

PRE-TRANSPLANT IMMUNIZATION GUIDELINES

SOLID ORGAN TRANSPLANT

December 2022

SickKids

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1.0 INTRODUCTION

PRE-TRANSPLANT IMMUNIZATION GUIDELINES:

The following tables are suggested immunization schedules for solid organ transplant candidates. They are meant as a guide only and may not be applicable to all patients. Please consult Infectious Diseases as appropriate for patient specific issues. Vaccines listed are those that are licensed for use in children <18 yrs of age. Please consult your local pharmacy for current cost of vaccines that are not covered by the Ontario Ministry of Health and Long Term Care (MOHLTC).

PRE-TRANSPLANT CONSIDERATIONS:

- Accelerated regimen schedules may be possible for some vaccines to facilitate optimal dosing and response with limited time prior to transplant. Refer to tables for the minimum age to receive each vaccine and interval recommended for accelerated scheduling.
- Defer transplant for 2 wks (if possible) following administration of INACTIVE vaccines to ensure adequate vaccine response.
- LIVE vaccines should be administered PRIOR to transplant when possible. Ideally transplant should not
 occur until at least 4 wks following live vaccine administration.

SIBLINGS AND OTHER FAMILY MEMBERS:

All siblings should be vaccinated per routine guidelines. It is also safe for siblings of solid organ transplant candidates to receive LIVE vaccines.

TRAVEL VACCINES:

Prior to travel, all transplant candidates should consult Infectious Diseases/Travel Clinic for recommended vaccinations. Travel Clinic consultations are not covered by the Ontario Ministry of Health and Long Term Care. Most travel vaccines are also not covered. Families will need to budget for the cost of consultation and vaccination. Some vaccines need to be administered several wks prior to travel in order to provide adequate protection. Families will need to plan consultations well ahead of their travel date.



| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | ROUTINE SCHEDULE (ONTARIO) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF DOSES REQUIRED | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | |
|---|--|--|--|-----------------------------|---|-------------------------------------|------------------------|--|
| DTaP-IPV-Hib Pediacel® Infanrix® IPV/Hib | 2, 4, 6 and 18 mths | 6 wks ^{1,6} | Doses 1, 2, 3 4 wks Dose 3 to 4 6 mths but 4th dose must be given at or after 12 mths of age ^{1, 2, 4, 6, 9} | As per routine schedule | YES In addition: Transplant candidates ≥5 yrs of age should receive one | | | |
| Tdap-IPV Adacel® Polio Boostrix® Polio | 4-6 yrs x1 dose | 4 yrs ^{1, 6, 14, 15} | N/A | | dose of Hib vaccine regardless of prior Hib vaccination history, at least 1 yr after any previous dose ^{1, 6} Defer transplant for 2 wks following | NOT done routinely | Covered by MOHLTC | |
| Tdap Adacel® Boostrix® | 14 years: 1 dose + booster in 10 yrs | 7 yrs ^{6, 13, 14} | N/A | | vaccine administration (if possible) to ensure adequate response | | | |

- D=diphtheria toxoid high dose; d=diphtheria toxoid low dose; ap or aP=acellular pertussis; T=tetanus toxoid; IPV or Polio=inactivated polio; Hib=haemophilus influenza type b; HB=hepatitis B.
- · DTap-HB-IPV-Hib: Infanrix-hexa® is not part of the Ontario routine immunization schedule and is NOT covered by MOHLTC.
- · Act-HIB® and Hiberix® are single entity haemophilus influenza b vaccines licenced for use in patients 2 mths and older.

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- The National Advisory Committee on Immunization (NACI) states that administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately.¹
- · NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites.1
- DTaP-IPV-Hib (Pediacel®) can be given at the same time as other routine vaccinations such as meningococcal C conjugate and hepatitis B.9

- National Advisory Committee on Immunization (NACI). Canadian Immunization Guide. Accessed June 22, 2022. http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php#toc.
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- CDC. Recommended immunization schedules for persons aged 0 through 18 yrs-2022 Accessed May 18, 2022 https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

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- 15. Sanofi Pasteur Ltd. Product Monograph Adacel-Polio®. April 2022.
- 16. GlaxoSmithKline Inc. Product Monograph Boostrix-Polio®. September 2022.
- 17. GlaxoSmithKline Inc. Product Monograph Infanrix-Hexa®. January 2021.
- 18. GlaxoSmithKline Inc. Product Monograph Hiberix® August 2019.
- 19. Sanfoi Pasteur Ltd. Product Monograph Act-HIB®. May 2019.

| NAME OF VACCINE PRODUCTS AVAILABLE | ROUTINE SCHEDULE | MINIMUM AGE FOR | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF Doses required | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST | COVERAGE IN ONTARIO |
|--|--|--|--|---|--|-----------------------|---|
| IN CANADA | (ONTARIO) | 1 ST DOSE | | | | VACCINATION | |
| Meningococcal quadrivalent ACW-135Y conjugate vaccine (Men-C-ACWY) Menactra® Menveo® Nimenrix® | Grade 7 OR HIGH RISK* (≥9 mths) | Nimenrix® 6 wks ^{1,7} Menveo® 9 mths ^{9,15} Menactra® 9 mths ^{4,8,15} | Nimenrix® 2 mths¹7 Menveo® 2 mths⁰ 4 mths⁰ Menactra® 3 mths®.15 Accelerated Men-C-ACWY schedule: ≥ 12 mths: 4 wks¹ | Men-C-ACWY ^Ψ 2 -11 mths: 2 or 3 doses, 8 wks apart, then booster between 12-23 mths, 8 wks from previous dose ^{1,2} 12-23 mths: 2 doses, 8 weeks apart ¹ ≥24 mths: 2 doses, 8 weeks apart ¹ | Transplant candidates are at HIGH RISK* of invasive meningococcal disease (IMD) due to impending immunouppression and should receive Men-C-ACWY vaccine** Routine Meningococcal Conjugate vaccine does not need to be administered in addtion to the quadrivalent vaccine¹ Defer transplant for 2 wks following administration to ensure adequate response | | Covered under MOHLTG school program (grade 7)² OR HIGH RISK* (≥9 mths)² |
| Serogroup B Meningococcal Vaccine 4CMenB Bexsero® MenB-fHBP Trumenba® (NOT interchangeable) | For HIGH RISK* only (2 mths- 17 yrs) ² | 4CMenB Bexsero® 2 mths12 MenB-fHBP Trumenba® 10 yrs21 | Bexsero®12 2-5 mths: 1 mth 6-23 mths: 2 mths >2 yrs: 1 mth Trumenba®21 HIGH RISK*: Dose 1 and 2: 1 mth Dose 2 and 3: 4 mths | Bexsero® 2-5 mths¹²: 3 doses, 1 mth apart then booster at 12-23 mths AND 6 mths after 3rd dose 6-11 mths¹²: 2 doses, 2 mths apart then booster at 12-23 mths AND 2 mths after 2nd dose 12-23 mths¹²: 2 doses, 2 mths apart then booster 12-23 mths after dose 2 >2 yrs¹²: 2 doses, 1 mth apart. Consider booster if continued risk of IMD Trumenba²¹ HIGH RISK* >10 yrs of age: 3 doses; 1 mth interval between 1st and 2nd dose, then 4 mth interval between 2nd and 3rd dose | YES Transplant candidates are at HIGH RISK* of invasive meningococcal disease (IMD) due to impending immune- suppression and should receive MenB-vaccine** Defer transplant for 2 wks following administration to ensure adequate response | NOT done routinely | Covered by MOHLTC for HIGH RISK* ONLY ² |

*HIGH RISK FOR INVASIVE MENINGOCOCCAL DISEASE (IMD) INCLUDE:

- 1. Functional/anatomic asplenia or sickle cell disease^{1, 2}
- 2. Complement, properdin, factor D or combined T and B cell deficiencies^{1, 2}
- 3. Cochlear implants (pre/post implant)²
- 4. HIV+1,2
- 5. Acquired complement deficiencies due to receipt of the terminal complement inhibitor eculizumab (Soliris™)¹,²
- Increased risk of exposure: travelers where meningococcal vaccine is recommended (meningitis belt of Sub-Saharan Africa) or required (Hajj, Mecca)¹

** Expert opinion

"Nimenrix" is funded by MOHLTC (June 2022). At the time of TRMC guideline update, NACI was reviewing its recommendations in view of Nimenrix® receiving approval for use in infants as young as 6 wks of age. (Previously Menveo® (Men-C-ACWY-CRM) was the vaccine of choice for children <2 yrs of age per NACI and CPS).

