Health Canada Endorsed Important Safety Information on ACLASTA* (zoledronic acid)

October 12, 2010

Dear Health Care Professional,

Subject: **Association of ACLASTA* (zoledronic acid 5 mg/100 mL) solution for intravenous infusion with renal dysfunction.**

Novartis Pharmaceuticals Canada Inc. ("Novartis"), in collaboration with Health Canada, would like to provide you with important renal safety information on renal dysfunction based on post-marketing experience with ACLASTA*. Therefore, Novartis would like to reinforce the current recommendations for selecting appropriate patients for ACLASTA*.

The ACLASTA* Product Monograph, has been revised to further emphasize precautions that should be taken into account to minimize the risk of renal adverse reactions:

- ACLASTA* has been associated with renal dysfunction manifested as deterioration in renal function and in rare cases, acute renal failure.
- Renal impairment has been observed following the administration of ACLASTA*, occasionally after a single administration.
- Renal failure requiring dialysis or with a fatal outcome has occurred especially in patients with history of renal impairment or other risk factors. Risk factors include advanced age, concomitant nephrotoxic medicinal products, concomitant diuretic therapy or dehydration occurring after ACLASTA* administration.

As of April 30, 2010 Novartis has received 265 spontaneous reports of renal impairment following administration of ACLASTA*, corresponding to a reporting rate of approximately 20 cases per 100,000 patient-years of exposure.

The following precautions should be taken to minimize the risk of renal adverse reactions:

- ACLASTA* should not be used in patients with severe renal impairment (creatinine clearance <30 mL/min).
- ACLASTA* should be used with caution when concomitantly used with other drugs that could impact renal function.
- Creatinine clearance should be calculated (e.g., Cockcroft-Gault formula) before each treatment with ACLASTA* followed by periodic monitoring of serum creatinine in patients with risk factors. Transient increase in serum creatinine may be greater in patients with underlying impaired renal function.
- Patients should be appropriately hydrated (500 mL or 2 glasses of water) prior to and following administration of ACLASTA*, especially elderly patients and those receiving diuretic therapy.
- A single dose of ACLASTA* should not exceed 5 mg and the duration of infusion should be no less than 15 minutes.

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 overdose symptoms or other serious or unexpected adverse reactions in patients receiving ACLASTA* 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: 0701E
Ottawa, Ontario, K1A 0K9
Telephone: 613-957-0337 or Fax: 613-957-0335
CanadaVigilance@hc-sc.gc.ca

To report an Adverse Reaction, consumers and health professionals may call toll free:
Telephone: 1-866-234-2345
Fax: 1-866-678-6789

Postage paid labels, the Canada Vigilance Reporting Forms and the Adverse Reaction Reporting Guidelines can be found on the MedEffect™ Canada Web site in the Adverse Reaction Reporting section. The Reporting Form is also in the *Canadian Compendium of Pharmaceuticals and Specialties.*

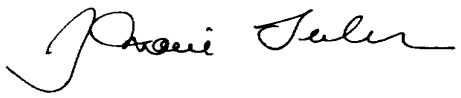
http://hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php

For other health product 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

To change your mailing address or fax number, contact Novartis Pharmaceuticals Canada Inc...

Should you have any questions or require additional information regarding the use of ACLASTA* (zoledronic acid), please contact Novartis Pharmaceuticals Canada Inc., Medical Information Department at 1-800-363-8883.

Sincerely,



Jean-Marie Leclerc, M.D. FRCP(C)
Chief Scientific Officer and Senior Vice-President Clinical and Regulatory Affairs

*ACLASTA is a registered trademark

References:
ACLASTA* is approved for the treatment and prevention of osteoporosis in postmenopausal women, to increase bone mass in men with osteoporosis, for treatment and prevention of glucocorticoid-induced osteoporosis and for the treatment of Paget's disease of bone.