FOCUS ON
COVID-19 Vaccines: mRNA Vaccines
6th revision: October 2021

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 messenger ribonucleic acid (mRNA) vaccines, including products authorized for use in Canada. This document will be updated as new information becomes available.

The Basics: mRNA Vaccines

mRNA vaccines have emerged as a promising alternative to conventional vaccine platforms. \(^2,3\) While efforts to develop a mRNA vaccine were initially limited by the transient nature of mRNA in human cells, major innovations over the last two decades have accelerated mRNA vaccine development. \(^2-4\)

What is mRNA?

Messenger ribonucleic acid (mRNA) is a type of transcript, which is used by our cells to transfer genetic information from DNA to make proteins. \(^2,5-7\)

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, mRNA vaccines work by delivering instructions to human cells to produce a viral protein, 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. There are two main types of RNA vaccines:

- **Non-replicating (or non-amplifying) RNA vaccines** are the simplest type and consist of mRNA coding for the viral antigen. Our cell machinery is used to make a specific viral antigen and once this is accomplished, the mRNA is cleared. \(^9,10\) COVID-19 mRNA vaccines are non-replicating RNA vaccines. \(^3,10\)

- **Self-replicating (or self-amplifying) RNA vaccines** consist of an RNA coding for the viral antigen and the virus’ replication machinery, allowing for abundant production of viral antigen. \(^9,10\)
Key messages: COVID-19 mRNA vaccines

1. You cannot get COVID-19 from an mRNA vaccine.

mRNA COVID-19 vaccines are non-infectious (they do not contain whole or live SARS-CoV-2); therefore there is no risk of an mRNA vaccine causing COVID-19.3-7

2. mRNA vaccines are a new vaccine platform, but not a new technology.

While mRNA therapeutics have been studied for over two decades, recent scientific advancements have improved mRNA stability and delivery which has been important for bringing mRNA vaccines and cancer mRNA therapeutics into clinical use.2,4,6,7

3. mRNA vaccines do not affect or interact with our DNA.

Human cells break down and get rid of mRNA as soon as they finish using its instructions. mRNA does not enter the nucleus of human cells, where our DNA is located, eliminating any risk of mRNA interacting with our DNA.2-7,11

4. Both mRNA COVID-19 vaccines used in Canada are safe and highly effective

The mRNA COVID-19 vaccines used in Canada (Pfizer-BioNTech Comirnaty® and Moderna Spikevax®) are both equally safe and highly effective for the prevention of symptomatic illness and severe outcomes, such as hospitalization and death.12-17 Both vaccines work in the same way to produce an immune response in our body.

Mechanism of action and immune response

COVID-19 mRNA vaccines use our normal cell processes to safely produce the SARS-CoV-2 spike glycoprotein antigen, which activates both antibody and cell-mediated immune responses.7,10,11

- mRNA vaccines are encapsulated in a lipid coat, commonly referred to as a lipid nanoparticle (LNP), which allows them to easily cross cell membranes into our cells.2-7

- Once inside our cells, mRNA is released into the cytoplasm where the body’s cell machinery makes copies of the SARS-CoV-2 spike glycoprotein antigen. The mRNA instructions are then rapidly broken down and disposed of by our cells.3-7,10,11

- 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.3,10,11

- Activation of cell-mediated immune responses are expected to play a central role in providing us with long-term protection.10 Antibody-mediated responses directed against the SARS-CoV-2 spike glycoprotein are believed to be important for blocking the virus from entering our cells.10

Advantages and limitations of mRNA vaccines

Recent advances in mRNA vaccine technology offer several advantages over classical vaccine platforms. Rapid and scalable manufacturing as compared to conventional vaccines, allows for quicker vaccine
production in response to novel pathogens, such as SARS-CoV-2, or novel SARS-CoV-2 variants of concern (VOC).\textsuperscript{3,4,11,18-19} Additionally, since mRNA vaccines produce both antibody and cell-mediated immune system responses, they are anticipated to provide longer-term protection.\textsuperscript{10} Clinical trial data and real-world vaccine effectiveness studies have demonstrated that COVID-19 mRNA vaccines are highly efficacious against confirmed symptomatic and severe COVID-19 disease. Growing evidence suggests mRNA vaccines provide protection against asymptomatic infection and SARS-CoV-2 transmission.\textsuperscript{20} Finally, mRNA vaccines are non-infectious so there is no risk of infection from the vaccine.\textsuperscript{3-7,11} Limitations of mRNA vaccine use relate to vaccine storage and handling requirements, including the need for freezing temperatures (due to mRNA being highly labile), and increased reactogenicity (i.e., side effects such as fever, muscle aches and fatigue), relative to some other vaccine platforms.\textsuperscript{3-5,12-1}

**COVID-19 mRNA vaccines**

In Canada, two COVID-19 mRNA vaccines were initially authorized for use under Health Canada’s \textit{Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19 (ISAD IO)} and on September 16\textsuperscript{th}, 2021 received full authorization under the \textit{Food and Drug Regulations}.\textsuperscript{21} Detailed characteristics of each vaccine are outlined in Table 1.
Table 1: Characteristics of COVID-19 mRNA vaccines authorized for use in Canada

