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To: **Physicians & Nurse Practitioners**

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Date: **March 29, 2021**

Subject: **AstraZeneca COVID-19 Vaccine Safety Update**

Very rare cases of Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) have been reported following administration of the AstraZeneca COVID-19 Vaccine in several European Economic Area countries. A combination of thrombosis and thrombocytopenia, in some cases accompanied by bleeding, has been observed very rarely in the post-market setting following vaccination with the AstraZeneca COVID-19 Vaccine. This includes severe cases presenting as venous thrombosis, occurring at unusual sites such as cerebral venous sinus thrombosis (CVST), mesenteric vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. **To date, similar cases have not been reported in Canada.**

Health Canada as the regulator of vaccines in Canada is completing a full risk assessment while more information and analysis are gathered from international partners. To date, such adverse events have not been reported in Canada. The National Advisory Committee on Immunization (NACI) has recommended the pause of the rollout for people under the age of 55. PEI has decided to temporarily pause the roll out of the AstraZeneca vaccine until more information is known.

Individuals who have been vaccinated with AstraZeneca COVID-19 Vaccine or COVISHIELD are being instructed to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg swelling and persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms including sudden onset of severe or persistent worsening headaches or blurred vision several days after vaccination, or who experience skin bruising (other than at the site of vaccination) or petechiae starting a few days or more after vaccination, should seek prompt medical attention.

Clinical Diagnosis and Treatment

Patients with severe symptoms should urgently seek care at their nearest emergency department. Patients with lesssevere symptoms may have initial investigations done in the primary care or outpatient setting.

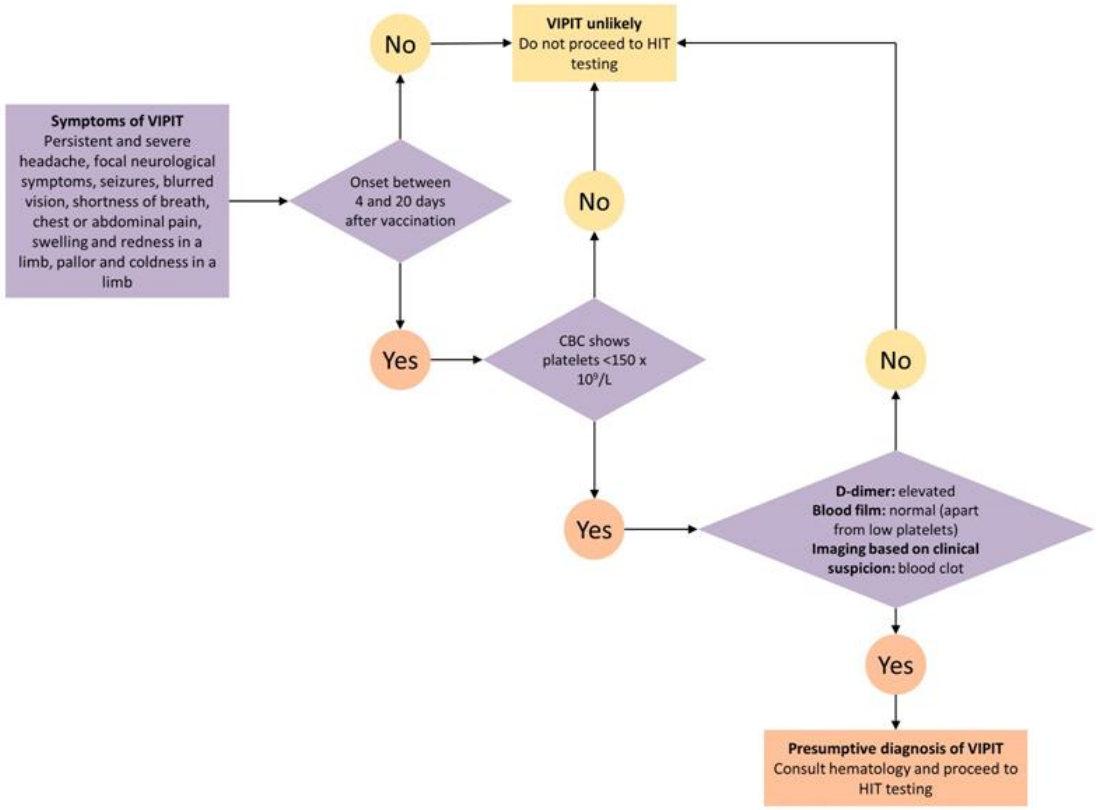
Clinicians should ask patients about their COVID-19 vaccine history and should draw a complete blood count (CBC). VIPIT is unlikely if symptoms of blood clotting fall outside of the 4 to 20 day time frame OR if the platelet count is $\geq 150 \times 10^9/L$.[6] VIPIT is more likely if symptoms of blood clotting fall within the 4 to 20 day time frame AND the

