COVID-19 Vaccine - ChAdOx1-S [recombinant] AstraZeneca/COVISHIELD Vaccine Biological Page

Section 7:	**Biological Product Information**		**Standard #: 07.205**
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	AstraZeneca COVID-19 Vaccine	**COVISHIELD COVID-19 Vaccine**
Manufacturer	AstraZeneca	Verity Pharmaceuticals Inc. & Serum Institute of India (In partnership with AstraZeneca)
Biological Classification	• Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS CoV 2 Spike (S) glycoprotein.	
Indications for Provincially Funded Vaccine	**Persons 40 years of age and older** • May be considered for individuals 18 years to 39 years of age for whom mRNA vaccines are contraindicated (e.g., anaphylaxis to PEG) OR eligible individuals who decline mRNA COVID-19 vaccine. • This vaccine is being offered in a phased approach. Please follow operational guidelines to assess eligibility. • Eligibility will be rolled out in cohorts by year of birth, therefore persons 39 years of age may receive this vaccine if born in an eligible year. **Notes:** • mRNA COVID-19 vaccine is preferentially recommended for eligible individuals who are at highest risk of severe illness and death and highest risk of exposure to COVID-19. • Individuals 40 years of age and older who choose to receive COVID-19 vaccine prior to their phased eligibility may receive AstraZeneca/COVISHIELD vaccine.	
Preferred Use	N/A	
Dose	0.5 mL	
Route	IM	
Schedule	2 doses • Dose 1: day 0 • Dose 2: day 84 (12 weeks)* *The interval between dose 1 and dose 2 should be extended up to 4 months (16 weeks/112 days) for all populations except the following if they have received AstraZeneca/COVISHIELD vaccine as a first dose: • Solid organ transplants (SOT) recipients - pre-transplant and post-transplant. • Hematopoietic stem cell transplants (HSCT) recipients - pre-transplant and post-transplant while in immunosuppressed state (post-HSCT individuals are generally considered to be immunocompetent after 3 years as long as they are not on immunosuppressive drugs). • Individuals with malignant hematologic disorders and non-hematologic malignant solid tumors prior to receiving or receiving active treatment which includes chemotherapy, targeted therapies, and immunotherapy (does not include individuals receiving solely hormonal therapy, radiation therapy or a surgical intervention). • Individuals on anti-CD20 monoclonal antibodies (such as rituximab, ocrelizumab, and ofatumumab).	

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	Immunization for these groups should occur at a time when the patients are most likely to mount immune responses. These individuals should receive their second dose 12 weeks after dose 1. *See below for rationale/evidence*. **Notes:** • Minimum spacing between doses is 28 days. Given that clinical trials have shown that longer spacing increases the efficacy of the vaccine compared to an interval of 4 weeks, this minimum spacing is not recommended. • Currently, no data on a maximum interval between doses or on medium- or long-term efficacy of COVID-19 vaccines are available. In general, regardless of the time between doses, interruption of a vaccine series does not require restarting the series. *Second dose for individuals under 40 years of age who have been immunized with AstraZeneca/COVISHIELD vaccine :* • For individuals with a contraindication or declination of mRNA COVID-19 vaccine, second dose of AstraZeneca/COVISHIELD vaccine will be given as per schedule. • For other individuals, decisions on the type of second dose will be determined based on the latest evidence and research.	
Rationale/Evidence for Extending the Interval Between Dose 1 and Dose 2	• Data from clinical trials show a high vaccine efficacy after the initial dose of the AstraZeneca vaccine. (See National Advisory Committee on Immunization - Recommendations on the use of COVID-19 Vaccine(s) for additional efficacy information). • Disease modelling has suggested that there is increased effectiveness in reducing the number of COVID-19 cases and achieving overall benefit by administering one dose to more people quickly when there is limited vaccine supply and widespread community transmission, compared to the strategy of saving early doses to ensure delivery of second dose according to manufacturers' recommendations. • In studies on vaccines for other infections, a longer time between the first and second dose can make the overall immune response to the vaccine better, while a shorter time between them can lower the overall response. • Published data from the AstraZeneca clinical trial indicated that delaying the second dose to greater than 12 weeks resulted in a better efficacy against symptomatic disease compared to shorter intervals between doses. • The rate of waning protection without the administration of the second dose is unknown, but short term sustained protection is consistent with immunological principles and vaccine science where it is not expected to see rapid waning of a highly effective vaccine in adults over a relatively short period of time. Extending the interval between doses was shown to be a good strategy through modelling, even in scenarios considering a six month interval and in theoretical scenarios where waning protection was considered. A second dose continues to be recommended.	
Rationale/Evidence for Exceptions to Extended Interval	• Emerging evidence shows suboptimal/poor immune responses after one dose in individuals with cancer or solid organ transplant. Immune response was greatly and rapidly increased by administering the second dose as per product monograph at 21 days (Pfizer vaccine was used in the study). • The exceptions are focused only on those with the most profound immune compromising conditions given the currently available evidence and the fact that increasing population level protection as quickly as possible also protects those with immune compromising conditions. • Those who are immunocompromised would be recommended to receive mRNA vaccine preferentially. For those who have received AstraZeneca/COVISHIELD as the first dose, second doses are recommended at 12 weeks. Clinical trials have shown that the longer spacing increases the efficacy of this vaccine compared to an interval of 4 weeks, therefore this spacing is recommended for those who are immunocompromised to ensure they have the greatest level of protection.	

