E-signed by

Jason Berg
Associate Director
Office of Policy, Risk Advisory and Advertising
Marketed Health Products Directorate
Health Canada
Tel.: 613-790-8384 Fax: 613-948-7996
E-mail: jason.berg@hc-sc.gc.ca

Attachment:

Summary Safety Review - Nexavar (sorafenib) - Assessing the Potential Risk of Tumour Lysis Syndrome

Summary Safety Review - Nexavar (sorafenib) - Assessing the Potential Risk of Tumour Lysis Syndrome

Product: Nexavar (sorafenib)

Potential Safety Issue: Tumour lysis syndrome (TLS), a condition that occurs when cancer cells are killed rapidly, releasing their contents into the blood, causing blood chemical imbalance and organ damage

Key Messages

- Health Canada's safety review found a possible link between the use of Nexavar and the risk of TLS.
- Health Canada reviewed the potential risk of TLS with the use of Nexavar, a prescription drug authorized for sale in Canada to treat advanced forms of liver, kidney and thyroid cancers. The safety review was triggered by a labelling update by the European Medicines Agency (EMA) and international case reports published in the medical literature.
- Health Canada is working with the manufacturer to update the product safety information in the Canadian product monograph (CPM) for Nexavar to include the risk of TLS. Health Canada will also inform healthcare professionals about this update through a Health Product InfoWatch communication.

Overview

Health Canada reviewed the potential risk of TLS with the use of Nexavar. The safety review was triggered by a labelling update made by the EMA and international case reports published in the medical literature.

Tumor lysis syndrome is a potentially life-threatening condition that can occur during cancer treatment. When cancer cells are killed by the cancer treatment, they release their contents (salts and proteins) into the blood. When cancer cells break down faster than the kidneys can remove these substances from the blood, it can cause changes to the chemical balance in the blood, which may result in damage to organs, most commonly the kidneys, heart and brain.

Use in Canada

- Nexavar is a prescription drug authorized for sale in Canada for the treatment of liver cancer (hepatocellular carcinoma) that cannot be treated by surgery, late-stage kidney cancer (renal cell carcinoma) and late-stage thyroid cancer (thyroid carcinoma).
- Nexavar has been marketed in Canada since 2006. It is currently available as 200 mg tablets.
- It is estimated that fewer than 100 patients are exposed to Nexavar yearly in Canada.

Safety Review Findings

- Health Canada reviewed information provided by the manufacturer, and from searches of the Canada Vigilance database^a, international databases and the scientific literature.
- At the time of the review, Health Canada had not received any Canadian reports of TLS in patients taking Nexavar.

^a Canadian reports can be accessed through the [Canada Vigilance Online Database](#).

- Health Canada reviewed 9 international cases of TLS in patients taking sorafenib, including 8 from the published literature¹⁻⁸. All 9 cases were found to be possibly linked to the use of sorafenib, although a potential contribution from spontaneous TLS (cancer cell break down in the absence of treatment) could not be ruled out.
- The reported time to the onset of TLS ranged from 3 to 34 days after starting treatment with sorafenib.
- Five deaths were reported among the 9 cases assessed. All 5 deaths were found to be possibly linked to TLS from sorafenib treatment. However, other causes of death, such as cancer progression, could not be ruled out.
- Health Canada reviewed 1 additional article published in the scientific literature⁹. A link between sorafenib and TLS could not be established due to study limitations.

Conclusions and Actions

- Health Canada's review found a possible link between the use of Nexavar and the risk of TLS.
- Health Canada is working with the manufacturer to update the CPM for Nexavar to include the risk of TLS.
- Health Canada will also inform healthcare professionals about this update through a Health Product InfoWatch Communication.
- Health Canada encourages consumers and healthcare professionals to [report](#) any side effects related to the use of Nexavar, and other health products, to the [Canada Vigilance Program](#).
- Health Canada will continue to monitor safety information involving Nexavar, as it does for all health products on the Canadian market, to identify and assess potential harms. Health Canada will take appropriate and timely action should new health risks be identified.

Additional Information

The analysis that contributed to this safety review included scientific and medical literature, Canadian and international information and what is known about the use of Nexavar both in Canada and internationally.

For additional information, [contact the Marketed Health Products Directorate](#).

References

1. Imam, S. Z., Zahid, M. F., & Maqbool, M. A. (2020). Sorafenib-induced tumor lysis syndrome in a patient with metastatic hepatocellular carcinoma. *Hematology/oncology and stem cell therapy*, 13(3), 168–170.
2. Kim S.Y., Kim, H.Y., Kim, Y.S., Lee S.M., Kim C.W. (2015). Tumor lysis syndrome following sorafenib treatment in hepatocellular carcinoma. *Yeungnam Univ J Med* 2015;32(1):47-49.
3. Kudo, C., Miura, M., Gamoh, M. et al. Tumor lysis syndrome after treatment with sorafenib for hepatocellular carcinoma. *Int Canc Conf J* 4, 147–150 (2015).
4. Yamashita, N., Ohho, A, Yamazaki, A, Kurokawa, M, Kinjo, M, Kajiwar, E., A Case of advanced hepatocellular carcinoma with tumor lysis syndrome after introduction of sorafenib. (2014). *J-Stage*, 55(4), 228-234.
5. Habib, G., & Nashashibi, M. (2013). Fatal Tumor Lysis Syndrome Following Sorafenib Treatment. *Journal Of Medical Cases*, 4(4), 269-270.
6. Abbass, K., Dewani, S., Markert, R., Kaplon, M. K., & Baumann, M. A. (2011). All that glitters: sorafenib. *Internal medicine (Tokyo, Japan)*, 50(7), 797.

7. Shiozawa, K., Watanabe, M., Takenaka, H., Nagai, H., Ishii, K., Sakai, K., & Sumino, Y. (2010). Tumor lysis syndrome after sorafenib for hepatocellular carcinoma: a case report (Abstract only). *Hepato-gastroenterology*, 57(101), 688–690.
8. Huang, W. S., & Yang, C. H. (2009). Sorafenib induced tumor lysis syndrome in an advanced hepatocellular carcinoma patient. *World journal of gastroenterology*, 15(35), 4464–4466.
9. Chou, J., Cheng, K., Akella, T., Lee, C. C., & Ju, T. (2021). Tumor lysis syndrome in patients with hepatocellular carcinoma: A systematic review of published case reports10.7759/cureus.19128