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FOCUS ON

COVID-19 Vaccines: Viral Vector-based Vaccines

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Introduction

The novel coronavirus disease (COVID-19) pandemic has stimulated unprecedented efforts to develop vaccines that provide protection against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1]

This Focus On is intended for health care providers and public health partners. It provides an overview of viral vector-based vaccines, including products authorized for use in Canada. This document will be updated as new information becomes available.

The basics: Viral vector-based vaccines

Viral vector-based vaccines have emerged as a promising alternative to conventional vaccine platforms.[2-4] Viral vector-based technology has been widely used for gene therapy, cancer therapeutics and animal vaccines for several decades, and most recently for two human Ebola vaccines.[3-7]

What is a viral vector?

A viral vector is a harmless, attenuated (weakened) virus that has been modified to act as a delivery system for transferring genetic instructions to our cells.[3-7]

Vaccines work by training our immune system to recognize and respond to infectious agents. For most vaccines, this is accomplished by delivering a weakened or inactivated virus or a component of the virus (such as a specific protein) to the body, which triggers an immune response.[2,3] In contrast, viral vector-based vaccines work by using a harmless, unrelated attenuated virus (a viral vector), to deliver genetic instructions (DNA) to human cells to produce a viral protein for the pathogen of interest, which is then recognized by the body as foreign.[2-8] These proteins, known as antigens, use the body's normal processes to safely produce an immune response.[2-8] There are two main types of viral vector-based vaccines:

- **Non-replicating (or replication-incompetent or replication-deficient) viral vector-based vaccines** are genetically modified so that they are unable to produce new viral particles. The viral vector enters our cells where our cell machinery is used to produce viral antigen once this is accomplished, the viral vector is cleared.[2,4,9] COVID-19 viral vector-based vaccines authorized for use in Canada are non-replicating vaccines.[9-12]

- **Self-replicating (or replication-competent) viral vector-based vaccines** are able to produce new viral particles in the cells they infect. These vectors use our host cell machinery to produce new viral particles, which go on to infect additional host cells and produce more viral antigen.[2,4,9] None of the COVID-19 viral vector-based vaccines authorized for use in Canada or other jurisdictions are replicating vaccines.[1]

Key messages: COVID-19 viral vector-based vaccines

1. You cannot get COVID-19 or other infections from a viral vector-based vaccine

Viral vector-based COVID-19 vaccines are non-infectious (they do not contain whole or live virus) and are modified so that the viral vector cannot replicate inside our cells.[2-7] Therefore, there is no risk of a viral vector-based vaccine causing COVID-19 or any other viral infection.[5-7]

2. Viral vector-based vaccines are a newer vaccine platform, but not new technology

Viral vector therapeutics (e.g., gene therapy, animal and human vaccines) have been studied for over four decades, with a well-established manufacturing and safety profile. Most recently, this technology has been used to develop vaccines to respond to recent Ebola outbreaks.[4-7]

3. Viral vector-based vaccines do not affect or interact with our DNA

Genetic material delivered by a viral vector is genetically stable and does not integrate or interact with our DNA.[3-7] Human cells break down and get rid of the viral vector and DNA as soon as they finish using its instructions.[5-7]

Mechanism of action and immune response

COVID-19 viral vector-based vaccines use our normal cell processes to safely produce the SARS-CoV-2 spike (S) glycoprotein antigen, which activates both **antibody** and **cell-mediated** immune responses.[2,3,8,9]

- Viral vector-based vaccines use a harmless, attenuated adenovirus as a vector to deliver genetic instructions (DNA) to our cells to make the SARS-CoV-2 spike glycoprotein. Adenoviruses are a group of DNA viruses that commonly cause colds.[2-7]

- During manufacturing, DNA coding for the SARS-CoV-2 spike glycoprotein is inserted into the adenoviral vector, which acts as a delivery system to bring the SARS-CoV-2 spike glycoprotein code to our cells. The adenoviral vector is genetically modified so that it cannot replicate or cause infection.[2-7,9]