platelet count is < 150 x 10^9/L, and such patients should be evaluated at their nearest emergency department for suspected VIPIT.

Patients with suspected VIPIT should go on to have blood work drawn including a D-dimer level and a blood film. When there is strong clinical suspicion of VIPIT, patients should also have diagnostic imaging to investigate for blood clots (including appropriate imaging to rule out cerebral sinus vein thrombosis (CSVT), if the patient presents with a persistent and severe headache). It is not known whether VIPIT, like heparin-induced thrombocytopenia (HIT), is associated with arterial thromboses, but arterial clots should be considered if patients have consistent symptoms. An elevated D-dimer, a normal blood film (apart from thrombocytopenia), and confirmation of a blood clot on diagnostic imaging makes the diagnosis of VIPIT presumptive.

The confirmatory diagnosis of VIPIT is made by testing for HIT. This testing should be done even if the patient has had no previous exposure to heparin. HIT testing involves two steps: identification of antibodies against the complex of platelet factor 4 and heparin; and confirmatory functional testing of the antibodies' ability to activate platelets.[1] The HIT antibody test appears very sensitive to VIPIT; if it is positive, VIPIT is confirmed, and if it is negative, VIPIT is unlikely.[1]

Diagnosing Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT)



A number of large hospital laboratories test for HIT antibodies, but only one lab in Canada performs confirmatory functional testing (the McMaster University Platelet Immunology Laboratory). Therefore, presumptive VIPIT should prompt an urgent hematology consultation (in person, virtually, or by phone) to arrange testing and start safe empiric treatment of blood clots (see below).

[1] Greinacher A, Selleng K, Warkentin TE. Autoimmune heparin-induced thrombocytopenia. *J Thromb Haemost*. 2017;15(11):2099-2114. https://doi.org/10.1111/jth.13813

Patients with presumptive and confirmed VIPIT should be treated similarly to HIT. The Box presents the treatment principles for patients with presumptive and confirmed VIPIT. Until VIPIT has been ruled out, anticoagulation with heparin (unfractionated heparin and low molecular weight heparins) should be avoided. Platelet transfusions should not be given.

Treating Blood Clots in Patients with Presumptive or Confirmed VIPIT

1. No Heparin
2. No platelet transfusion
3. First line anti coagulants: direct oral anti-Xa inhibitors[2] (e.g. rivaroxaban, apixaban, edoxaban)
4. Consult hematology
5. IVIG 1g/kg[3] daily for 2 days for severe or life-threatening blood clots

Health Canada continues to evaluate the situation and we are committed to providing you with updates on the situation in the coming days.

A reminder that any serious adverse events following immunization must be reported to the CPHO, even presumptive VIPIT presentations. Please reach out to our office at **(902) 368-4996** if you have questions and concerns in the coming days.

[2] The dose of direct oral anti-Xa inhibitor is identical to the dose used to treat uncomplicated deep vein thromboses. If the patient has severe renal impairment that makes direct oral anticoagulants unsafe, advice from a hematologist should be sought to guide use of parenteral anticoagulants that are safe to use in HIT.

[3] It is important to dampen the prothrombotic response with intravenous immunoglobulin (IVIG). Administration of high dose IVIG (1 g/kg of body weight daily for two days) is appropriate and can be guided by the consulting hematologist