PublicHealth
WELLINGTON-DUFFERIN-GUELPH
Stay Well.

UPDATE

SUBJECT:	**Second Doses for AstraZeneca/COVISHIELD Vaccine Recipients**
Date:	May 21, 2021
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To:	Primary Care Providers, Physicians, Pharmacies
From:	Dr. Matthew Tenenbaum, Associate Medical Officer of Health

Last week, the Ministry of Health announced that first doses of the AstraZeneca/COVISHIELD vaccine would be paused due to an increase in the reported rate of vaccine-induced immune thrombotic thrombocytopenia (VITT). To date, physicians and pharmacists in WDG have already delivered first doses of this vaccine to over 20,000 patients, many of whom already have appointments booked for their second dose.

At this point, public health units are awaiting further information from the Ministry of Health regarding second doses. However, it is likely that your patients will be able to choose between two different options[1]:

1. Receiving a second dose of AstraZeneca/COVISHIELD; or
2. Receiving a 'mixed schedule' with an mRNA vaccine (e.g. Pfizer) as the second dose

WDGPH is working to gather information about the options that will be made available in order to ensure that your patients receive the best possible care. **It is important that your patients know that they will likely have two good options for their second dose**. Some patients may have a strong preference for one of the two options.

How will clients who received AstraZeneca/COVISHIELD in primary care or pharmacy receive a second dose of COVID vaccine?

WDGPH expects that pharmacists and primary care providers will have the option of completing the two-dose series for their clients with either an mRNA vaccine or with AstraZeneca/COVISHIELD. Pharmacists and primary care providers will be expected to counsel each client about the risk/benefit of both options and allow the client to make an informed choice. More information about options for ordering second dose vaccines will be available soon.

Possible Option #1: Receiving a Second Dose of AstraZeneca/COVISHIELD

While there is still a risk of VITT, early data suggests that the risk after a second dose is lower than after a first dose.

Our current understanding of the second-dose VITT risk is based on data from the United Kingdom's Yellow Card reporting system (analogous to Canada's AEFI reporting system). As of May 12, 2021, 309 cases of VITT were reported among 23.9 million first-dose recipients and 9.0 million second dose recipients.[2] The reporting rate was approximately 12.3 per million for first doses, versus 1.7 per million for second doses (Table 1). However, these reporting rates are likely to change as additional cases are reported.

Table 1: Thromboembolic events with concurrent thrombocytopenia following AstraZeneca included in UK Yellow Card reporting (up to May 12, 2021).[2]

	First Doses*	Second Doses	Total
Reported cases of thromboembolic events with concurrent thrombocytopenia	294	15	309
Total doses administered (estimated)	23.9 million	9.0 million	32.9 million
Reporting rate	~12.3 per million doses	~1.7 per million doses	

* includes first and unknown doses.

Possible Option #2: Receiving a Second Dose with an mRNA Vaccine ('Mixed Schedule')

Providing a second dose with a different vaccine, such as an mRNA vaccine, may be a reasonable option for patients who do not wish to receive the AstraZeneca/COVISHIELD vaccine. The practice of *heterologous prime-boost immunization* (i.e. using two different vectors or delivery systems expressing the same antigen) has been shown to increase humoral and T-cell immunity in animal models, and may produce a more effective immunity in humans than using multiple doses of the same vaccine (*homologous prime-boost*).[3,4]

Several trials are currently evaluating the use of 'mixed schedules' for COVID-19 vaccines. These include the Com-COV and Com-COV2 trials in the UK.[5] Early safety and reactogenicity data from the Com-COV trial found that participants who received a mixed schedule (of Pfizer and AstraZeneca) were more likely to experience mild-moderate side effects such as chills and muscle aches.[6] This may indicate that the mixed schedule generated a potent immune response. Efficacy and immunogenicity data is expected in the coming weeks.

In Spain, the Combivacs study evaluated the impact of the Pfizer vaccine when given as a second dose, following AstraZeneca. According to preliminary results reported in the media, participants who received their second dose with Pfizer had significantly higher levels of neutralizing antibodies than participants who received a second AstraZeneca shot.[7]

In Canada, the MOSAIC study will assess the impact of using mixed vaccine schedules and extended dose intervals.[8] Enrolment will begin shortly, and it is unlikely that data will be available in the near term to inform practice.

The National Advisory Committee on Immunization is expected to provide a recommendation on the use of mixed schedules in the coming weeks. Their recommendation would take the available data into account but would also be informed by expert opinion.

References:

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