



JANSSEN-ORTHO

PUBLIC ADVISORY
Health Canada Endorsed Important Safety Information on
ORTHOCLONE OKT*3 (muromonab-CD3)

May 17, 2004

RE: Important New Safety Information on ORTHOCLONE OKT*3 (muromonab-CD3)

This is to inform you that Janssen-Ortho Inc., in consultation with Health Canada, has informed Canadian hospitals of important new safety information concerning ORTHOCLONE OKT*3 (muromonab-CD3). This drug is used to treat acute rejection from liver, kidney, and heart transplants that do not respond to other therapies.

Please note the following new safety information for the use of ORTHOCLONE OKT*3 in children (age up to 17 years):

- **ORTHOCLONE OKT*3 is not approved for use in children in Canada.**
- **Children treated with ORTHOCLONE OKT*3 may be at increased risk of nervous system complications, most notably a build-up of excess fluid in the brain (cerebral edema) that may result in a fatal condition called cerebral herniation.**
- **Children treated with ORTHOCLONE OKT*3 may also be at increased risk of lymphomas (cancers of the lymph system) and infections.**

Since 1986, a total of nine (9) cases of cerebral edema have been reported around the world in children, with subsequent cerebral herniation and death in 6 of the 9 cases. The majority of the cases of cerebral herniation in pediatric patients occurred within a few hours to one day after the first injection. Signs of cerebral edema and cerebral herniation may include the sudden appearance of:

- severe headache,
- seizures,
- impaired mental function,
- drowsiness and lethargy,
- coma.

Patients with high blood pressure and excess fluid build-up in their bodies (fluid overload) are at increased risk of developing these conditions.

In Canada, two (2) cases of cerebral edema in children have been reported following treatment with ORTHOCLONE OKT*3. However, there have been no Canadian cases of death due to cerebral herniation in either children or adults. In addition, the use of ORTHOCLONE OKT*3 has declined in Canada, with only 25 patients receiving the drug in 2003.

The identification, characterization, and management of marketed health product-related adverse reactions are dependent on the active participation of health care professionals in adverse reaction reporting programmes. Any occurrences of cerebral edema, lymphoma, infection or other serious and/or unexpected adverse reactions in patients receiving ORTHOCLONE OKT*3 (muromonab-CD3) should be reported to Janssen-Ortho Inc. or Health Canada at the following addresses:

Janssen-Ortho Inc.
19 Green Belt Drive
Toronto, Ontario
M3C 1L9
Or call toll free 1-800-567-3331
Or e-mail to dsscan@joica.jnj.com
Or fax to 416-449-2658

Any suspected adverse reaction can also be reported to:

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)
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

cadrmpp@hc-sc.gc.ca

For other inquiries: please refer to contact information.

The [AR Reporting Form](#) and the [AR 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/hpfb-dgpsa/tpd-dpt/adverse_e.html

http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adr_guideline_e.html

This advisory is in addition to a letter issued to all hospitals discussing the above-mentioned safety information. This letter can be accessed at Health Canada's Web site (http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_advisories_e.html), as well as the company web site: <http://www.janssen-ortho.com>. In addition, the prescribing

information (Product Monograph) for ORTHOCLONE OKT*3 is being revised to provide physicians with updated safety information for this product.

Patients who have any questions about ORTHOCLONE OKT*3 should contact their physician.

Sincerely,

A handwritten signature in black ink, appearing to read "Wendy Arnott". The signature is stylized and cursive.

Wendy Arnott, Pharm.D.
Vice President
Regulatory, Safety and Quality

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