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Contraindications/ Precautions	**Contraindications:** • Persons under 18 years of age • Known severe hypersensitivity to any component of the vaccine ○ One non-medicinal ingredient in the vaccine that has the potential to cause type 1 hypersensitivity reactions is polysorbate 80. Polysorbate 80 may be found in medical preparations (e.g. vitamin oils, tablets, anticancer agents) and cosmetics. • Anaphylactic or other allergic reactions to previous dose of AstraZeneca or COVISHIELD COVID-19 vaccine. **Precautions:** • Individuals receiving anticoagulant therapy or those with a bleeding disorder that would contraindicate intramuscular injection should not be given the vaccine unless the potential benefit clearly outweighs the risk of administration. • Administration should be postponed in individuals suffering from acute severe febrile illness. • Prior to receiving the AstraZeneca/COVISHIELD vaccine, individuals should be informed of what is currently known about the risk of the rare but serious events characterized by thrombosis with thrombocytopenia that were reported following immunization of the vaccine in order to help them make an informed decision.	

Immunocompromised and Auto-Immune Disorders	• At this time, there is an absence of evidence on the use of COVID-19 vaccine in immunocompromised individuals and those with auto-immune disorders. These groups were not included in large enough numbers in the initial trials to provide solid information.
	• COVID-19 vaccine may be offered to individuals in the eligible group who are immunosuppressed due to disease or treatment and those with an auto-immune disorder if a risk assessment with their primary health care provider or medical specialist determines that the benefits outweigh the potential risks. Risks would include that:
	  ○ Immunocompromised persons may have a diminished immune response to the vaccine and
	  ○ There is a theoretical concern that viral vector vaccines may elicit an inflammatory response and possibly exacerbate existing autoimmune diseases.
	• However, with the exception of SOT and HSCT clients, the individual may also be immunized without consulting their primary health care provider or medical specialist following their acknowledgment of the risks mentioned above and the absence of evidence on the use of COVID-19 vaccine in these populations.
	  ○ Response for immunizers if individual has not consulted with their primary health care provider: “The vaccine studies have not tested whether this vaccine is safe or effective for you. We recommend that you do not receive the immunization until you have discussed the potential risks and benefits with your doctor. However, it is your choice whether to proceed without consulting your doctor.”
	• SOT and HSCT clients require consultation with primary health care provider or medical specialist prior to immunization, including timing of when vaccine should be given.
	• Additional resources:
	  ○ COVID-19 Scientific Advisory Group Rapid Evidence Report.	

Pregnancy	• The safety and efficacy of AstraZeneca COVID-19 vaccine in pregnancy women has not yet been established. • At this time, there is an absence of evidence on the use of COVID-19 Vaccine in pregnant individuals. These groups were not included in large enough numbers in the initial trials to provide solid information. • COVID-19 vaccine may be offered to individuals in the eligible group who are pregnant if a risk assessment with their primary health care provider or obstetrician determines that the benefits outweigh the potential risks for the woman and fetus. ○ However, the individual may also be immunized without consulting their primary health care provider or obstetrician following their acknowledgment of the absence of evidence on the use of COVID-19 vaccine in this population.	