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Pfizer-BioNTech Comirnaty® COVID-19 Vaccine</th>
<th>Moderna Spikevax® COVID-19 Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Pfizer Inc., BioNTech Manufacturing GmbH</td>
<td>ModernTX, Inc.</td>
</tr>
<tr>
<td>Generic Name</td>
<td>BNT162b</td>
<td>mRNA-1273</td>
</tr>
<tr>
<td>Vaccine Platform</td>
<td>LNP-encapsulated, non-replicating, nucleoside-modified mRNA vaccine(^{12,13})</td>
<td>LNP-encapsulated, non-replicating, nucleoside-modified mRNA vaccine(^{14-16})</td>
</tr>
<tr>
<td>Antigenic Target</td>
<td>Pre-fusion SARS-CoV-2 spike (S) glycoprotein(^{12,13})</td>
<td>Pre-fusion SARS-CoV-2 spike (S) glycoprotein(^{14,16})</td>
</tr>
<tr>
<td>Authorized Ages for Use</td>
<td>12 years of age and older(^{13,17})</td>
<td>12 years of age and older(^{16,2})</td>
</tr>
<tr>
<td>No. of Doses Administered</td>
<td>2 doses(^{13})</td>
<td>2 doses(^{14,16})</td>
</tr>
<tr>
<td>Dosage</td>
<td>30 µg of mRNA per 0.3 mL dose(^{13})</td>
<td>100 µg of mRNA per 0.5 mL dose(^{16})</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>No(^{12,13})</td>
<td>No(^{14-16})</td>
</tr>
<tr>
<td>Diluent</td>
<td>Yes(^{12,13})</td>
<td>No(^{14-16})</td>
</tr>
<tr>
<td>Schedule</td>
<td>Authorized Interval: 21 days (3 weeks)(^{13,17}) Extended Interval: 16 weeks(^{17}) Minimum Interval: 19 days(^{17})</td>
<td>Authorized interval: 28 days (4 weeks)(^{16,17}) Extended Interval: 16 weeks(^{17}) Minimum Interval: 21 days(^{17})</td>
</tr>
<tr>
<td>Route of Administration</td>
<td>Intramuscular (IM)(^{12,13})</td>
<td>Intramuscular (IM)(^{16})</td>
</tr>
<tr>
<td>Storage Conditions</td>
<td>- 90 °C to - 60 °C until expiry date(^{13})</td>
<td>- 25 °C to - 15 °C until expiry date(^{16}) (a)</td>
</tr>
</tbody>
</table>

Notes:
\(a\) On September 29, 2021, out of an abundance of caution, Ontario issued a preferential recommendation for the use of Pfizer-BioNTech Comirnaty® vaccine for individuals 18-24 years of age, and the continued use of Pfizer-BioNTech Comirnaty® vaccine for individuals 12-17 years of age, based on an analysis of data from Ontario’s Adverse Event Following Immunization (AEFI) vaccine safety surveillance system. 25,27
\(b\) Vials stored at - 25 °C to - 15 °C for up to 2 weeks may be returned one time to the recommended storage conditions of - 90 °C to - 60 °C.
Vaccine effectiveness and safety

Both mRNA COVID-19 vaccines authorized for use in Canada were shown to be equally safe and highly effective against symptomatic COVID-19 disease and severe outcomes, such as hospitalization and death. Clinical trials and real-world vaccine effective studies demonstrates very high vaccine efficacy (≥ 94 %) and vaccine effectiveness following a complete series. Both vaccines offer strong protection against all VOC’s currently circulating in Canada, with a small reduction in vaccine effectiveness observed against the B.1.617.2 (Delta) VOC.

In clinical trials, the most common side effects following vaccination with mRNA 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. These side effects are typically mild and resolve within a few days. Reports of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining around the heart) following COVID-19 mRNA vaccines have been identified through post-marketing safety surveillance. Canada’s National Advisory Committee on Immunization (NACI) and other countries such as the United Kingdom and United States, continue to recommend a complete series of mRNA vaccine be offered to all eligible individuals. Health Canada has updated the Pfizer-BioNTech Comirnaty® and Moderna Spikevax® product monographs to include information on these conditions. On September 29, 2021, out of an abundance of caution, Ontario issued a preferential recommendation for the use of Pfizer-BioNTech Comirnaty® vaccine for individuals 18-24 years of age, and the continued use of Pfizer-BioNTech Comirnaty® for individuals 12-17 years of age, based on an analysis of data from Ontario’s Adverse Event Following Immunization (AEFI) vaccine safety surveillance system. For more information on myocarditis and pericarditis following mRNA vaccines see Public Health Ontario’s At a Glance: Myocarditis and Pericarditis Following COVID-19 mRNA Vaccines, the Enhanced Epidemiological Summary: Myocarditis and Pericarditis Following Vaccination with COVID-19 mRNA Vaccines in Ontario: December 13, 2020 to August 7, 2021 and the NACI Recommendations on the use of COVID-19 vaccines.
References


Summary of Revisions

First published: December 17, 2020

This document is current to October 6, 2021. New material in this revision is highlighted in the table below.

<table>
<thead>
<tr>
<th>Section</th>
<th>Revision</th>
<th>Implementation Date</th>
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</thead>
<tbody>
<tr>
<td>COVID-19 mRNA vaccines</td>
<td>Updated to reflect full authorization of the Pfizer-BioNTech Comirnay® and Moderna Spikevax® COVID-19 vaccines under the <em>Food and Drug Regulations</em>.</td>
<td>06/10/2021</td>
</tr>
<tr>
<td>Table 1</td>
<td>Updated to include vaccine trade names, generic names, updated Health Canada authorized ages for Moderna Spikevax®, and storage and handling conditions for Pfizer-BioNTech Comirnay®. Addition of footnote on Ontario’s preferential recommendation for use of Pfizer-BioNTech Comirnay® COVID-19 vaccine in individuals aged 18-24 years.</td>
<td>06/10/2021</td>
</tr>
<tr>
<td>Vaccine Effectiveness and Safety</td>
<td>Addition of footnote on Ontario’s preferential recommendation for use of Pfizer-BioNTech Comirnay® COVID-19 vaccine in individuals aged 18-24 years and accompanying resources.</td>
<td>06/10/2021</td>
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