

# Recommendations: Hepatitis B Catch-up Schedule for Adolescents 16-18 Years

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## Overview

The COVID-19 pandemic limited public health ability to deliver school-based immunization programs. This caused many students to fall behind on routine immunizations, including hepatitis B, which is offered to all students in grade 7 in Ontario.

A complete hepatitis B immunization series is a 3-dose schedule with the exception of adolescents aged 11 to <16 years, for whom a 2-dose 1.0mL schedule is authorized. If a dose is missed, the Canadian Immunization Guide (CIG) recommends completing the series using the age-appropriate dose and schedule.<sup>1</sup> In practice, this means that older adolescents and adults (anyone aged ≥16 years) who received only one dose between the ages of 11 to <16 years are recommended to complete the series with two additional doses. This has also been the standard practice implemented in Ontario, although prior to the pandemic, this scenario was relatively uncommon.

Due to pandemic-related disruptions, many students initiated but did not complete their hepatitis B immunization series, and are now presenting for their next dose two or more years later. Additionally, to help facilitate hepatitis B catch-up and align program eligibility with Ontario's other school-based programs, beginning in the 2022-2023 school year, students will have until grade 12 to complete their hepatitis B immunization series.<sup>2</sup> Following this expansion of eligibility a greater number of older students may face this scenario going forward. The Ministry of Health (MOH) asked the Ontario Immunization Advisory Committee (OIIAC) to provide advice on whether adolescents aged 16 to 18 years who received their first dose of the hepatitis B vaccine between ages 11 to <16 years can continue with a 2-dose schedule (i.e., complete the series with only one additional dose). The OIIAC met on June 1, 2022 to review and discuss the evidence and other considerations to inform advice on hepatitis B catch-up immunization schedules for adolescents in Ontario. This document provides a summary of the evidence, considerations, and the OIIAC's recommendations.

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## Recommendations

Adolescents who have missed dose(s) of the hepatitis B immunization series should complete the series using the age-appropriate dose and schedule, as recommended by the CIG, based on their age at presentation.

1. If an adolescent received their first dose of a 2-dose schedule of Recombivax HB (10 µg, 1.0mL) or Engerix-B (20 µg, 1.0mL) vaccine between ages 11 to <16 years and present to complete the series at 16 to 18 years, they should complete a 3-dose schedule and receive two additional doses of Recombivax HB (5 µg, 0.5mL) or Engerix-B (10 µg, 0.5mL). The second dose should be administered immediately and the third dose after a five-month interval.
2. If an adolescent received one dose of 1.0mL hepatitis B vaccine between ages 11 to <16 years, but inadvertently received a second 1.0mL dose at 16 to 18 years, the second dose is still valid. A third dose using an age-appropriate dose should be provided to complete the series. In this scenario, the third dose should be 0.5mL of Recombivax HB (5 µg) or Engerix-B (10 µg), based on age and be administered at least five months after the second dose.

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## Background

Coverage estimates for hepatitis B immunization since the beginning of the pandemic in March 2020 were substantially lower than in previous years.<sup>3</sup> Due to the COVID-19 pandemic, at the end of the 2019-20 school year, 56% of grade 7 students initiated but did not complete their school-based immunization series (only 25% received all recommended doses for their age), and fewer initiated and completed their series in 2020-21. In comparison, 67% of grade 7 students received all recommended doses of the hepatitis B vaccine by the end of the 2018-2019 pre-pandemic school year.<sup>4</sup> These estimates represent coverage assessed at the end of the school year and do not reflect immunization administered as part of catch-up activities that occurred after the school year ended. Some students from the 2019-20 cohort affected by pandemic school closures are turning 16 years old this year and presenting for their second dose, outside the age indication for the 2-dose adolescent immunization schedule. Beginning in the 2022-2023 school year, students who missed one or both doses of hepatitis B vaccine in grade 7 will have until the end of grade 12 to complete their immunization series through their public health unit or primary care provider under Ontario's publicly-funded program.

There are two monovalent hepatitis B vaccines authorized for use in Canada: Recombivax HB and Engerix-B.<sup>5</sup> Hepatitis B immunization schedules authorized by Health Canada vary in dose and antigen content in relation to the age of the vaccine recipient. For adolescents aged 11 to <16 years, a 2-dose schedule of Recombivax HB 10 µg and Engerix-B 20 µg in a 1.0mL dose are also authorized (Table 1). This 2-dose schedule is used in school-based hepatitis B immunization programs in Ontario.

The CIG provides guidance for catch-up immunization schedules and recommends that the hepatitis B vaccine, using the age-appropriate dose and schedule, should be provided to all children and adolescents who missed previous dose(s) on the routine schedule.<sup>5</sup> Based on this guidance, adolescents aged 16 to 18 years who initiated the 2-dose series at 11 to <16 years are recommended to complete the 3-dose schedule with two additional doses of Recombivax HB (5 µg, 0.5mL) or Engerix-B (10 µg, 0.5mL).