Provincial recommendations may vary based on available vaccine products. Choice of vaccine and recommended schedules vary with age¹

CONTRAINDICATIONS:

In persons with history of anaphylaxis after a previous dose of the vaccine and in patients with proven hypersensitivity/ anaphylaxis to any component of the vaccine or its container.¹

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- The National Advisory Commmitee on immunization (NACI) states that administering the most widely used live and
 inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions
 similar to those observed when the vaccines are administered separately.¹
- NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites.¹
- Men-C-C products, Menactra® and Bexsero® can be given with other routine childhood immunizations, in a different
 injection site with a separate needle and syringe¹. Per NACI, Menveo® administration at the same time as Pneu-C-13
 requires further study.¹ However, the Menveo® product monograph indicates concomitant administration with other
 routine childhood immunizations is appropriate (separate injection site and syringe).®
- Co-administration of Men-C-ACYW-CRM (Menveo) and Tdap may result in a lower immune response to the pertussis antigens than when Tdap vaccine is given alone; however, the clinical significance of this is unknown.¹
- Tdap vaccine given one mth after Men-C-ACYW-CRM induces the strongest immunologic response to pertussis antigens.¹

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- Publicly funded immunization schedules for Ontario-June 2022. Accessed October 4, 2022 https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf.
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- http://publications.gc.ca/collections/collection_2014/aspc-phac/HP40-103-2014-eng.pdf.
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- Report from Advisory Committee on Immunization Practices (ACIP): Decision not to recommend routine
 vaccination of all children aged 2-10 yrs with quadrivalent meningococcal conjugate vaccine.

 MMWR Morbidity and Mortality Weekly Report 2008: 57: 462-465.
- 8. Sanofi Pasteur Ltd. Product Monograph Menactra®. November 2017.
- 9. Novartis Vaccines and Diagnostics Inc. Product Monograph Menveo™. June 2020.
- 10. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clinical Infectious Diseases* 2014; 58: e44-100.

- 11. Allen UD. Minimizing infection risks after paediatric organ transplant: advice for practitioners. Canadian Paediatric Society Infectious Diseases and Immunization Committee. *Paediatric Child Health* 2013;18(3): 143-8.
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- Kumar D. Immunizations following solid-organ transplantation. Current Opinion in Infectious Disease 2014; 27: 329-335.
- 14. L'Huillier AG, Kumar D. Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Human Vaccines and Immunotherapeutics* 2015; 11: 2852-63. 15.
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- 17. GlaxoSmithKline Inc. Product Monograph Nimenrix®. September 2020.
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- 19. Pfizer Canada Product Monograph NeisVac-C®. October 2021.
- American Academy of Pediatrics (AAP) Committee on Infectious Diseases. Kimberlin DW (ed) Red Book: 2021-2024 Report of the Committee on Infectious Diseases (32nd edition). Itasca, IL: American Academy of Pediatrics.
- 21. Pfizer Canada Product Monograph Trumenba®. October 2022.
- 22. Canadian Pediatric Society. Update on invasive meningococcal vaccination for Canadian children and youth. July 2020. Accessed June 02, 2021.

https://www.cps.ca/en/documents/position/invasive-meningococcal-vaccination

| 2.3 INACTIVE VACCINES: PNEUMOCOCCAL – PRE-TRANSPLANT GUIDELINES | | | | | | | | | |
|---|---|--|-----------------------------------|---|---|-------------------------------------|---|--|--|
| NAME OF VACCINE Products available in Canada | ROUTINE SCHEDULE (ONTARIO) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF DOSES REQUIRED | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | | |
| Pneumococcal Conjugate Vaccine (Pneu-C) Prevnar® 13 (Pneu-C-13) Vaxneuvance® (Pneu-C-15) Synflorix® (Pneu-C-10) | 2, 4, 6 and 12-15 mths ^{1,2} for HIGH RISK* 2, 4 and 12 mths for other children ¹ | 6 wks ^{1, 5, 13} | 8 wks ^{1, 2} | 3-4 doses for HIGH RISK* (schedule dependent on age) <5 yrs: follow MOHLTC schedule for HIGH RISK* (see Tables 1 and 2 on next page) >5yrs, NOT previously immunized: 2 doses Pneu-C, 6-8 wks apart*, then 1 dose Pneu-P (8 wks after last Pneu-C dose¹) followed by 2nd Pneu-P dose 5 yrs later¹ | YES Transplant candidates are at HIGH RISK* of invasive pneumococcal disease (IPD) due to impending immunouppression ^{1, 2} Defer transplant for 2 wks following vaccine administration to ensure adequate response | NOT done routinely | Covered by MOHLTC per routine schedule for ≤5 yrs age² (Prevnar® 13 only) 4th dose covered for transplant candidates² | | |
| Pneumococcal Polysaccharide Vaccine (Pneu-P) Pneumovax® 23 (Pneu-P-23) | 2 doses for HIGH RISK* ≥2 yrs NOT routine for other children | 2 yrs ^{1, 6} | 5 yrs ^{1, 2} | ≥2 yrs: 1 dose, 8 wks after Pneu-C administration (after completion of age appropriate Pneu-C series) ^{1,2} THEN 2nd dose ≥5 yrs after first dose | | | 2 doses covered by MOHLTC for transplant candidates ≥2 yrs age ² | | |

- *NACI: Children 2 months to less than 18 years of age at increased risk of invasive pneumococcal disease (IPD) should receive pneumococcal conjugate (Pneu-C) vaccine, with pneumococcal polysaccharide (Pneu-P) vaccine as a booster dose to increase the serotype coverage¹
- · Children at increased risk of IPD *include* those who have: chronic medical conditions (example: heart, kidney, liver or lung disease), are transplant candidates, have sickle cell disease/sickle cell hemoglobinopathies, have other types of functional or anatomic asplenia, have HIV infection, are immunocompromised (e.g., primary immunodeficiencies; malignancies, immunosuppressive therapy, use of long-term systemic corticosteroids, nephrotic syndrome), have chronic medical conditions (e.g., diabetes mellitus or CSF leak) and children with cochlear implants/receiving cochlear implants.¹

*Expert opinion: Note that expert opinion based on local study data listed in this table differs from that of NACI, which recommends patients >5 yrs receive 1 dose of Pneu-C-13 followed by 2 doses of Pneu-P-23, the first given >8 wks after Pneu-C-13 and the second >5 yrs after the first.¹

At the time of TRMC guideline update, NACI was reviewing Pneu-C-15 data in paediatrics and had not yet issued guidance.

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- The National Advisory Committee on Immunization (NACI) states that administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately.¹
- · NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites.1
- Prevnar® 13 can be given with any of the following vaccine antigens, either as monovalent or combination vaccines: diphtheria, tetanus, acellular pertussis, Haemophilus influenzae type b, inactivated poliomyelitis, hepatitis B, meningococcal serogroup C, measles, mumps, rubella and varicella.⁵

TABLE 1: CHILDREN <5 YRS NOT PREVIOUSLY IMMUNIZED WITH THE PNEUMOCOCCAL CONJUGATE VACCINE

| AGE AT FIRST DOSE | APPLIES TO | PREVNAR® 13 (Pneu-C-13) MINIMUM INTERVALS |
|-------------------------|------------|--|
| 6 wks-6 mths | HIGH RISK | Dose 1: age ≥6 wks Dose 2: 8** wks after 1st dose Dose 3: 8** wks after 2nd dose Dose 4: 8 wks after 3rd dose AND at age ≥12 mths |
| 7-11 mths | All | Dose 1: Day 0 Dose 2: 8 wks after 1st dose Dose 3: 8 wks after 2nd dose AND at age ≥12 mths |
| 12-23 mths | All | Dose 1: Day 0 Dose 2: 8 wks after 1st dose |
| 24-59 mths (2-5 yrs) | All | 1 dose only |

- · Adapted from Publicly Funded Immunization Schedules for Ontario June 2022² Table 17
- **4 wks minimal interval recommended by vaccine manufacturers but NACI recommends minimal interval to be 8 wks.

