Health Canada Endorsed Important Safety Information on
[Pr] Myfortic* (mycophenolate sodium) Enteric-Coated tablets

NOVARTIS

December 21 , 2009

Dear Health Care Professional:

Subject: Reports of Pure Red Cell Aplasia in Patients Treated with Myfortic* (mycophenolate sodium)

Novartis Pharmaceuticals Canada Inc., in consultation with Health Canada, would like to inform you of important new safety information regarding reports of pure red cell aplasia (PRCA) in patients treated with Myfortic* (mycophenolate sodium) in combination with other immunosuppressive agents.

Myfortic*, an immunosuppressive agent, is currently indicated for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants, administered in combination with cyclosporine, and corticosteroids.

- Cases of PRCA have been reported worldwide in patients treated with Myfortic* in combination with other immunosuppressive agents. As of October 31, 2009, there have been no Canadian cases of PRCA reported in patients receiving Myfortic*.
- The mechanism for Myfortic-associated PRCA is unknown. In some cases PRCA was found to be reversible with dose reduction or cessation of Myfortic therapy. In transplant patients however, reduced immunosuppression may place the graft at risk.
- PRCA is usually treated by treating the underlying condition (disease) or discontinuing the drug that causes PRCA.

Myfortic* (mycophenolate sodium), delivers the active moiety mycophenolic acid (MPA), an immunosuppressive agent. MMF is converted to mycophenolic acid (MPA), the active ingredient in Myfortic*, following oral administration.

PRCA

PRCA is a type of anaemia that develops secondary to failure of erythropoiesis. Erythropoiesis is a process by which red blood cells (RBCs) are produced from immature precursors in the bone marrow. PRCA describes a condition in which RBC precursors in bone marrow are nearly absent, while megakaryocytes and white blood cell precursors are usually present at normal levels. PRCA may be idiopathic or occur as a manifestation of an underlying condition. Approximately 5% of all cases of PRCA are drug induced. Patients with PRCA may present with fatigue, lethargy, and/or abnormal paleness of the skin (pallor). Anaemia is the primary clinical concern in PRCA. The degree of anaemia can range from subclinical to severe. Anaemia in acute self-limited PRCA is barely noticeable; however, profound anaemia can occur in chronic acquired PRCA and in congenital PRCA. Patients with severe anaemia have symptoms and signs of uncompensated anaemia and present with weakness, tachycardia, and dyspnoea.

Myfortic* and PRCA

As of October 31, 2009, between 5 and 10 cases of PRCA out of an estimated cumulative worldwide exposure of 208,978 patient-years have been reported in patients receiving Myfortic* (mycophenolate sodium) in combination with other immunosuppressive agents (such as tacrolimus, cyclosporine, corticosteroids). None of these cases are from Canada. The mechanism for Myfortic-associated PRCA is not well understood but may be related to immunosuppression. In some cases, PRCA was found to be reversible with dose reduction or discontinuation of MPA therapy. When PRCA occurs in a patient on multiple immunosuppressants the relative

contribution of the drugs to PRCA and the prophylaxis of rejection must be considered before a decision is made to discontinue the drug.

Canadian Product Monograph for Myfortic* has recently been revised to include this new safety finding. A copy of most up-to-date Product Monograph can be found at:

http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp.

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 cases of serious PRCA, or other serious or unexpected adverse reactions in patients receiving Myfortic* should be reported to Novartis Pharmaceuticals Canada Inc., or Health Canada at the following addresses:

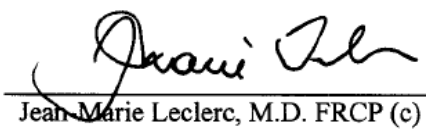
Novartis Pharmaceuticals Canada Inc.
385 Bouchard Blvd.
Dorval, Quebec H9S 1A9
Phone: 1-800-363-8883 (Medical Information)

Any suspected adverse reaction can also be reported to:
Canada Vigilance Program
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
Ottawa, Ontario, K1A 0K9
Tel: 613-957-0337 or Fax: 613-957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866-234-2345, Fax: 866-678-6789,
CanadaVigilance@hc-sc.gc.ca

The Adverse Reaction Reporting Form and the Adverse Reaction Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties.*
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei_form-eng.php
http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_fs-if/2009-ar-ei-guide-prof/index-eng.php

For other inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate (MHPD)
E-mail: mhpd_dpsc@hc-sc.gc.ca
Tel: 613-954-6522, Fax: 613-952-7738

Should you have any questions or require additional information regarding the use of Myfortic*, please contact Novartis Pharmaceuticals Canada Inc., at 1-800-363-8883 from 8:30 to 4:30 Monday to Friday Eastern Standard Time.



Jean-Marie Leclerc, M.D. FRCP (c)
Chief Scientific Officer and Senior Vice-President Clinical and Regulatory Affairs
Novartis Pharmaceuticals Canada Inc.
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