**Table 1: Recommended Dosages and Routine Schedules for Monovalent Hepatitis B Vaccines for Adolescents in Canada**

Age (years)	Number of doses	Recombivax HB µg of hepatitis B surface antigen (HBsAg)	Recombivax HB Volume (mL)	Recombivax HB Schedule (months)	Engerix-B µg of hepatitis B surface antigen (HBsAg)	Engerix-B Volume (mL)	Engerix-B Schedule (months)
11 to <16	2	10	1.0	0, 4-6	20	1.0	0, 6
11 to <16	3	5	0.5	0, 1, 6	10	0.5	0, 1, 6*
16 to 19	3	5	0.5	0, 1, 6	10	0.5	0, 1, 6*

\*In addition to the schedules noted above, an accelerated schedule of 0, 1, 2, and 12 months, which may be offered when rapid protection is needed (e.g., travel to endemic countries), is also outlined in the CIG for Engerix-B.

**Source:** Public Health Agency of Canada; National Advisory Committee on Immunization. Canadian immunization guide [Internet]. Evergreen ed. Ottawa, ON: Government of Canada; 2020 [modified 2022 May 20; cited 2022 Jul 11]. Part 4 – Active vaccines: hepatitis B vaccine. Table 3: Recommended dosages and schedules for hepatitis b-containing vaccines. Available from: <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-7-hepatitis-b-vaccine.html>

## Evidence Summary and Considerations

The following summary provides an overview of the evidence reviewed and considerations discussed by the OIAC.

### Recommendations by International Jurisdictions

An international jurisdictional scan of advisory groups confirmed that the CIG guidance was consistent with the approach recommended by other groups, including the Australia Technical Advisory Group on Immunisation (ATAGI), the United States Advisory Committee on Immunization Practices (ACIP), and the World Health Organization (WHO).<sup>6-8</sup> The ACIP specifically highlights that, “when scheduled to receive the second dose, adolescents aged >15 years should be switched to a 3-dose series, with doses 2 and 3 consisting of the [0.5mL dose] administered on an appropriate schedule.”

### Immunogenicity

Public Health Ontario (PHO) Library Services designed searches for published literature (OVID MEDLINE and NIH iSearch COVID-19 Portfolio for Preprints) to identify available evidence on the immune response of a two-dose 1.0 mL schedule among adolescents aged ≥16 years. Reference lists of relevant organizations’ foundational hepatitis B documents were also reviewed for relevant data, and the vaccine manufacturers were contacted for further information on immunogenicity and recommendations on catch-up immunization schedules. From 1,599 records retrieved by the search, only four studies were relevant to the research question, only one of which was specific to the age group of interest.<sup>9</sup> The remaining three studies were among young adults and were included to help further contextualize the immune response of a 2-dose schedule among individuals older than the authorized age indication.<sup>10-12</sup> Risk of bias was assessed for all four included studies by two independent reviewers.<sup>13,14</sup>

The most relevant study was a randomized controlled trial conducted in the United States comparing the immune response of a 2- versus 3-dose schedule of Recombivax HB across different volumes and antigen contents among adolescents aged 16 to 19 years.<sup>9</sup> The study found that a 2-dose 1.0mL schedule of 10 µg resulted in 93% and 95% of vaccinees reaching the minimum threshold antibody response ( $\geq 10$  mIU/mL) when the second dose was administered at four and six months, respectively. In comparison, 99% of adolescents aged 16 to 19 years vaccinated with the standard 3-dose schedule of 5 µg 0.5mL reached the threshold and this group had the strongest immune response compared to all others. The three studies among young adults found that a 2-dose schedule resulted in at least 95% of participants reaching the minimum antibody threshold. However, these studies did not compare the immune response of a 2- versus 3-dose schedule so it is unknown whether the schedules would provide equal protection.

## Additional Considerations

- Although a 2-dose hepatitis B schedule may be more feasible to complete than a 3-dose schedule, other school-based immunization programs have successfully followed similar practices where older adolescents require a different number of doses for series completion (i.e., human papillomavirus [HPV] vaccine), supporting the approach to continue to provide two additional doses of hepatitis B for series completion of older adolescents.
- Changes in practice should be supported by enough evidence to suggest there is moderate-to-high certainty of a net benefit to the population of interest.<sup>15</sup> If enough support exists for this practice change, informing parents and adolescents of the reasons, and subsequently obtaining consent, would be essential, and how to best implement this requires careful consideration. The systematic literature search suggested there was limited evidence with only one study retrieved measuring the immune response of a 2-dose hepatitis B schedule among adolescents aged 16 to 18 years. The study found that a 2-dose schedule may not provide equivalent protection to the standard 3-dose schedule.<sup>9</sup>
- Acceptability of the practice change to routine vaccination schedules among parents and adolescents is also important. Alterations to routine schedules and recommendations may cause confusion and raise concerns about what led to changes.<sup>16</sup>
- Continuing to follow the existing practice outlined in the CIG for series completion of older adolescents would provide direction for other immunization scenarios that occasionally arise (i.e., the inadvertent administration of 1.0mL as a second dose for older adolescents).

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## About the Ontario Immunization Advisory Committee

The OIAC is a multidisciplinary scientific advisory body that provides evidence-based advice to Public Health Ontario (PHO) on vaccines and immunization matters including vaccine program implementation in Ontario, priority populations and clinical guidance. The focus of the OIAC's work is on publicly-funded vaccines and immunization programs in Ontario, including COVID-19 and those under consideration for new programming. For more information about the OIAC and its members contact [secretariat@oahpp.ca](mailto:secretariat@oahpp.ca)

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