Health Canada Endorsed Important Safety Information on TEMODAL® (temozolomide)

MERCK

May 7, 2014

Dear Health Care Professional:

Subject: Association of TEMODAL® (temozolomide) with the risk of hepatic injury

Merck Canada Inc., in consultation with Health Canada, would like to inform you of new warnings for TEMODAL® (temozolomide) regarding cases of hepatic injury, including fatal hepatic failure reported post-marketing.

TEMODAL® is an antineoplastic agent indicated for the treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment. It is also indicated for treatment of adult patients with glioblastoma multiforme or anaplastic astrocytoma and documented evidence of recurrence or progression after standard therapy.[1]

- Cases of hepatic injury, including fatal hepatic failure, have been reported in patients receiving temozolomide. Liver toxicity may occur several weeks after initiation of treatment or after temozolomide discontinuation.
- Liver function tests should be performed
  - prior to treatment initiation;
  - after each treatment cycle;
  - midway during the treatment cycle for patients on a 42 day treatment cycle.
- For patients with significant liver function abnormalities, the benefits and risks of continuing treatment should be carefully considered.

In total, 44 cases of hepatic injury, including fatal hepatic failure (19 cases) were identified in patients receiving temozolomide from market introduction (19 January 1994) through 15 March 2013. The cases of fatal hepatic failure were reported with an approximate onset of 42 to 77 days following initiation of treatment with temozolomide. Non-fatal cases of liver toxicity were also reported with times to onset of up to 112 days following initiation of treatment with temozolomide.

The Temodal® (temozolomide) Product Monograph has been revised to include updated information on the risk of hepatic injury and specific recommendations for monitoring of liver function.

A copy of the most up-to-date Product Monograph for TEMODAL®, is available at http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp or www.merck.ca.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of serious hepatic injury or other serious or unexpected adverse reactions in patients receiving TEMODAL® should be reported to Merck Canada Inc. or Health Canada.

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To correct your mailing address or fax number, contact Merck Canada Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax

For other health product inquiries related to this communication, contact Health Canada at:
Marketed Health Products Directorate
E-mail: mhpd_dpsc.public@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

If you have any questions regarding this important information or for any medical inquiries on Merck Canada products, please call the Merck Canada Medical Information Centre at 514-428-8600 or 1-800-567-2594, or Health Canada at the number listed above.

Sincerely,

Mauricio Ede, M.D.
Executive Director, Medical Affairs

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References:

1. TEMODAL® (temozolomide) Product Monograph, April 14, 2014