TABLE 2: CHILDREN <5 YRS OF AGE WHO HAVE INTERRUPTED OR INCOMPLETE VACCINATION WITH THE PNEUMOCOCCAL CONJUGATE VACCINE

| CURRENT AGE | APPLIES TO | NUMBER OF Pneu-C-13 DOSES Previously received | NUMBER OF Pneu-C-13 DOSES NEEDED TO COMPLETE SERIES |
|--------------------------|---------------|--|--|
| 2-6 mths | HIGH RISK* | 1 dose | Dose 2: 2 mths after 1st dose Dose 3: 2 mths after 2nd dose Dose 4: 2 mths after 3rd dose AND at age ≥12 mths |
| | KISK. | 2 doses | Dose 3: 2 mths after 2nd dose Dose 4: 2 mths after 3rd dose AND at age ≥12 mths |
| 7-11 mths | All | 1 dose | Dose 2: 2 mths after 1st dose Dose 3: 2 mths after 2nd dose AND at age ≥12 mths |
| | | 2 doses | Dose 3: 2 mths after 2nd dose AND at age ≥12 mths |
| | | 1 dose at age <12 mths | Dose 2: 2 mths after 1st dose Dose 3: 2 mths after 2nd dose |
| | | 1 dose at age ≥12 mths | Dose 2: 2 mths after 1st dose |
| 12-23 mths | AII | 1 dose at age <12 mths AND 2nd dose at age ≥12 mths | Dose 3: 2 mths after 2nd dose |
| | | 2 or more doses at age <12 mths | 1 dose, 2 mths after the most recent dose |
| 24-59 mths (2-<5 yrs) | All | Any incomplete series | 1 dose, 2 mths after the most recent dose |

Adapted from Publicly Funded Immunization Schedules for Ontario June 2022² Table 23

- National Advisory Committee on Immunization (NACI). Canadian Immunization Guide. Accessed November 28, 2021 and September 29, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/ Publicly_Funded_ImmunizationSchedule.pdf
- Publicly funded immunization schedules for Ontario-June 2022. Accessed September 29 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf
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| | 2.4 INACTIVE VACCINES: HEPATITIS A – PRE-TRANSPLANT GUIDELINES | | | | | | | | | |
|--|--|--|---|---|---|---|------------------------|--|--|--|
| NAME OF VACCINE Products available in Canada | ROUTINE SCHEDULE (ONTARIO) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF DOSES REQUIRED | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | |
| Hepatitis A Avaxim® Avaxim Ped® Havrix® Havrix Jr® Vaqta® Vaqta Ped® (Can be used interchangeably) | 6 mths ¹ | Monovalent vaccines 6 mths ¹ | 2 doses See table 1 for schedule | Recommended for liver transplant candidates, and for other organ candidates meeting HIGH RISK* criteria¹ Hepatitis A vaccine may be given either as a monovalent product or in combination with hepatitis B; dosing is different NACI does not recommend the use of | Recommended for liver transplant candidates, and for other organ candidates meeting HIGH RISK* criteria¹ Hepatitis A vaccine may be given either as a monovalent product or in combination with hepatitis B; dosing is different NACI does not recommend the use of NO** | Covered by ON MOHLTC only for patients >1 yr old with chronic liver | | | | |
| Combination Hep A/B Vaccines Twinrix® Twinrix® Junior | ation 3 Vaccines | | Twinrix® 6 mths Twinrix® Junior 1 mth between first and second dose; 6 mths between first and third dose | See table 2 for schedule | immunosuppressed or hyporesponsive patients (example ESRD dialysis patients) ¹ Defer transplant for 2 wks following vaccine administration to ensure adequate response ¹ | | disease | | | |

^{*}HIGH RISK includes persons travelling to endemic countries, individuals living in communities at risk of hepatitis A (HA) outbreaks or in which HA is endemic1

^{**}High response rate to immunization makes routine post immunization serologic testing unnecessary in healthy populations. Commercial assay kits are not universally reliable for detecting vaccine-induced antibody^{1,2}

| HEPATITIS A | TABLE 1: CANADIAN IMMUNIZATION GUIDE (NACI)- HEPATITIS A DOSING RECOMMENDATIONS FOR MONOVALENT HEPATITIS A VACCINES ¹ | | | | | | | | | | |
|-------------|---|--------|-----------------------------|------------------|--|--|--|--|--|--|--|
| VACCINE | VACCINE ANTIGEN* VOLUME SCHEDULE (BOOSTER) AGE ^t | | | | | | | | | | |
| Avaxim® | 160 antigen units HAV | 0.5 mL | 0, (6-36) mths | 12 yrs and older | | | | | | | |
| Avaxim Ped® | 80 antigen units HAV | 0.5 mL | 0, (6-36) mths | 6 mths-<16 yrs | | | | | | | |
| Havrix® | 1440 ELISA units HAV | 1 mL | 0, (6-12) mths [‡] | 19 yrs and older | | | | | | | |
| Havrix Jr® | 720 ELISA units HAV | 0.5 mL | 0, (6-12) mths | 6 mths-<19 yrs | | | | | | | |
| Vaqta® | 50 units HAV | 1 mL | 0, (6-18) mths | 18 yrs and older | | | | | | | |
| Vaqta Ped® | 25 units HAV | 0.5 ml | 0, (6-18) mths | 6 mths-<18 yrs | | | | | | | |

^{*}There is no international standard for HAV measurement. Each manufacturer uses its own units of measurement.

- Comparable to the results reported in clinical trials of children more than 12 mths, all reviewed studies have consistently shown that vaccination of infants 6-12 mths with inactivated HA vaccines is immunogenic and safe.
- · Product monographs for Avaxim Ped, Havrix Jr and Vaqta Ped indicate 12 mths as the lower age limit.

| | TABLE 2: TWINRIX® AND TWINRIX® JR DOSING SCHEDULE¹ | | | | | | | | | |
|--------------|--|----|-----------------|-----------------------|-------------|-----------------|--|--|--|--|
| ACE | TWINRIX® | | | | TWINRIX JR® | | | | | |
| AGE | ANTIGEN* | mL | SCHEDULE (MTHS) | ANTIGEN* | mL | SCHEDULE (MTHS) | | | | |
| 1 yr-<16 yrs | 720 ELISA units | 1 | 0, 6-12 | 360 ELISA units | 0.5 | 0, 1, 6 | | | | |
| 16-<19 yrs | - | - | - | 360 ELISA units | 0.5 | 0, 1, 6 | | | | |

CONTRAINDICATIONS:

In persons with a history of anaphylaxis after previous administration of a HA-containing vaccine and in persons
with proven immediate or anaphylactic hypersensitivity to any component of the product or its container.¹¹
TWINRIX® and TWINRIX® Junior: latex in plunger stopper of pre-filled syringe, neomycin, yeast¹¹

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- The National Advisory Committee on Immunization (NACI) states that administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately.¹
- NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites.¹
- Since HAVRIX® is an inactivated vaccine, its concomitant use with other inactivated vaccines is unlikely to result in interference with immune responses. When concomitant administration of other vaccines is considered necessary, the vaccines must be given with different syringes and at different injection sites.¹⁰

^tAges for which the vaccine is approved

^{*}Studies have shown that 720 ELISA units provides an effective booster dose in those over 19 yrs of age

- National Advisory Committee on Immunization (NACI). Canadian Immunization Guide. Accessed June 22, 2022. http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php#toc.
- Publicly funded immunization schedules for Ontario-June 2022. Accessed September 29, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf
- 3. Danziger-Isakov L, Kumar D, AST Infectious Diseases Community of Practice. Vaccination in solid organ candidates and recipients. *Clin Transplant*. 2019; 33(9): e13563.
- 4. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clinical Infectious Diseases* 2014; 58: e44-100.
- 5. Abuali MM, Arnon R, Posada R. An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. *Pediatric Transplant* 2011; 15: 770-7.
- Kumar D. Immunizations following solid-organ transplantation. Current Opinion in Infectious Disease 2014; 27: 329-335.

- 7. L'Huillier AG, Kumar D. Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Human Vaccines and Immunotherapeutics* 2015; 11: 2852-63.
- American Academy of Pediatrics (AAP) Committee on Infectious Diseases. Kimberlin DW (ed)
 Red Book: 2021-2024 Report of the Committee on Infectious Diseases (32nd edition). Itasca, IL:
 American Academy of Pediatrics 373-381.
- 9. Martin K, Drabble A, Manlhiot C, Dipchand Al. Response to hepatitis A and B vaccination after pediatric heart transplant. *Pediatric Transplant*ation 2012; 16: 699-703.
- 10. GlaxoSmithKline Inc. Product Monograph Havrix®. March 2021.
- 11. GlaxoSmithKline Inc. Product Monograph Twinrix®. November 2018.
- 12. Sanofi Pasteur Ltd. Product Monograph Avaxim Pediatric®. May 2021.

| | 2.5 INACTIVE VACCINES: HEPATITIS B – PRE-TRANSPLANT GUIDELINES | | | | | | | | | |
|---|--|---|---|--|---|--|--|--|--|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | ROUTINE SCHEDULE (ONTARIO) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF Doses required | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | |
| Hepatitis B Engerix® B OR Recombivax HB® (Can be used interchangeably) | Grade 7 (12 yrs) 2 doses (0, 6 mths) | Newborn ¹ | Varied accelerated schedules available ACCELERATED SCHEDULES 4 dose 0, 7, 21-28 days, and booster at 6-12 mths 3 dose 0, 1, >2 mths² | 3 dose schedule preferred 0, 1, 6 mths ¹ | *See tables 1 and 2 below for dosing If functionally immunosuppressed or hyporesponsive, consider double the microgram dose for age and use 3 or 4 dose schedule (example chronic renal failure, dialysis, congenital immunodeficiency, patients receiving | YES 6-8 wks* (range 1-6 mths¹) post series Annually post series to assess ongoing immunity | Monovalent vaccines covered by ON MOHLTC school program (grade 7): 2 doses only Covered <7 yrs age immigrated from countries of high prevalence or exposed to | | | |
| Combination Hepatitis B Vaccines: Hepatitis A +B: Twinrix® Twinrix® Junior DTaP-HB-IPV-Hib INFANRIX Hexa™ | | 1 yr ¹¹ NACI: 6 mths ¹ for urgent cases | See Table 3 for Twinrix® and Twinrix® Junior intervals | See Table 3 for Twinrix® and Twinrix® Junior dosing | immunosuppressive therapy) ¹ NACI does not recommend the use of Twinrix® or Twinrix® Junior or Infanrix Hexa® in functionally immunosuppressed or hyporesponsive patients (example chronic renal failure, dialysis patients) ¹ Defer transplant for 2 wks following vaccine administration to ensure adequate response ¹ | If suboptimal response (titre <10 mIU/mL) repeat 3 dose series (higher dose if req'd) If non-responsive with repeat series, consult ID | or exposed to hepatitis B Doses 2 and 3 covered for patients ² : -on dialysis or receiving frequent blood products -listed for transplan 3 doses covered for patients with chroni liver disease ² | | | |

