Health Canada Endorsed Important Safety Information for all systemic formulations of diclofenac-containing medicines including VOLTAREN® / VOLTAREN® SR (diclofenac sodium), VOLTAREN RAPIDE® (diclofenac potassium), and ARTHROTEC® (diclofenac sodium/misoprostol)

October 6, 2014

Dear Health Care Professional,

Subject: **Update to cardiovascular safety information and decrease in recommended maximum daily dose for all systemic formulations of diclofenac-containing medicines including VOLTAREN® / VOLTAREN® SR (diclofenac sodium), VOLTAREN RAPIDE® (diclofenac potassium), and ARTHROTEC® (diclofenac sodium/misoprostol).**

Novartis Pharma Canada Inc. ("Novartis Canada") and Pfizer Canada Inc. ("Pfizer Canada"), in collaboration with Health Canada, are informing you of revisions made to the Product Monographs for all diclofenac-containing systemic medicines (tablets and suppositories) including VOLTAREN/VOLTAREN SR (diclofenac sodium), VOLTAREN RAPIDE (diclofenac potassium), ARTHROTEC (diclofenac sodium/misoprostol).

This safety update does not refer to topical formulations of diclofenac, such as gel or eye drops.

Diclofenac (diclofenac sodium) is indicated for the symptomatic treatment of rheumatoid arthritis and osteoarthritis. Diclofenac (diclofenac potassium) is indicated for the short-term treatment of acute, mild to moderately severe pain that may be accompanied by inflammation, in conditions such as: musculoskeletal and/or soft tissue trauma including sprains, postoperative pain following dental extraction, episiotomy or dysmenorrhea.

Health Canada is currently updating the labelling of all systemic formulations of diclofenac-containing medicines as follows:

- Diclofenac (tablets and suppositories), particularly at higher doses (150 mg per day), is associated with an increased risk of serious cardiovascular adverse events (such as myocardial infarction, stroke or thrombotic events which can be fatal) that is comparable to COX-2 inhibitors. Evidence suggests that the risk may increase with the dose and duration of use.

- The maximum recommended daily dose of systemic diclofenac has been reduced from 150 mg per day to 100 mg per day for all indications, excluding VOLTAREN RAPIDE which allows for a 200 mg dose only on the first day of treatment for dysmenorrhea. To minimize the potential risk for an adverse cardiovascular event, the lowest effective dose should be used for the shortest possible duration.

- Treatment with diclofenac is not recommended in patients with pre-existing cardiovascular disease (CVD) or cerebrovascular disease, or presenting risk factors for CVD. For these patients, treatment options other than non-steroidal anti-inflammatory drugs (NSAIDs), particularly COX-2 inhibitors and diclofenac, should be considered first.

Meta-analyses of randomized clinical trials comparing several different NSAIDs suggest that diclofenac systemic formulations, particularly at high doses, is associated with an increased risk of cardiovascular adverse events that is comparable to COX-2 inhibitors. Large population-based observational studies conducted in the general population also support these findings. From January 1, 2008 to December 31, 2012 (approximately 353 X 1000 patient treatment-years), Health Canada received 39 reports of serious cardiovascular events potentially associated with systemic diclofenac use. One of these cases had a fatal outcome.

A Public Communication (PC) to inform patients of this new safety information has also been posted on Novartis Canada, Pfizer Canada and Health Canada websites. Please visit www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/index-eng.php

In this public communication, patients have been advised to contact their health care provider if their current daily dose is more than 100 mg per day.

Please refer to VOLTAREN / VOLTAREN SR (diclofenac sodium) and VOLTAREN RAPIDE (diclofenac potassium) Product Monographs at the following links for complete details: http://www.novartis.ca/en/products/pharmaceuticals/index.shtml

Please refer to the ARTHROTEC (diclofenac sodium/misoprostol) Product Monograph at the following link for complete details: http://www.pfizer.ca/en/our_products

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Any case of serious or unexpected adverse reactions in patients receiving VOLTAREN / VOLTAREN SR (diclofenac sodium), VOLTAREN RAPIDE (diclofenac potassium), ARTHROTEC (diclofenac sodium/misoprostol) or the generic versions of diclofenac-containing products should be reported to Novartis Canada, Pfizer Canada, the appropriate generic company or Health Canada.

Contact information for manufacturer of VOLTAREN / VOLTAREN SR and VOLTAREN RAPIDE
Novartis Pharma Canada Inc.
385 Bouchard Blvd., Dorval, (QC) H9S 1A9
Phone: 1-800-363-8883 (Medical Information)

Contact information for manufacturer of ARTHROTEC
Pfizer Canada Inc.
17300 Trans-Canada Highway
Kirkland, QC H9J 2M5
Telephone: 1-800-463-6001

Health Canada contact
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

Sincerely,

Original signed by

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