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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 and 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 with longer-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 operational benefits including a single dose product series (i.e., Janssen (Johnson and Johnson) COVID-19 vaccine) and less stringent storage and handling conditions (i.e., refrigerated temperatures, due to greater product stability) relative to other vaccine platforms.[4,10-17]

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 November 2021, Health Canada under the *Food and Drug Regulations* granted full authorization to two COVID-19 viral vector-based vaccines: the AstraZeneca Vaxzevria COVID-19 vaccine and Janssen (Johnson and Johnson) COVID-19 vaccine.[18,19]

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[a]	Janssen (Johnson & Johnson) COVID-19 Vaccine[b]
Manufacturer	AstraZeneca Canada Inc.	Janssen Inc.
Generic Name	ChAdOx1-S (recombinant)	Ad26.COV2.S (recombinant)
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]
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]

Trade Name	AstraZeneca Vaxzevria COVID-19 Vaccine[a]	Janssen (Johnson & Johnson) COVID-19 Vaccine[b]
Diluent	No[10,11]	No[12]
Schedule[c]	Authorized Interval: 4 to 12 weeks[10,11,17] Optimal interval: At least 8 weeks[17] Minimum Interval: 28 days[10,11,17]	N/A
Route of Administration	Intramuscular (IM)[10,11]	Intramuscular (IM)[12c]
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]	May be stored and/or transported at -25°C to -15°C until expiry date[12] 2°C to 8°C for up to 6 months, not exceeding the expiry date[12] Post-puncture, 2°C to 8°C for up to 6 hours OR at room temperature (up to 25°C) for up to 3 hours[12] Do not freeze[12] Keep vials in original packaging to protect from light[12]

[a] 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.[19,20] AstraZeneca Vaxzveria is available in limited quantities in Ontario to those with a contraindication to receiving a COVID-19 mRNA vaccine.

[b] Janssen COVID-19 vaccine is available in limited quantities in Ontario, and is available on request for eligible populations.

[c] The authorized interval is the dosing schedule approved by Health Canada, based on evidence from clinical trials. The recommended optimal interval between doses is provided by National Advisory Committee on Immunization (NACI) and is included in their recommendations following review of available data and based on expert advice.

Vaccine Effectiveness and Safety

In clinical trials, 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 (Johnson and Johnson)) and 82% (AstraZeneca Vaxzevria) with an interval of >12 weeks between doses), and high vaccine effectiveness against severe outcomes following a complete series (AstraZeneca Vaxzevria 70%., Janssen (Johnson and Johnson 89.4%) during a time when variants of concern (VOC), Alpha and Delta were prominant.[12-17,22] Preliminary data from the United Kingdom Health Security Agency found that after 2 doses of the AstraZeneca Vaxzevria vaccine, VE against symptomatic Omicron infection was 45 to 50%; this then dropped to almost no effect from 20 weeks after the second dose.[23] Among those who had received two doses of AstraZeneca Vaxzevria, there was almost no protection against symptomatic disease caused by Omicron 20 to 24 weeks after dose 2.[24] Twenty-five or more weeks after two doses of AstraZeneca Vaxzevria COVID-19 vaccine, VE was approximately 25 to 35% against hospitalization following infection with the Omicron VOC.[23] There are currently no peer-reviewed studies reporting on the effectiveness of Janssen (Johnson and Johnson) against severe disease caused by Omicron.[22]

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 (Johnson and Johnson) COVID-19 vaccines have been identified through post-marketing safety survillance.[17] Health Canada has updated the AstraZeneca Vaxzevria and Janssen (Johnson and Johnson) COVID-19 vaccine product monographs to include information on these conditions.[10-12,25] On May 11, 2021, Ontario paused the administration of first doses of the AstraZeneca Vaxzevria COVID-19 vaccine.[26]