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	○ Response for immunizers if individual has not consulted with their primary health care provider: "The vaccine studies have not tested whether this vaccine is safe or effective for you. We recommend that you do not receive the immunization until you have discussed the potential risks and benefits with your doctor. However, it is your choice whether to proceed without consulting your doctor." • Additional resources: ○ Society of Obstetricians and Gynecologists of Canada Statement on COVID-19 Immunization in Pregnancy. • It would be prudent to delay pregnancy by 28 days or more after the administration of the complete two-dose vaccine series of a COVID-19 vaccine.	
Lactation	• It is unknown whether AstraZeneca COVID-19 vaccine is excreted in human milk. A risk to the newborns/infants cannot be excluded. • At this time, there is an absence of evidence on the use of COVID-19 vaccine in breast feeding individuals. These groups were not included in large enough numbers in the initial trials to provide solid information. • COVID-19 vaccine may be offered to individuals in the eligible group who are breastfeeding if a risk assessment with their primary health care provider or medical specialist determines that the benefits outweigh the potential risks for the mother and infant. ○ However, the individual may also be immunized without consulting their primary health care provider or medical specialist following their acknowledgment of the absence of evidence on the use of COVID-19 vaccine in this population. ○ Response for immunizers if individual has not consulted with their primary health care provider: "The vaccine studies have not tested whether this vaccine is safe or effective for you. We recommend that you do not receive the immunization until you have discussed the potential risks and benefits with your doctor. However, it is your choice whether to proceed without consulting your doctor."	
Other Considerations	• Individuals with a history of lab confirmed COVID-19 infection who have no contraindications can be provided COVID-19 vaccine. • Individuals presenting for immunization do not need to be tested for previous COVID-19 infection. • Immunization of individuals who may be currently infected with SARS-CoV-2 is not known to have a detrimental effect on the illness. ○ However, individuals with COVID-19-like symptoms should not go to an immunization/venue in order to minimize the risk of COVID-19 transmission and their immunization should be deferred. For individuals who are isolated due to COVID-19-like symptoms, immunization should be deferred until the test result is back and negative and the person is otherwise eligible based on the acuity of their symptoms (i.e. no acute severe febrile illness). If tested positive, immunization should be deferred until at least after the isolation period is over.	
Updated Safety Information: Risk of Thrombosis with Thrombocytopenia	• A combination of thrombosis and thrombocytopenia, in some cases accompanied by bleeding, has been observed very rarely in Europe and Canada following immunization with AstraZeneca COVID-19 Vaccine. • This includes severe cases presenting as venous thrombosis, including unusual sites such as cerebral venous sinus thrombosis, mesenteric vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. • This adverse event is being referred to as Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT). • This entity is associated with the development of antibodies that "activate" platelets, which stimulate the formation of clots and result in thrombocytopenia. • The exact mechanism by which the AstraZeneca vaccine triggers VITT is still under investigation. At this time, no other risk factors have consistently been identified in patients who develop VITT. • Cases have been reported in women and men in all age groups. • The global frequency of VITT has been estimated at approximately 1 case in 100,000 to 250,000 doses of vaccine administered.	

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	• Health Canada has assessed the available data and after a thorough, independent assessment of the currently available scientific data, Health Canada has concluded that these very rare events may be linked to use of the vaccine. This is in line with the findings of other regulators. As a result, the Department has updated warnings in the product information to inform Canadians of the possible side effects and to provide information about the signs and symptoms and when to seek prompt medical attention following immunization.
	• Healthcare professionals should be alert to the signs and symptoms of thromboembolism and or thrombocytopenia and be aware of VITT including how to diagnose and treat the condition.
	• Those immunized should be instructed to seek immediate medical attention if they develop symptoms of thromboembolism and/or thrombocytopenia between days 4 and 28 following receipt of the AstraZeneca vaccine such as:
	  ○ shortness of breath,
	  ○ chest pain,
	  ○ leg swelling,
	  ○ persistent abdominal pain,
	  ○ severe or persistent worsening headaches,
	  ○ blurred vision, or
	  ○ skin bruising beyond the site of immunization or petechiae
	See:
	• Important Safety Information on AstraZeneca COVID-19 Vaccine and COVISHIELD: Risk of Thrombosis with Thrombocytopenia
	• Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT) Following AstraZeneca COVID-19 Vaccination.
	• Health Canada provides update on safety review of AstraZeneca and COVISHIELD COVID-19 vaccines	

Possible Reactions	**Common** • Pain, tenderness, redness, bruising, warmth, itching, swelling, and induration at the injection site • Fever, chills • Fatigue, malaise • Headache, arthralgia, myalgia • Nausea, vomiting, diarrhea **Uncommon** • Hyperhydrosis • Decreased appetite • Lymphadenopathy • Pruritis • Rash • Dizziness • Somnolence **Rare:** • Anaphylaxis • Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT). • As with any immunization, unexpected or unusual side effects can occur. Refer to product monograph for more detailed information.	
Composition	Each 0.5 mL dose contains: COVID-19 Vaccine (ChAdOx1-S* recombinant) 5 x 10^{10} viral particles *Recombinant, replication-deficient chimpanzee adenovirus vector encoding the unmodified SARS-CoV-2 Spike (S) glycoprotein (GP) produced in genetically modified human embryonic kidney (HEK) 293 cells by recombinant DNA technology. Essential Amino Acids • L-Histidine • L-Histidine hydrochloride monohydrate	