- Once inside our cells, DNA encoding the SARS-CoV-2 spike glycoprotein is released from the viral vector in the cell's nucleus where the body's cellular machinery makes a transcript called messenger RNA (mRNA). This transcript is then released into the cytoplasm of our cells where it is used to make the SARS-CoV-2 spike glycoprotein antigens. The viral vector, DNA fragment and mRNA transcript are then rapidly broken down and disposed of by our cells.[2-9]

- Next, the SARS-CoV-2 spike glycoprotein antigen is temporarily displayed on the surface of our cells, where it is recognized as foreign and activates B (antibody-mediated) and T (cell-mediated) cells of the immune system.[2,3,8,9]

- **Antibody-mediated** responses directed against the SARS-CoV-2 spike glycoprotein are believed to be important for blocking the virus from entering our cells.[8] Activation of **cell-mediated** immune responses are expected to play a central role in providing us long-term protection.[8]

Advantages and limitations of viral vector-based vaccines

Recent advances in viral vector-based vaccine technology offer several advantages over classical vaccine platforms. Adenoviral vector-based vaccines are highly immunogenic and trigger strong antibody and cell-mediated immune system responses that are anticipated to provide longer-term protection.[2,3,8] Viral vector-based vaccines offer several operational benefits including a single dose product series (i.e., Janssen) and less stringent storage and handling conditions (i.e., refrigerated temperatures, due to greater product stability) relative to other vaccine platforms.[4,10-18]

Limitations of viral vector-based vaccines include diminished immune responses and vaccine effectiveness in individuals with pre-existing immunity to the viral vector.[3,4,6,7] Since adenoviruses are a common cause of colds, individuals with pre-existing adenoviral immunity achieved through natural infection may neutralize the viral vector and mount a limited immune response; however this limitation is overcome for COVID-19 vaccines by using adenovirus serotypes that rarely cause infections or using a non-human adenovirus.[3,4,6,7]

COVID-19 viral vector-based vaccines

In Canada, two COVID-19 viral vector-based vaccines have been authorized for use under Health Canada's Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19.[5] Detailed characteristics of each vaccine are outlined in **Table 1**.

Table 1: Characteristics of COVID-19 viral vector-based vaccines authorized for use in Canada

Trade Name	AstraZeneca Vaxzevria™ COVID-19 Vaccine	Janssen (Johnson & Johnson) COVID-19 Vaccine[a]
Manufacturer	AstraZeneca Canada Inc.[b]	Janssen Inc. (Johnson & Johnson)
Vaccine Platform	Recombinant, replication-deficent (non-replicating) chimpanzee adenovirus (ChAdOx1) vector-based vaccine[10,11,13,14]	Recombinant, replication-incompetent (non-replicating) adenovirus serotype 26 (Ad26) vector-based vacine[12,15,16]
Antigenic Target	SARS-CoV-2 spike (S) glycoprotein[10,11]	Pre-fusion SARS-CoV-2 spike (S) glycoprotein[12,15,16]
Health Canada Authorized Ages for Use	18 years of age and older	18 years of age and older
No. of Doses Administered	2 doses[10,11]	1 dose[12]
Dosage	5 x 10^{10} viral particles per 0.5 mL dose[10,11]	5 x 10^{10} viral particles per 0.5 mL dose[12]
Adjuvant	No[10,11]	No[12]
Diluent	No[10,11]	No[12]
Schedule	Authorized Interval: 4 to 12 weeks[10,11,17] Extended Interval: 16 weeks[10,11,17,18] Minimum Interval: 28 days[10,11,17]	N/A
Route of Administration	Intramuscular (IM)[10,11]	Intramuscular (IM)[12]
Storage Conditions	2 ˚C to 8 ˚C[10,11] Post-puncture, 2 ˚C to 8 ˚C for up to 48 hours OR at room temperature (up to 30 ˚C) for up to 6 hours Do not freeze[10,11] Keep vials in original packaging to protect from light[10,11]	2 ˚C to 8 ˚C[12] Post-puncture, 2 ˚C to 8 ˚C for up to 6 hours OR at room temperature (up to 30 ˚C) for up to 3 hours Do not freeze[12] Keep vials in original packaging to protect from light[12]