Based on the lower efficacy and vaccine effectiveness of viral vector vaccines, and the increased risk of very rare, serious adverse events (e.g., VITT, Guillain Barré Syndrome (GBS), and capillary leak syndrome (CLS)) Canada's National Advisory Committee on Immunization (NACI) has made a strong recommendation for the preferential use of mRNA COVID-19 vaccine series in all authorized age groups.[17] NACI recommends that a complete primary series of a viral vector COVID-19 vaccine (AstraZeneca Vaxzevria, Janssen (Johnson and Johnson)) may be offered to individuals in the authorized age group, only when all other authorized COVID-19 vaccines are contraindicated or inaccessible.[17]

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 COVID-19 vaccine: Canadian Immunization Guide.[17]

References

1. World Health Organization. COVID-19 vaccine tracker and landscape [Internet]. Geneva: World Health Organization; 2021 [cited 2021 Mar 15]. Available from: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

2. van Riel D, de Witt E. Next-generation vaccine platforms for COVID-19. Nat Mater. 2020;19(8):810-20. Available from: https://doi.org/10.1038/s41563-020-0746-0

3. Krammer F. SARS-CoV-2 vaccines in development. Nature. 2020;586(7830):516-27. Available from: https://doi.org/10.1038/s41586-020-2798-3

4. Robert-Guroff M. Replicating and non-replicating viral vectors for vaccine development. Curr Opin Biotechnol. 2007;18(6):546-56. Available from: http://doi.org/10.1016/j.copbio.2007.10.010

5. Health Canada. Viral vector-based vaccines for COVID-19 [Internet]. Ottawa, ON: Government of Canada; 2020 [modified 2020 Dec 11; cited 2021 Dec 07]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines/type-viral-vector.html

6. Centers for Disease Control and Prevention. Vaccines & immunizations: understanding and explaining viral vector COVID-19 vaccines [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2020 [updated 2021 Oct 18; cited 2021 Mar 05]. Available from: https://www.cdc.gov/vaccines/covid-19/hcp/viral-vector-vaccine-basics.html

7. Gavi. What are viral vector-based vaccines and how could they be used against COVID-19? [Internet]. Geneva: Gavi; 2020 [cited 2021 Mar 05]. Available from: https://www.gavi.org/vaccineswork/what-are-viral-vector-based-vaccines-and-how-could-they-be-used-against-covid-19

8. Poland GA, Ovsyannikova IG, Kennedy RB. SARS-CoV-2 immunity: review and applications to phase 3 vaccine candidates. Lancet. 2020;396(10262):1595-606. Available from: https://doi.org/10.1016/S0140-6736(20)32137-1

9. Public Health Agency of Canada; Salvadori M, Killikelly A. COVID-19 vaccine candidates in development special focus on mRNA and viral vector platforms [Internet]. Presented at: PHO Grand Rounds. 2020 Oct 01 [cited 2021 Mar 05]; Toronto, ON. Available from: https://www.publichealthontario.ca/-/media/event-presentations/2020/pho-rounds-covid-19-vaccine-candidates.pdf?la=en

10. AstraZeneca Canada Inc. Product monograph including patient medication information: AstraZeneca COVID-19 vaccine [Internet]. Missisauga, ON: AstraZeneca; 2021 [modified 2021 Nov 19; cited 2021 Dec 07]. Available from: https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-pm-en.pdf

11. Verity Pharmaceutricals Inc. Product monograph including patient medication information: COVISHIELD COVID-19 vaccine (ChAdOx1-S [recombinant]) [Internet]. Mississauga, ON: Verity Pharmaceutricals Inc.; 2021 [modified 2021 Aug 13; cited 2021 Dec 07]. Available from: https://covid-vaccine.canada.ca/info/pdf/covishield-pm-en.pdf

12. Janssen Inc. Product monograph including patient medication information: Janssen COVID-19 vaccine [Internet]. Toronto, ON: Janssen Inc.; 2021 [modified 2021 Nov 23; cited 2021 Dec 07]. Available from: https://covid-vaccine.canada.ca/info/pdf/janssen-covid-19-vaccine-pm-en.pdf

13. Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021;397(10269):99-111. Available from: https://doi.org/10.1016/s0140-6736(20)32661-1

14. Voysey M, Costa Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single dose administration, and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine. SSRN 3777268 [Preprint]. 2021 Feb 01 [cited 2021 Mar 16]. Available from: https://doi.org/10.2139/ssrn.3777268

15. Sadoff J, Le Gars M, Shukarev G, Heerwegh D, Truyers C, de Groot AM, et al. Interim results of phase 1-2a trial of Ad26.COV.S covid-19 vaccine. N Eng J Med. 2021;384(19):1824-35. Available from: http://doi.org/10.1056/NEJMoa2034201

16. Sadoff J, Le Gars M, Shukarev G, Heerwegh D, Truyers C, de Groot AM, et al. Safety and immunogenicity of the Ad26.COV2.S COVID-19 vaccine candidate: interim results of phase 1/2a, double-blind randomized, placebo-controlled trial. medRxiv 20199604 [Preprint]. 2020 Sep 25 [cited 2021 Mar 16]. Available from: https://doi.org/10.1101/2020.09.23.20199604

17. Government of Canada. COVID-19 vaccine: Canadian Immunization Guide. [Internet]. Ottawa, ON: Government of Canada; 2021 [modified 2022 Jan 22; cited 2022 Feb 02]. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html

18. Health Canada. Drug and vaccine authorizations for COVID-19: list of authorized drugs, vaccines, and expanded indications. [Internet]. Ottawa, ON: Government of Canada; 2021 [cited 2021 Dec 07]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/list-drugs.html

19. *Food and Drug Regulations*, CRC, c 870. Available from: https://laws-lois.justice.gc.ca/eng/regulations/c.r.c.,_c._870/index.html

20. Government of Canada; Health Canada. Interim order respecting the importation, sale and advertising of drugs for use in relation to COVID-19 (ISAD IO) [Internet]. Ottawa. ON: Government of Canada; 2020 [archived; cited 2021 Sep 27]. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/interim-order-import-sale-advertising-drugs.html

21. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 vaccine effectiveness over time - what we know so far [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [modified 2021 Oct 28; cited 2021 Dec 07]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/covid-wwksf/2021/11/wwksf-vaccine-effectiveness-over-time.pdf?sc_lang=en

22. McMaster Health Forum; Coronavirus Variants Rapid Response Network. COVID-19 living evidence Ssnthesis #6. Version 31 [Internet]. Hamilton, ON: McMaster University; 2022 [cited 2022 Mar 04]. Available from: https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-syntheses/covid-19-living-evidence-synthesis-6.31---what-is-the-efficacy-and-effectiveness-of-available-covid-19-vaccines-in-general-and-specifically-for-variants-of-concern.pdf?sfvrsn=3929a111_7

23. UK. Health Security Agency. COVID-19 vaccine surveillance report, week 8 [Internet]. London, UK: Crown Copyright; 2022 [cited 2022 Mar 08]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1057599/Vaccine_surveillance_report_-_week-8.pdf

24. Andrews N, Stowe J, Kirsebom F, Toffa S, Gallagher RE, Gower C et al. Covid-19 vaccine effectiveness against the Omicron (B.1.1.529) variant [Internet]. N Eng J Med. 2022 Mar 02 [Epub ahead of print]. Available from: https://doi.org/10.1056/NEJMoa2119451

25. Government of Canada. Vaccines for COVID-19 [Internet]. Ottawa, ON: Government of Canada; 2020 [cited 2022 Feb 02]. Available from: https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19/vaccines.html

26. Ontario. Ministry of Health. COVID-19 vaccine administration [Internet]. Toronto, ON: Government of Ontario; 2021 [modified 2021 Nov 26; cited 2021 Dec 08]. Available from: https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID-19_vaccine_administration.pdf

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