TABLE 1: CANADIAN IMMUNIZATION GUIDE (NACI) – HEPATITIS B STANDARD DOSING RECOMMENDATIONS1 FOR PAEDIATIC PATIENTS (3 OR 4 DOSE SCHEDULE ONLY):

| RECIPIENTS | | RECOMBIVAX HB® | | | ENGERIX® B | | | |
|--|----|----------------|-----------------|----|------------|-------------------------------|--|--|
| | μg | mL | SCHEDULE (MTHS) | μg | mL | SCHEDULE (MTHS) | | |
| Infants (regardless of mothers' HBV status) | 5 | 0.5 | 0, 1, 6** | 10 | 0.5 | 0, 1, 6 0R 0, 1, 2, 12 | | |
| 12 mths- 19 yrs | 5 | 0.5 | 0, 1, 6** | 10 | 0.5 | 0, 1, 6 OR 0, 1, 2, 12 | | |

^{*}Thimerosal preservative-free preparation is recommended

TABLE 2: HEPATITIS B-REVISED DOSING GUIDELINES FOR FUNCTIONALLY IMMUNOSUPPRESSED OR HYPORESPONSIVE PATIENTS (ADAPTED FROM CANADIAN IMMUNIZATION GUIDE-NACI) NOTE: DOSES LISTED ARE DOUBLE THE ROUTINE AGE RECOMMENDED DOSE

| RECIPIENTS | | | RECOMBIVAX HB® | | | ENGERIX® B |
|--|----|----|---|----|----|--|
| | μg | mL | SCHEDULE (MTHS) | μg | mL | SCHEDULE (MTHS) |
| Infants (regardless of mothers' HBV status) | 10 | 1 | 0, 1, 6** | 20 | 1 | 0, 1, 6 0R 0, 1, 2, 12 |
| 12 mths- <16 yrs | 10 | 1 | 0, 1, 6** OR 0, 1, 2, 12 for dialysis, chronic renal failure, and some immunocompromised individuals | 20 | 1 | 0, 1, 6 OR 0, 1, 2, 12 |
| 16-<20 yrs | 10 | 1 | 0, 1, 6** OR 0, 1, 2, 12 for dialysis, chronic renal failure, and some immunocompromised individuals | 40 | 2 | 0, 1, 2, 6 ¹ particularly for ESRD/dialysis patient |

^{*}Thimerosal preservative-free preparation recommended;

^{**}Although higher dose with a schedule of 0, 1 and >2 mths is approved, the preferred schedule is 0, 1, and 6 mths

^{*}Expert opinion

^{**}Although higher dose with a schedule of 0, 1 and >2 mths is approved, the preferred schedule is 0, 1, and 6 mths

| | TABLE 3: TWINRIX® AND TWINRIX JR® DOSING SCHEDULE ¹¹ | | | | | | | | | | |
|------------------|---|----|-----------------|-------------|-----|-----------------|--|--|--|--|--|
| AGE | | | TWINRIX® | TWINRIX JR® | | | | | | | |
| | μg | mL | SCHEDULE (MTHS) | μg | mL | SCHEDULE (MTHS) | | | | | |
| 1 yr- <16 yrs | 20 | 1 | 0, 6-12 | 10 | 0.5 | 0, 1, 6 | | | | | |
| 16-<19 yrs | - | - | - | 10 | 0.5 | 0, 1, 6 | | | | | |

There are no data to support the use of Twinrix® and Twinrix® Jr on an accelerated schedule in children¹¹

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- The National Advisory Committee on Immunization (NACI) states that administering the most widely used live and
 inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions
 similar to those observed when the vaccines are administered separately.¹
- NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites.¹
- According to the National Advisory Committee on Immunization (NACI), RECOMBIVAX HB® (hepatitis B vaccine [recombinant]) may be administered simultaneously with other vaccines at different sites. A separate needle and syringe should be used for each vaccine.¹⁴

CONTRAINDICATIONS:

- In persons with a history of anaphylaxis after previous administration of a HB-containing vaccine and in persons
 with proven immediate or anaphylactic hypersensitivity to any component of the product or its container.¹¹
- TWINRIX® and TWINRIX® Junior: latex in plunger stopper of pre-filled syringe, neomycin, yeast.¹¹

- NACI. Canadian Immunization Guide. Accessed June 22, 2022. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-7-hepatitis-b-vaccine.html
- Publicly funded immunization schedules for Ontario-June 2022 Accessed September 29, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ ImmunizationSchedule.pdf
- 3. Danziger-Isakov L, Kumar D, AST Infectious Diseases Community of Practice. Vaccination of solid organ candidates and recipients. *Clin Transplant*. 2019; 33(9): e13563
- 4. European Consesnsus Group on Hepatitis B Immunity. Are booster immunisations needed for lifelong hepatitis B immunity? Lancet 2000; 355: 561-565.
- Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clinical Infectious Diseases 2014; 58: e44-100.
- Abuali MM, Arnon R, Posada R. An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. *Pediatric Transplant* 2011; 15: 770-7.

- Kumar D. Immunizations following solid-organ transplantation. Current Opinion in Infectious Disease 2014; 27: 329-335.
- 8. L'Huillier AG, Kumar D. Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Human Vaccines and Immunotherapeutics* 2015; 11: 2852-63.
- 9. Leung DH, Ton-That M, Economides JM, Healy CM. High prevalence of hepatitis B non-immunity in vaccinated pediatric liver transplant recipients. *American Journal of Transplantation* 2015; 15: 535-540.
- 10. Martin K, Drabble A, Manlhiot C, Dipchand Al. Response to hepatitis A and B vaccination after pediatric heart transplant. *Pediatric Transplant* 2012; 16: 699-703.
- 11. GlaxoSmithKline Inc. Product Monograph Twinrix®. November 2018.
- American Academy of Pediatrics (AAP) Committee on Infectious Diseases. Kimberlin DW (ed)
 Red Book: 2021-2024 Report of the Committee on Infectious Diseases (32nd edition). Itasca, IL:
 American Academy of Pediatrics. 381-399.
- 13. GlaxoSmithKline Inc. *Product Monograph Engerix B®*. October 2020.
- 14. Merck Canada Inc. Product Monograph Recombivax®. May 2012.
- 15. Chong P, Avery R. A Comprehensive Review of Immunization Practices in Solid Organ Transplant and Hematopoietic Stem Cell Transplant Recipients. Clinical Therapeutics. 2017; 39(8): 1581-1598

| | 2.6 INACTIVE VACCINES: HUMAN PAPILLOMA VIRUS – PRE-TRANSPLANT GUIDELINES | | | | | | | | | | | |
|--|--|--|---|--|--|-------------------------------------|--|--|--|--|--|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | ROUTINE SCHEDULE (ONTARIO) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF DOSES REQUIRED | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | | | |
| Human Papilloma Virus Gardasil® 9 (9-valent HPV 9 type 6, 11, 16, 18, 31, 33, 45, 52, 58) Cervarix® (Bivalent HPV 2 type 16, 18) | Grade 7 females and males | 9 yrs ^{1,2} Gardasil® 9 Approved in both females and in males between 9 and 45 yrs ³ Cervarix® Approved in females between 9 and 45 yrs ^{1,6} | 3 dose series 4 wks between first and second dose ^{1, 2, 3} 12 wks between second and third dose ^{1, 2, 3} Third dose at least 24 wks after first dose ^{1, 2, 3} 2 dose series 5 mths between first and second dose ³ | Gardasil® 9 3 doses: 0, 2 and 6 mths ^{1,2,3} Immunocompetent patients 9-<15 yrs of age at time of first injection may receive HPV vaccine on a 2 dose schedule (0 and 6 mths) ¹ If schedule interrupted, series does not need to be restarted ⁵ , however ideally all 3 doses should be completed within a 1 yr period ³ | YES Recommend if patient >9 yrs of age and is a transplant candidate ^{1,4,5,9} | NO | Gardasil® 9 Covered under ON MOHLTC school program (grade 7-12) for immunocompro- mised: 3 doses Cervarix® Not covered in Ontario | | | | | |

