Summary Safety Review - Nexavar (sorafenib) - Assessing the Potential Risk of Thrombotic Microangiopathy

Product: Nexavar (sorafenib)

Potential Safety Issue: Thrombotic microangiopathy (TMA), a group of rare, but serious and life-threatening conditions, involving the formation of clots in small blood vessels

Key Messages

- **Nexavar (sorafenib) is a prescription drug authorized for sale in Canada to treat advanced forms of liver, kidney and thyroid cancers.**
- **Health Canada reviewed the potential risk of TMA with the use of Nexavar. The safety review was triggered by a labelling update in the United States (U.S.) and international case reports published in the medical literature.**
- **Health Canada's review concluded that there may be a link between the use of Nexavar and the risk of TMA.**
- **Health Canada will work with the manufacturer to update the Canadian product safety information (Canadian product monograph [CPM]) for Nexavar to include the risk of TMA.**

Overview

Health Canada reviewed the potential risk of TMA with the use of Nexavar. This safety review was triggered by a U.S. Food and Drug Administration update to the product safety information for Nexavar to include the risk of TMA, as well as international case reports published in the medical literature.

Thrombotic microangiopathy is a group of rare, but serious and life-threatening conditions, involving the formation of clots in the small blood vessels. These clots can cause damage to organs and body systems by blocking proper blood flow. Thrombotic microangiopathy is a medical emergency and requires rapid intervention. A number of factors, including congenital conditions (those present at birth), infection, cancer and drugs, can cause TMA.

Use in Canada

- Nexavar is a prescription drug authorized 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.
- The yearly number of prescriptions dispensed by Canadian retail pharmacies for Nexavar decreased from approximately 1,700 prescriptions in 2016 to approximately 700 prescriptions in 2021.

Safety Review Findings

- Health Canada reviewed information provided by the manufacturer, and information resulting from searches of the Canada Vigilance database[a] and the published literature.
- Health Canada reviewed 28 cases (1 Canadian, 27 international) of TMA in patients taking Nexavar. Of the 28 cases, 12 (all international) met the criteria for further assessment to determine if there was a link between the use of Nexavar and TMA.
- All 12 cases, including 6 published in the scientific literature[1-6], were found to be possibly linked to the use of Nexavar. Three deaths were reported (2 of which were assessed as having a possible link to Nexavar and 1 unlikely to be linked).
- There were no Canadian cases of TMA found to be linked to the use of Nexavar.

Conclusions and Actions

- Health Canada's review of the available information concluded that there may be a link between the use of Nexavar and the risk of TMA.
- Health Canada will work with the manufacturer to update the CPM for Nexavar to include the risk of TMA.
- 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

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a. Canadian reports can be accessed through the Canada Vigilance Online Database.