

**Health Canada Endorsed Important Information on  
AREPANRIX™ H1N1 vaccine (AS03-Adjuvanted H1N1 Pandemic Influenza Vaccine)**



November 12, 2009

**Subject: AREPANRIX™ H1N1 Vaccine Authorization for Sale and Post-Market Activities**

Dear Health Care Professional,

GlaxoSmithKline Inc., in consultation with Health Canada, would like to inform you of important information regarding the authorization for sale and post-market activities for AREPANRIX™ H1N1 vaccine (AS03-Adjuvanted H1N1 Pandemic Influenza Vaccine).

- Health Canada has authorized the sale of AREPANRIX™ H1N1 vaccine on October 21, 2009 based on limited clinical testing in humans under the provision of an Interim Order.
- Health Canada considers that the benefit/risk profile of AREPANRIX™ H1N1 vaccine is favourable.
- GlaxoSmithKline Inc. is conducting additional studies in Canada and elsewhere to provide further information regarding the benefit/risk ratio of AREPANRIX™ H1N1 vaccine.
- As with all vaccines, health care professionals should report serious or unexpected adverse events following immunization.

Authorization for Sale of AREPANRIX™ H1N1 Vaccine in Canada

On October 13, 2009, an Interim Order was issued by the Minister of Health at the request of the Public Health Agency of Canada to allow the authorization for sale of a vaccine for the novel influenza A H1N1 virus due to the current influenza A H1N1 pandemic. An Interim Order is issued by the Minister of Health under Section 30.1 of the *Food and Drugs Act* in rare situations where the Minister believes that immediate action is required to deal with a significant risk, direct or indirect, to human health, public safety, or the environment.

The authorization for sale for AREPANRIX™ H1N1 vaccine was based on quality and available non-clinical and clinical information submitted for AREPANRIX™ H1N1 vaccine, PANDEMRIX™ vaccine (a similar influenza A H1N1 adjuvanted vaccine manufactured by GlaxoSmithKline in Dresden, Germany and currently available in Europe), and supporting quality and safety data from a similar adjuvanted vaccine that was developed in the pre-pandemic period using an influenza A H5N1 strain.

AREPANRIX™ H1N1 vaccine is indicated for active immunization against the H1N1 2009 influenza

strain in an officially declared pandemic situation. Recommendations made by the Public Health Agency of Canada should also be taken into consideration. For detailed information on Indications and Clinical Use, Dosage and Administration, Contraindications, Warnings and Precautions, and Adverse Reactions, please consult the Product Information Leaflet for AREPANRIX™ H1N1 vaccine available at the Health Canada website ([www.hc-sc.gc.ca](http://www.hc-sc.gc.ca), under H1N1 flu virus regulatory information or at <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/legislation/interimorders-arretesurgence/prodinfo-vaccin-eng.php>) and at the GlaxoSmithKline Inc website ([www.gsk.ca](http://www.gsk.ca)).

### Clinical Data

Preliminary reactogenicity data are available from two studies that evaluated the safety of PANDEMRIX™ vaccine in healthy subjects aged 18-60 years. Transient pain at the site of injection was the most frequently reported solicited adverse event (approximately 90% of subjects). Other very common adverse events after one 3.75 µg dose include myalgia, fatigue, headache and arthralgia.

Two clinical studies conducted with PANDEMRIX™ vaccine in healthy subjects aged 18 to 60 years showed immune responses post-dose 1 which exceeded the immunogenicity criteria for a pandemic influenza vaccine as defined by international licensing authorities. In the clinical study using the approved marketed formulation of PANDEMRIX™, the immune response after one dose of 3.75 µg adjuvanted vaccine indicated seroprotection rate of 100% compared to 93.9% with a non-adjuvanted formulation of H1N1 vaccine, three weeks following vaccination.

Although not part of the initial Health Canada approval process, clinical data in elderly and children between 6 and 36 months of age is available showing similar results as in the above mentioned population.

A number of additional clinical studies are underway in adults and children to further evaluate the safety and immunogenicity of AREPANRIX™ H1N1 vaccine. Information on these clinical trials is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov). Results from these studies will be assessed by Health Canada as they become available and the Product Information Leaflet for AREPANRIX™ H1N1 vaccine will be updated accordingly. Healthcare professionals should consult the Health Canada or GlaxoSmithKline Inc. website for the most-up-to-date Product Information Leaflet.

AREPANRIX™ H1N1 vaccine contains the adjuvant system AS03 which is an oil-in-water emulsion composed of squalene (naturally occurring substance found in plants, animals and humans), tocopherol (vitamin E oil), and polysorbate 80 (Tween 80), an emulsifier also used in other vaccines. The adjuvant system AS03 has been tested in more than 41,000 subjects in GlaxoSmithKline's influenza programmes including H5N1, H1N1 and candidate adjuvanted seasonal influenza flu vaccines. Available data show these adjuvanted vaccines to be generally well tolerated with acceptable safety profiles. The AS03 adjuvant is used to boost the immune response generated by the vaccine.

Healthcare professionals should report all serious adverse events following immunization with AREPANRIX™ H1N1 vaccine, including adverse events of special interest such as anaphylaxis, Bell's palsy, convulsion, demyelinating disorders (acute disseminated encephalomyelitis, multiple sclerosis, optic neuritis, transverse myelitis), encephalitis, Guillain-Barre syndrome, neuritis and vasculitis. Laboratory-confirmed H1N1 infections in a vaccinated patient should be reported as a vaccination failure. The occurrence of thrombocytopenia or autoimmune disorders following immunization with AREPANRIX™ H1N1 vaccine should also be reported.

Managing marketed health product-related adverse events depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse events are generally presumed to underestimate the risks associated with health product treatments. Any case of serious or unexpected adverse events in patients receiving AREPANRIX™ H1N1 vaccine should be reported to your local public health authorities. Reports may also be sent directly to the Public Health Agency of Canada or GlaxoSmithKline at the following addresses:

The Adverse Event Following Immunization Reporting Form and its User Guide can be found on the Health Canada web site or in The Canadian Compendium of Pharmaceuticals and Specialties.

<http://www.phac-aspc.gc.ca/im/ae-fi-form-eng.php>

The site also links to each provincial/territorial jurisdiction for information on where to send adverse event reports.

**Any suspected adverse event can also be reported to:**

The Public Health Agency of Canada

Vaccine Safety Section

130 Colonnade Road

Address Locator: 6502A

Ottawa, Ontario, K1A 0K9

Tel: 1-866-844-0018

Fax: 1-866-844-5931

[caefi@phac-aspc.gc.ca](mailto:caefi@phac-aspc.gc.ca)

Or

GlaxoSmithKline Inc.

7333 Mississauga Road

Mississauga, Ontario

L5N 6L4

Tel.: 1-800-387-7374

[www.gsk.com](http://www.gsk.com)

**For other inquiries related to this communication, please contact Health Canada at:**

email: [BGTD\\_ORA\\_Enquiries@hc-sc.gc.ca](mailto:BGTD_ORA_Enquiries@hc-sc.gc.ca)

Tel : 613-957-1722

Sincerely,

*original signed by*

Dr. Tjark Reblin, MD, MBA

Vice President, Medical Division and Chief Medical Officer

GlaxoSmithKline Inc.