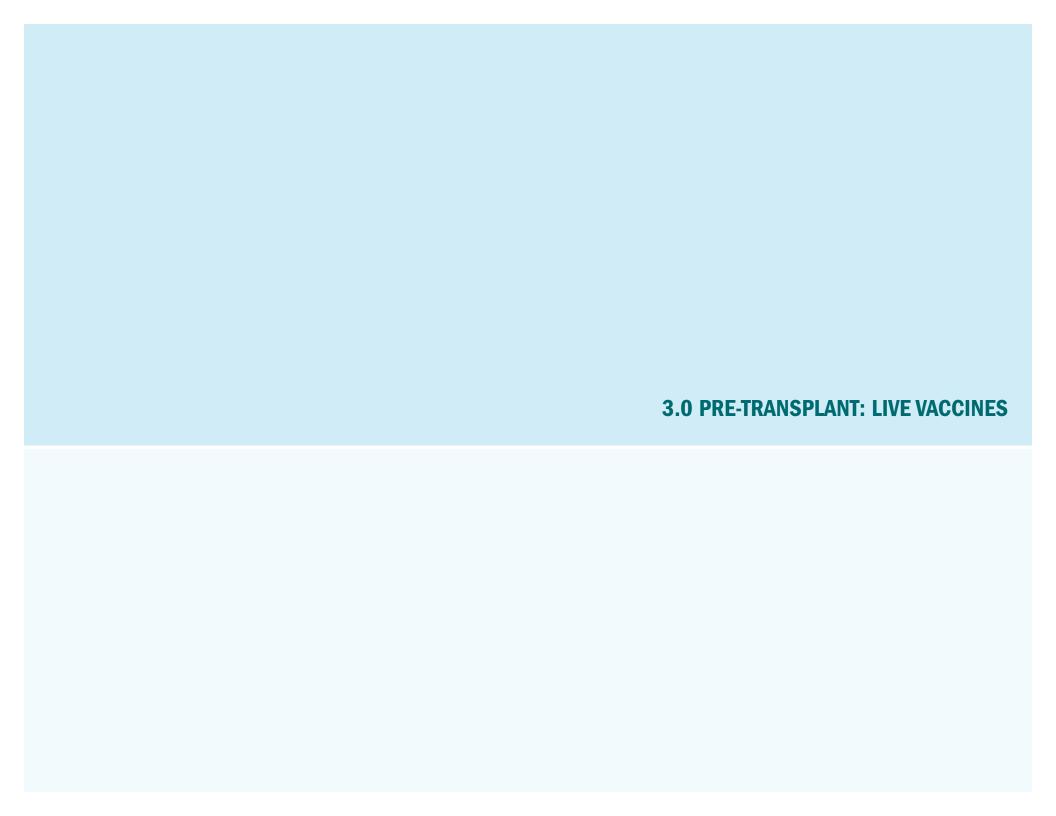
- · Dose 0.5 mL IM
- · Higher incidence of fainting in younger individuals; observe patients for full 15 minutes post dose.

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- The National Advisory Committee on Immunization (NACI) states that administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately.¹
- · NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites.¹
- · GARDASIL® 9 may be administered concomitantly (at a separate injection site) with Menactra* [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel* [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)], and Poliomyelitis (inactivated) Vaccine.³

- NACI. Canadian Immunization Guide. Accessed November 28, 2021 and June 22, 2022. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-9-human-papillomavirus-vaccine.html
- Publicly funded immunization schedules for Ontario-June 2022. Accessed September 29, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf
- 3. Merck Canada Inc. Product Monograph Gardasil® 9. April 2022.
- 4. Abuali MM, Arnon R, Posada R. An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. *Pediatric Transplant* 2011; 15: 770-7.
- CDC. Recommended immunization schedules for persons aged 0 through 18 yrs-2022.
 Accessed May 18, 2022. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html
- 6. GlaxoSmithKline. Product Monograph Cervarix®. February 2019

- American Academy of Pediatrics (AAP) Committee on Infectious Diseases. Kimberlin DW(ed)
 Red Book: 2021-2024 Report of the Committee on Infectious Diseases (32nd edition). Itasca, IL:
 American Academy of Pediatrics. 443-447.
- 8. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clinical Infectious Diseases* 2014; 58: e44-100.
- 9. Danziger-Isakov L, Kumar D, AST Infectious Diseases Community of Practice. Vaccination of solid organ transplant candidates and recipients. *Clin Transplant* 2019; 33 (9) e13563.
- Kumar D. Immunizations following solid-organ transplantation. Current Opinion in Infectious Disease 2014; 27: 329-335.
- 11. L'Huillier AG, Kumar D. Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Human Vaccines and Immunotherapeutics* 2015; 11: 2852-63.
- 12. Kidney disease: improving global outcomes. KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation. *Transplantation* 2020; 104 (Suppl 4): S1-103.



| | 3.1 LIVE VACCINES: MEASLES, MUMPS, RUBELLA – PRE-TRANSPLANT GUIDELINES | | | | | | | | | | | | |
|--|--|--|---|--|---|---|------------------------|--|--|--|--|--|--|
| NAME OF VACCINE Products available In Canada | ROUTINE SCHEDULE (ONTARIO) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF DOSES REQUIRED | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | | | | |
| Priorix® (MMR) MMR-II® (MMR) | MMR at 12 mths | 6 mths⁴ | 4 wks-6 wks ^{4, 5, 6, 7, 9, 10} in consultation with Infectious Diseases | If first dose given <12 mths, 2 additional | YES | May be done prior to vaccination Post-serology NOT | | | | | | | |
| Priorix-Tetra® (MMR-V) ProQuad® (MMR-V) ³ | MMRV at 4-6 yrs ² | Priorix-Tetra® 9 mths8 ProQuad® 12 mths3 | 4 wks ^{3,4,8,16} In consultation with Infectious Diseases | | Ideally defer transplant for 4 wks following vaccine administration ^{1, 6} | routinely recommended ⁴ Consider post serology if first dose <12 mths or if functionally immunosuppressed ^{4,5} | Covered by MOHLTC | | | | | | |

- · Upper limit for MMR-V products is 12 yrs of age.
- Use of immune globulin or other antibody-containing blood products: Delay immunization for 3 to 11 mths depending on the product to avoid vaccine failure secondary to passively acquired varicella/measles antibodies [https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-11-blood-products-human-immune-globulin-timing-immunization.html].
- · Blood products of human origin contain significant amounts of antibodies to infectious agents such as measles virus and varicella zoster virus (VZV). Administration of IVIG preparations can interfere with the immune responses to live virus vaccines given concomitantly with or shortly before or after the vaccine. The duration of interference with the immune response to the vaccine is related to the amount of antibody in the Ig preparation.^{4,16}
- · If the interval between administration of any of these vaccines and subsequent administration of an IVIG preparation is less that the recommended intervals, immunization should be repeated at 3 mths or longer, unless serologic test indicates that the antibodies were produced. 4.16 [https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-11-blood-products-human-immune-globulin-timing-immunization.html].
- Egg allergy is NOT a contraindication to MMR or MMRV vaccine-trace amount of egg protein appears insufficient to elicit a hypersensitivity reaction in egg allergic individuals.⁴

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- Measles, mumps and rubella vaccine may be given at the same time as the inactivated polio vaccine (IPV), diphtheria, tetanus and pertussis vaccines (DTPw/DTPa) and Haemophilus influenzae type b (Hib) as well as hepatitis A and B, meningococcal B, meningococcal C conjugate, meningococcal polysaccharide groups Ac, C, W- 135 and Y conjugate and pneumococcal polysaccharide vaccines if they are administered at separate injection sites.^{4,8,9,10}
- Per NACI, a minimum interval of 4 wks between 2 varicella-containing vaccines is acceptable under exceptional circumstances. With resepct to other live vaccinations: NACI recommends that if the live vaccines were not given concomitantly, a minimum interval of 4 wks interval should be observed between admnistration of other live vaccines.

- 1. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clinical Infectious Diseases* 2014: 58: e44-100.
- Publicly funded immunization schedules for Ontario-June 2022. Accessed September 29, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ ImmunizationSchedule.pdf
- 3. Merck Canada Inc. Product Monograph ProQuad®. June 2020.
- NACI. Canadian Immunization Guide. Accessed Nov 28, 2021 and June 22, 2022. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines.html
- Danziger-Isakov L, Kumar D. AST Infectious Diseases Community of Practice. Vaccination of solid organ transplant candidates and recipients. Clin Transplant 2019: 33 (9) e13563.
- 6. Abuali MM, Arnon R, Posada R. An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. *Pediatric Transplant* 2011; 15: 770-7.
- 7. L'Huillier AG, Kumar D. Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Human Vaccines and Immunotherapeutics* 2015; 11: 2852-63.
- 8. GlaxoSmithKline Inc. Product Monograph PRIORIX-TETRA™. August 2019.
- 9. GlaxoSmithKline Inc. Product Monograph PRIORIX®. August 2019.
- 10. Merck Canada Inc. Product Monograph MMR-II®. March 2021.