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	Stabilizer • Magnesium chloride hexahydrate • Polysorbate 80 • Ethanol • Disodium edetate dihydrate (EDTA) Others • Sucrose • Sodium chloride • Water for injection No adjuvants or preservatives	
Blood/Blood Products	Contains no human blood/blood products	
Bovine/Porcine Products	Contains no bovine/porcine products.	
Latex	Does not contain latex.	
Interchangeability	• Currently, no data exists on the interchangeability of COVID-19 vaccines. • The vaccine series should be completed with AstraZeneca or COVISHIELD vaccine.	
Administration with Other Products	• In the absence of evidence, COVID-19 vaccines should not be given simultaneously with other live or inactivated vaccines due to the potential for immune interference and the need to be able to monitor for potential symptoms of COVID-19 and COVID-19 vaccine adverse events without potential confounding from adverse events following other vaccines. • If a COVID-19 vaccine is inadvertently administered at the same time as another vaccine, neither dose should be repeated. • In the absence of evidence, it would be prudent to wait for a period of at least 28 days between the administration of a dose of COVID-19 vaccine and the administration of another vaccine (except in the case where another vaccine is required for post-exposure prophylaxis). • In the absence of evidence, it would be prudent to wait for a period of at least 14 days after the administration of another vaccine before administrating a COVID-19 vaccine. • Currently there is no data on the impact of the COVID-19 vaccines on tuberculin skin testing or IGRA (QFT) test results. There is a theoretical risk that COVID-19 vaccines may temporarily affect cell-mediated immunity, resulting in false-negative tuberculin skin testing or IGRA (QFT) test results. o If tuberculin skin testing or an IGRA test is required for baseline screening, it should be administered and read before administration of any COVID-19 vaccine or delayed for at least 28 days after a dose of COVID-19 vaccine. o Immunization with COVID-19 vaccines may take place at any time after all steps of tuberculin skin testing (including read) have been completed. o If tuberculin skin testing is required for other reasons (e.g., contact tracing, immigrants, query LTBI), testing should not be delayed, as these are theoretical considerations. However, re-testing (at least 28 days after a dose of COVID-19 vaccine) of individuals with negative results for whom there is high suspicion of TB infection may be prudent in order to avoid missing cases due to potentially false-negative results. • Timing of administration and potential interference between COVID-19 vaccine and monoclonal products are currently unknown and the primary care provider or medical specialist should be consulted on a case-by-case basis. • Timing of administration and potential interference between COVID-19 vaccine and convalescent plasma as part of COVID-19 treatment are currently unknown and the primary care provider or medical specialist should be consulted on a case-by-case basis. • Viral vector COVID-19 vaccines may be given at any time before or after an immunoglobulin preparation (including RhIg) or blood product has been administered. There is no recommended minimum interval between these products and COVID-19 vaccine.	

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Appearance	• The solution is colourless to slightly brown, clear to slightly opaque and particle free.	
Storage	• Can be stored in a refrigerator between +2°C to +8°C storage until expiry. • Punctured vials can be stored at room temperature up to +30°C for 6 hours. • Punctured vials can be stored in a refrigerator (+2 to +8ºC) for 48 hours. • Punctured vials can be re-refrigerated, but the cumulative storage time at room temperature must not exceed 6 hours, and the total cumulative storage time must not exceed 48 hours. After this time, the vial must be discarded. • Do not freeze.	
Packaging	**Vaccine:** • 10 doses per vial • 5 mL of solution in a 10-dose vial (clear type I glass) with stopper (elastomeric with aluminum overseal) • 10 vials per package	
Preparation/ Reconstitution	• No reconstitution is required.	
Vaccine Code	COVAUVec	COVIISVec
Antigen Code	COVID-19-5	COVID-19-8
Licensed for	18 years of age and older.	

Program Notes:

- 2021 February 26: Licensed for use in Canada
- 2021 March 10: Implemented in Alberta
- 2021 March 29: Indications for use changed to 55 years of age and older. Pause on use in individuals under 55 years of age.
- 2021 April 19: Indications for use changed to 40 years of age and older.
- 2021 April 21: Exceptions to extended interval to include SOT, HSCT, and individuals with malignant hematologic disorders and non-hematologic malignant solid tumors receiving specific types of active treatment, and individuals on anti-CD20 monoclonal antibodies who have received AstraZeneca/COVISHIELD vaccine as the first dose.

Related Resources:

- Alberta Health Services Website (2020). COVID-19 Vaccine Information.

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