[a] Janssen COVID-19 vaccine was authorized under the ISAD IO on March 5th, 2021, but has not be distributed for use in Canada.[19]

[b] Health Canada had authorized two manufacturers under the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19 (ISAD IO) to produce the COVID-19 vaccine ChAdOx1-S: AstraZeneca (trade name AstraZeneca Vaxzevria™ COVID-19 vaccine) and Verity Pharmaceuticals and the Serum Institute of India (SSI) (trade name COVISHIELD vaccine).[19] The COVISHIELD vaccine provided a temporary supply to Canadians; it was not transitioned to the Food and Drug Regulations when the ISAD IO expired on September 16, 2021.[20,19]

Vaccine Effectiveness and Safety

Both viral vector-based COVID-19 vaccines authorized for use in Canada were shown to be safe and effective against symptomatic COVID-19 disease and severe outcomes, such as hospitalization and death.[14-19] Clinical trials and real-world vaccine effectiveness studies demonstrated vaccine efficacy, between 67% (Janssen) and 82% (AstraZeneca Vaxzevria™) with an interval of > 12 weeks between doses), and high vaccine effectiveness against severe outcomes following a complete series.[12-17] Emerging evidence suggests that the AstraZeneca Vaxzevria™ COVID-19 vaccine provides good protection against the B.1.1.7 (Alpha) and B.1.617.2 (Delta) variants of concern (VOCs), with a small reduction in vaccine effectiveness against symptomatic B.1.617.2 (Delta) infection as compared to B.1.1.7 (Alpha).[17, 20] The Janssen vaccine offers protection against symptomatic, moderate to severe infection with B.1.351 (Beta) VOC; however, there is growing evidence that the AstraZeneca vaccine offers limited protection against the B.1.351 (Beta) VOC.[17]

In clinical trials, the most common side effects following vaccination with viral vector-based vaccines included pain at the injection site, headache and fatigue, with systemic symptoms (e.g., fatigue, headache, muscle pain, joint pain, chills and fever) reported more frequently after the second dose.[12-17] These side effects are typically mild and resolve within a few days. Very rare reports of thrombosis (blood clotting) with new onset thrombocytopenia (low levels of platelets) called Thrombosis with Thrombocytopenia Syndrome (TTS) or Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) following vaccination with AstraZeneca Vaxzevria™ and Janssen COVID-19 vaccines have been identified through post-marketing safety survillance.[17] On May 11, 2021, Ontario paused the administration of first doses of the AstraZeneca Vaxzevria™ COVID-19 vaccine. Canada's National Advisory Committee on Immunization (NACI) preferentially recommends offering mRNA COVID-19 product for initiation and/or completion of a COVID-19 vaccine series.[17] Health Canada has updated the AstraZeneca Vaxzevria™ and Janssen COVID-19 vaccine product monographs to include information on these conditions.[10-12] For more information see Public Health Ontario's COVID-19 Viral Vector Vaccines and Rare Blood Clots - Vaccine Safety Surveillance in Action, Ontario's COVID-19 Science Advisory Table scientific briefs on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) Following Adenovirus Vector COVID-19 Vaccination, and the NACI Recommendations on the use of COVID-19 vaccines.[17] Health Canada has also updated the AstraZeneca Vaxzevria™ product monograph to include information on very rare reports of Guillain-Barré Syndrome (GBS) and capillary leak syndrome (CLS) following vaccination with AstraZeneca Vaxzevria™.[10,17]

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Summary of Revisions

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This document is current to September 23, 2021. New material in this revision is highlighted in the table below.

Section	Revision	Implementation Date
Vaccine Safety and Effectiveness	Addition of reference Ontario's COVID-19 Science Advisory Table Scientific Brief on VITT.	23/09/2021
Table 1	Addition of vaccine manufacturer and trade names. Addition of reference Ontario's COVID-19 Science Advisory Table on VITT.	23/09/2021

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