- Kawano Y, Suzuki M, Kawada J, Kimura H, Kamei H, Ohnishi Y, Ono Y, Uchida H, Ogura Y, Ito Y. Effectiveness and safety of immunization with live-attenuated and inactivated vaccines for pediatric liver transplantation recipients. *Vaccine* 2015; 33: 1440-45.
- Shinjoh M, Hoshino K, Takahashi T, Nakayama T. Updated data on effective and safe immunizations with live-attenuated vaccines for children after living donor liver transplantation. Vaccine 2015; 33: 701-707.
- 13. L'Huillier AG, Posfay-Barbe KM. Live viral vaccines in immunocompromised patients. Future Virology 2014; 9: 161-171.
- 14. Verolet CM, Posfay-Barbe KM. Live Virus Vaccines in Transplantation: Friend or Foe? *Current Infectious Disease Reports* 2015: 17: 472-83.
- 15. Kumar D. Immunizations following solid-organ transplantation. *Current Opinion in Infectious Disease* 2014; 27: 329-335.
- 16. CDC. Recommended immunization schedules for persons aged 0 through 18 yrs-2022
 Accessed May 18, 2022. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html
- 17. American Academy of Pediatrics. Immunization in immunocompromised children. In: Red Book: 2021-2024 Report of the Committee on Infectious Diseases, 32nd ed, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH. (Eds), American Academy of Pediatrics, Itasca, IL.
- 18. Kano H, Mizuta K, Sakakihara Y, et al. Efficacy and safety of immunization for pre-and post-liver transplant children. Transplantation 2002; 74: 543-50.

| | 3.2 LIVE VACCINES: VARICELLA – PRE-TRANSPLANT GUIDELINES | | | | | | | | | | | |
|--|--|--|--|--|---|---|-------------------------|--|--|--|--|--|
| NAME OF VACCINE Products available In Canada | ROUTINE Schedule (Ontario) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF Doses required | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | | | |
| Varivax® III (Varicella only) Varilrix® (Varicella only) | Varicella at 15 mths ¹⁵ | 12* mths (varicella alone) | Varivax® 4 wks ^{8, 10, 12, 13, 25} Varilix® 6 wks ²⁶ | 2 doses recommended Initial dose as varicella vaccine; second dose in combination with MMR (MMR-V) | YES Ideally defer transplant for 4 wks following vaccine administration ^{1, 10} | YES Check serology minimum 4-6 wks ^{8, 11} following last dose | Covered under MOHLTC | | | | | |
| Priorix-Tetra® (MMR-V) ProQuad® (MMR-V) | MMR-V at 4-6 yrs ¹⁵ | Priorix-Tetra® 9 mths³ ProQuad® 12 mths² | 4 wks ^{2, 10, 14, 16, 17} | | | | | | | | | |

- *Varicella vaccine may be given at 9 mths^{3,8,11,12,26} in consultation with Infectious Diseases.
- · Upper limit for MMR-V products is 12 yrs of age.
- Use of immune globulin or other antibody-containing blood products: Delay immunization for 3 to 11 mths depending on the product to avoid vaccine failure secondary to passively acquired varicella/measles antibodies.

 https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-11-blood-products-human-immune-globulin-timing-immunization.html
- Blood products of human origin contain significant amounts of antibodies to infectious agents such as measles virus and varicella zoster virus (VZV). Administration of IVIG preparations can interfere with the immune responses to live virus vaccines given concomitantly with or shortly before or after the vaccine. The duration of interference with the immune response to the vaccine is related to the amount of antibody in the Ig preparation.^{13,14}
- If the interval between administration of any of these vaccines and subsequent administration of an IVIG preparation is less that the recommended intervals, immunization should be repeated at 3 mths or longer, unless serologic test indicates that the antibodies were produced.^{13, 14} https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-11-blood-products-human-immune-globulin-timing-immunization.html
- · Refer to product monographs for information regarding potential allergens such as neomycin, gelatin and egg protein.
- · Contraindicated in patients with history of anaphylaxis after previous administration of the vaccine or with proven immediate/anaphylactic hypersensitivity to any component of the product.
- Egg allergy is NOT a contraindication to MMR-V vaccine-trace amount of egg protein appears insufficient to elicit a hypersensitivity reaction in egg allergic individuals. ¹⁴
- · Close contacts should be vaccinated against varicella if they do not have a previous history of chicken pox. Isolate contacts from the transplant recipient if they develop a varicella-like rash (>50 lesions).^{7,27}

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- · Varicella vaccine can be administered concomitantly with diphtheria and tetanus toxoids and pertussis vaccine adsorbed (DTaP) and Haemophilus b (Hib) conjugate vaccine.
- MMR vaccine can be administered concomitantly with diphtheria and tetanus toxoids and pertussis vaccine adsorbed, Haemophilus b conjugate vaccine and inactivated polio (IPV) vaccine if given at separate sites. 4,9,10
- MMR-V vaccines: Priorix Tetra® can be given at the same time as DTaP, Hib and IP vaccines if administered at separate sites.3 ProQuad® can be given at the same time as Hib, Hepatitis B, Hepatitis B,
- Per NACI, a minimum interval of 4 wks between 2 varicella-containing vaccines is acceptable under exceptional circumstances. With resepct to other live vaccinations: NACI recommends that if the live vaccines were not given concomitantly, a minimum interval of 4 wks interval should be observed between admnistration of other live vaccines. 14

- Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clinical Infectious Diseases 2014; 58: e44-100.
- 2. Merck Canada Inc. Product Monograph ProQuad®. June 2020.
- 3. GlaxoSmithKline Inc. Product Monograph PRIORIX-TETRA™. August 2019.
- 4. Shinjoh M, Hoshino K, Takahashi T, Nakayama T. Updated data on effective and safe immunizations with live-attenuated vaccines for children after living donor liver transplantation. Vaccine 2015; 33: 701-707.
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- 7. Pergam SA, Limaye AP, AST Infectious Disease Community of Practice. Varicella zoster virus in solid organ transplant recipients. *Clin Transplant*. 2019; 33: e13622.
- 8. Danziger-Isakov L, Kumar D, AST Infectious Diseases Community of Practice. Vaccination of solid organ transplant candidates and recipients. *Clin Transplant* 2019; 33 (9) e13563.
- L'Huillier AG, Posfay-Barbe KM. Live viral vaccines in immunocompromised patients. Future Virology 2014;
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- 10. Abuali MM, Arnon R, Posada R. An update on immunizations before and after transplantation in the pediatric solid organ transplant recipient. *Pediatric Transplant* 2011: 15: 770-7.
- 11. L'Huillier AG, Kumar D. Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Human Vaccines and Immunotherapeutics* 2015; 11: 2852-63.
- 12. Verolet CM, Posfay-Barbe KM. Live Virus Vaccines in Transplantation: Friend or Foe? Current Infectious Disease Reports 2015; 17: 472-83.
- 13. CDC. Recommended immunization schedules for persons aged 0 through 18 yrs-2022.

 Accessed May 18, 2022 https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

- 14. NACI. Canadian Immunization Guide. Accessed Sept 18, 2021 and June 22, 2022 https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines.html
- 15. Publicly funded immunization schedules for Ontario-June 2022. Accessed September 29, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf
- 16. American Academy of Pediatrics. Immunization in immunocompromised children. In: Red Book: 2021-2024 Report of the Committee on Infectious Diseases, 32nd ed, Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH. (Eds), American Academy of Pediatrics, Itasca IL.
- Kumar D. Immunizations following solid-organ transplantation. Current Opinion in Infectious Disease 2014;
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- 18. Mizuta K, Urahashi T, Ihara Y, et al. Varicella zoster virus disease after pediatric living donor liver transplantation: is it serious? *Transplantation Proceedings* 2012; 44: 780-783.
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- 23. Weinberg A, Horslen SP, Kaufman SS, et al. Safety and immunogenicity of varicella-zoster virus vaccine in pediatric liver and intestine transplant recipients. *American Journal of Transplantation* 2006; 6: 565-8.
- Donati M, Zuckerman M, Dhawan A, et al. Response to varicella immunization in pediatric liver transplant recipients. Transplantation 2000; 70: 1401-4.
- 25. Merck Canada Inc. Product Monograph Varivax® III. May 2020.
- 26. Glaxo Smith Kline Inc. Product Monograph Varilix®. August 2019.
- 27. Seward JF, Zhang JX, Maupin TJ, Mascola L, Jumaan AO. Contagiousness of varicella in vaccinated cases: A household contact study. *JAMA* 2004; 292: 704-708.

| | 3.3 LIVE VACCINES: ROTAVIRUS – PRE-TRANSPLANT GUIDELINES | | | | | | | | | | | |
|---|---|--|-----------------------------------|--|--|-------------------------------------|---|--|--|--|--|--|
| NAME OF VACCINE Products available In Canada | ROUTINE Schedule (Ontario) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF DOSES REQUIRED | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | | | |
| Rotavirus oral vaccine Rotarix® RotaTeq® (Not interchangeable) | Rotarix® 2 and 4 mths ^{1,2,4} RotaTeq® 2, 4, 6 mths ^{1,2,5} | 6 wks ^{2, 4, 5} | 4 wks ^{2, 4, 5} | Rotarix® 2 doses² All doses completed by <25 wks of age ^{1,2,4} RotaTeq® 3 doses All doses completed by <32 wks of age ^{1,2,5} | YES As per suggested schedule if no contraindication Ideally defer transplant for 4 wks following vaccine administration ^{1, 6} | NO | Rotarix® Covered by MOHLTC for infants: 6-25 wks of age | | | | | |

- · Contraindicated with history of intussusceptions^{4,5}, severe combined immunodeficiency disorder (SCID).^{2,4,5}
- Infants with moderate to severe gastroenteritis should have rotavirus vaccine deferred until clinical condition improves, unless deferral will result in first dose being given >15 wks.² If an incomplete dose is administered for any reason (for example, infant spits or regurgitates the vaccine) a replacement dose should NOT be administered.²
- · Live virus sheds in stool; care with diaper changes.^{4,5}
- · Typically NOT be given in hospital due to risk of transmission.
- · Siblings may receive vaccine however careful handwashing recommended. Older transplant recipients should not change/handle their vaccinated sibling's diapers for 10 days following vaccine dose.²

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

• Rotavirus oral vaccines may be given at the same time as other routine vaccinations (diphtheria, tetanus, pertussis, Haemophilus influenzae type b, inactivated polio, hepatitis B, pneumococcal vaccines as well as meningococcal serogroup C conjugate vaccine).

- Publicly funded immunization schedules for Ontario-June 2022 Accessed October 4, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf
- 2. National Advisory Committee on Immunization. (NACI). Canadian Immunization Guide. Accessed November 28, 2021 and June 22, 2022. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines.html
- CDC. Recommended immunization schedules for persons aged 0 through 18 yrs-2022.
 Accessed May 18, 2022. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html
- 4. Rotarix® Product Monograph. Glaxo Smith Kline. July 2021.
- 5. RotaTeq® Product Monograph. Merck. January 2018.



| | | | 4.0 INFLUENZ | ZA VACCINES: PRE-TRANSPLANT GUI | DELINES | | · |
|---|----------------------------------|--|-----------------------------------|---|--|-------------------------------------|--|
| NAME OF VACCINE Products available In Canada | ROUTINE SCHEDULE (ONTARIO) | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL BETWEEN DOSES | NUMBER OF DOSES REQUIRED | RECOMMEND PRE-TRANSPLANT | SEROLOGY PRE/POST VACCINATION | COVERAGE IN ONTARIO |
| Influenza Vaccine availability may vary annually Quadrivalent Inactivated: Flulaval® Tetra Fluzone® Quad Flucelvax® Quad Influvac® Tetra Afluria® Tetra (age ≥5 yrs) Trivalent Inactivated, Adjuvanted: Fluad Pediatric™ (age 6-23 mths) | Yearly | 6 mths ¹ | Annual | 6 mths-<9 yrs, no previous influenza vaccination: 2 doses, 4 wks apart ^{1, 2, 5} 6 mths-<9 yrs, previous influenza vaccination: 1 dose ¹ ≥9 yrs: 1 dose ¹ | YES Quadrivalent vaccine preferred for paediatric patients | NO | Covered by MOHLTC for all patients at risk |
| Live-attenuated Influenza Vaccine (LAIV) quadrivalent: FluMist® | Yearly | 2 yrs¹ | Annual | 2 to < 9 yrs, no prior influenza vaccination: 2 doses, 4 wks apart ^{1,2,3,6} 2 to < 9 yrs, previous influenza vaccination: 1 dose ¹ ≥9 yrs:1 dose ¹ | Reserve FluMist® for needle averse patients; less data regarding efficacy in the CKD population Recommendations may vary across international jurisdictions. Defer transplant for 2 wks following vaccine administration to ensure adequate response9,10 | | |

• If a quadrivalent vaccine is not available, any of the available trivalent vaccines licensed for the pertinent age group should be used.1

CONCOMITANT ADMINISTRATION OF VACCINES LISTED IN THIS TABLE:

- The National Advisory Committee on Immunization (NACI) states that administering the most widely used live and inactivated vaccines during the same patient visit has produced seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately.¹
- NACI recommends that vaccines administered simultaneously should be given using separate syringes at separate sites.¹
- · As a precaution, siblings who have been vaccinated with LAIV should avoid contact with recently transplanted patients who are still in hospital for one wk following LAIV dose. 9, 27, 31

CONTRAINDICATIONS:

- · Persons who have developed an anaphylactic reaction to a previous dose of influenza vaccine or any of its components (with the exception of egg*), have developed Guillain-Barre Syndrome (GBS) within 6 wks of influenza vaccination.
- *Egg allergic individuals can be vaccined with influenza vaccine with inactivated TIV and QIV or LAIV without an influenza skin test and with the full dose of the vaccine.¹ There is low risk of adverse reaction to trace amounts of ovalbumin exist in the current influenza vaccines.¹
- · Consult individual product monographs for specific warnings in this regard.

- National Advisory Committee on Immunization (NACI). Canadian Immunization Guide chapter on influenza and statement on seasonal influenza vaccine for 2022-2023: Nov 28, 2021 and September 29, 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023.html#a5.¹
- Publicly funded immunization schedules for Ontario-June 2022. Accessed June 22, 2022. https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf
- 3. Kumar D, Blumberg EA, Danziger-Isakov L, Kotton CN, Halasa NB, Ison MG, et al. Influenza Vaccination in the Organ Transplant Recipient: Review and Summary of Recommendations. *American Journal of Transplantation* 2011: 11: 2020-2030.
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- CDC. Recommended immunization schedules for persons aged 0 through 18 yrs-2022.
 Accessed May 18, 2022. http://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf.
- Gavalda J, Cabral E, Perez-Romero P, Len O, Aydillo T, Campins M et al. Immunogenicity of pandemic influenza A H1N1/2009 adjuvanted vaccine in pediatric solid organ transplant recipients. Pediatric Transplantation 2013: 17: 403-406.
- GiaQuinta S, Michaels MG, McCullers JA, Wang, L, Fonnesbeck C, O'Shea A et al. Randomized, double-blind comparison of standard-dose vs. high-dose trivalent inactivated influenza vaccine in pediatric solid organ transplant patients. Pediatric Transplantation 2015: 19: 219-228.
- 8. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clinical Infectious Diseases 2014; 58: e44-100.
- 9. Benden C, Danziger-Isakov LA, Astor T, et al. Variability in immunization guidelines in children before and after lung transplantation. *Pediatric Transplant*ation 2007; 11: 882-887.
- Danziger-Isakov L, Kumar D, AST Infectious Diseases Community of Practice. Vaccination of solid organ transplant candidates and recipients. Clin Transplant 2019; 33 (9) e13563.
- Kumar D. Immunizations following solid-organ transplantation. Current Opinion in Infectious Disease 2014;
 329-335.
- 12. L'Huillier AG, Kumar D. Immunizations in solid organ and hematopoeitic stem cell transplant patients: A comprehensive review. *Human Vaccines and Immunotherapeutics* 2015; 11: 2852-63.
- Kidney disease: improving global outcomes. KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation. Transplantation 2020; 104 (Suppl 4): S1-103r.

- L'Huillier AG, Posfay-Barbe KM. Live viral vaccines in immunocompromised patients. Future Virology 2014;
 161-171.
- 15. Martin ST, Torabi MJ, Gabardi S. Influenza in solid organ transplant recipients. *The Annals of Pharmacotherapy* 2012; 46: 255-264.
- 16. Cordero E, Manuel O. Influenza vaccination in solid-organ transplant recipients. *Current Opinion in Organ Transplantation* 2012; 17: 601-608.
- 17. AstraZeneca Canada Inc. Product Monograph FluMist® Quadrivalent April 2022.
- 18. Avery RK. Influenza vaccines in the setting of solid-organ transplantation: are they safe? Current Opinion in Infectious Diseases 2012; 25: 464-468.
- Moore DL, Canadian Pediatric Society, Infectious Disease and Immunization Committee. Vaccine recommendations for children and youth for the influenza season. Accessed May 18, 2021. https://www.cps.ca/en/documents/position/vaccine-recommendations-2020-2021-influenza-season.
- Haller W, Buttery J, Laurie K, Beyerle K, Hardikar W, Alex G. Immune response to pandemic H1N1 2009 influenza a vaccination in pediatric liver transplant recipients. Liver Transplantation 2011; 17: 914-920.
- Danziger-Isakov LA, Husain S, Mooney ML, Hannan MM. The novel 2009 H1N1 influenza virus pandemic: unique considerations for programs in cardiothoracic transplantation. *Journal of Heart and Lung Transplantation* 2009: 28: 1341-1347.
- 22. Kumar D, Morris MI, Kotton CN, et al. Guidance on novel influenza A/H1N1 in solid organ transplant recipients. American Journal of Transplantation 2010; 10: 18-25.
- Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and Control of Seasonal Influenza with Vaccines.
 MMWR Recomm Rep 2016; 65: 1.
- 24. Kamboj M, Sepkowitz KA. Risk of transmission associated with live attenuated vaccines given to healthy persons caring for or residing with an immunocompromised patient. Infect Control Hosp Epidemiol 2007; 28: 702.
- 25. Sanofi Pasteur Ltd. Product Monograph Fluzone® Quad. April 2022.
- 26. GlaxoSmithKline Inc. Product Monograph Fluviral® Tetra. April 2022.
- 27. American Academy of Paediatrics Committee on Infectious Diseases; Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH (eds). RedBook 2021-2024 Report of the Committee on Infectious Diseases 32nd edition.
- 28. Segirus Canada Inc. Product Monograph Flucelvax® Quad. May 2022.
- 29. BGB Pharma ULC. Product Monograph Influvac® Tetra. May 2022.
- 30. Seqirus Canada Inc. Product Monograph Afluria® Tetra. May 2022.



| | 5.1 ENTEROTOXIGENIC E COLI – PRE-TRANSPLANT TRAVEL GUIDELINES | | | | | | | | | | |
|--|---|---|--|-----------------------------------|--------------------------------------|--|---------------------------------------|--|--|--|--|
| NAME OF VACCINE Products available In Canada | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL PRIOR TO TRAVEL | NUMBER OF DOSES REQUIRED | MINIMUM INTERVAL BETWEEN DOSES | INDICATION PRE-TRANSPLANT | SEROLOGY REQUIRED PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | | |
| Enterotoxigenic E coli Dukoral® (Oral, inactivated) | 2 yrs¹ | 2 wks¹ | Primary immunization 2 doses* 1st dose 2 wks before departure; 2nd dose 1 wk following first dose and at least 1 wk before departure Booster Every 3 mths if in area of ongoing risk ² . If more than 5 yrs have passed since primary immunization or last booster dose, repeat primary series. ² | 1 wk ^{1, 2} | YES If indicated ² | NO | Not routinely covered by ON-MOHLTC | | | | |

*If 6 wks elapses between doses patient will need to repeat the primary series.

Dukoral dose is prepared differently for younger children. See below:

- · Open the white sachet of powder and pour into 150 ml (5 oz) of cool water.
- · Stir gently with spoon to dissolve.
- · Do not use any other liquid.
- · For children aged 2-6 yrs, pour away half of the powder/water mixture before adding the vaccine component.1

- 1. Valneva Canada Inc. Dukoral® product monograph October 2020.
- National Advisory Committee on Immunization (NACI). Canadian Immunization Guide. Cholera and enterotoxigenic escherichia coli (ETEC) travellers' diarrhea vaccine. Accessed Nov 28, 2021, and June 17 2022
- Danziger-Isakov, L., and D. Kumar. "Vaccination of solid organ transplant candidates and recipients: Guidelines from the American society of transplantation infectious diseases community of practice." Clin Transplant 2019; 33 (9) e13563.
- 4. CDC Yellow Book 2020: Immunocompromised travelers-severe immunosuppression (non HIV-related; adult).
- Buchan CA, Nelson Lotton C. Travel medicine, transplant tourism, and the solid organ transplant recipient-Guidelines from the American Society of Transplantation infectious diseases community of practice. Clin Transplant 2019 Sep; 33(9): e13529; doi: 10.111/ctr.13529.
- Patel RP, Liang SY, Koolwal P and Kulhmann FM. "Travel Advice for the Immunocompromised Traveler: Prophylaxis, Vaccination, and Other Preventive Measures." *Therapeutics and Clinical Risk Management TCRM* (2015): 217.

| | 5.2 HEPATITIS A – PRE-TRANSPLANT TRAVEL GUIDELINES | | | | | | | | | | |
|---|--|--|--|---|---|--|---|--|--|--|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL PRIOR TO TRAVEL | NUMBER OF DOSES REQUIRED | MINIMUM INTERVAL BETWEEN DOSES | INDICATION PRE-TRANSPLANT | SEROLOGY REQUIRED PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | | |
| Hepatitis A AVAXIM® PED HAVRIX® HAVRIX® JR VAQTA® VAQTA® PED (Interchangeable) IM inj | 6 mths ² | 2-4 wks Vaccination up until the day of travel may still provide some | 2 doses (Refer to dosing table below) | 6 mths | YES If indicated Recommended for ALL transplant candidates | NO | Not covered routinely by ON MOHLTC except for HIGH RISK* individuals | | | | |
| Combination Hepatitis A Vaccines Hep A + Hep B Twinrix® Twinrix® Junior | 12 mths ¹² | protection ² | Twinrix® 2 doses Twinrix® Junior 3 doses | Twinrix® 6 mths Twinrix® Jr 1 mth between 1st and 2nd dose; 6 mths between 1st and 3rd dose | *NACI does not recommend the use of Twinrix® and Twinrix® Jr in patients who are functionally immunosuppressed or hyporesponsive (e.g. ESRD dialysis patients)² | | Not covered routinely by ON MOHLTC | | | | |

| HEPATITIS A | TABLE 1: CANADIAN IMMUNIZATION GUIDE (NACI)- HEPATITIS A DOSING RECOMMENDATIONS FOR MONOVALENT HEPATITIS A VACCINES ¹ | | | | | | | | | | | |
|-------------|--|--------|-----------------------------|-------------------------|--|--|--|--|--|--|--|--|
| VACCINE | ANTIGEN* | VOLUME | SCHEDULE (BOOSTER) | AGE ^t | | | | | | | | |
| Avaxim® | 160 antigen units HAV | 0.5 mL | 0, (6-36) mths | 12 yrs and older | | | | | | | | |
| Avaxim Ped® | 80 antigen units HAV | 0.5 mL | 0, (6-36) mths | 6 mths-<16 yrs | | | | | | | | |
| Havrix® | 1440 ELISA units HAV | 1 mL | 0, (6-12) mths [‡] | 19 yrs and older | | | | | | | | |
| Havrix Jr® | 720 ELISA units HAV | 0.5 mL | 0, (6-12) mths | 6 mths-<19 yrs | | | | | | | | |
| Vaqta® | 50 units HAV | 1 mL | 0, (6-18) mths | 18 yrs and older | | | | | | | | |
| Vaqta Ped® | 25 units HAV | 0.5 ml | 0, (6-18) mths | 6 mths-<18 yrs | | | | | | | | |

^{*}There is no international standard for HAV measurement. Each manufacturer uses its own units of measurement.

- Comparable to the results reported in clinical trials of children more than 12 mths, all reviewed studies have consistently shown that vaccination of infants 6-12 mths with inactivated HA vaccines is immunogenic and safe.
- The manufacturer of Twinrix and Twinrix Jr has not authorized use of the combination products in children <1 yr of age.
- *HIGH RISK includes patients with chronic liver disease, patients awaiting liver transplants, and individuals living in communities at risk of hepatitis A (HA) outbreaks or in which HA is endemic²

- Publicly funded immunization schedules for Ontario-June 2022. Accessed September 29, 2022 https://www.health.gov.on.ca/en/pro/programs/immunization/docs/Publicly_Funded_ImmunizationSchedule.pdf
- National Advisory Committee on Immunization. (NACI). Canadian Immunization Guide. Accessed Nov 28, 2021 and June 17, 2022. http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php#toc.
- Summary of NACI Statement Update on the recommended use of Hepatitis A Vaccine. Canada Communicable Disease report (CCDR) 42-9; accessed June 25, 2021 and May 18, 2022. https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/mthly-issue/2016-42/ccdr-volume-42-9-september-1-2016/ccdr-volume-42-9-september-1-2016-scientific-writing-6.html
- 4. NACI: Immunization of Immunocompromised Persons: Vaccination of solid organ transplant candidates and recipients.
- 5. Kumar D and Humar A. The AST Handbook of Transplant Infections: Recommendations for Travel-related Vaccinations and Medications for Transplant Travelers (2021).
- 6. CDC Yellow Book 2020: Immunocompromised travelers-severe immunosuppression (non HIV-related; adult).
- 7. Buchan CA, Kotton, CN. "Travel medicine, transplant tourism and the solid organ transplant recipient-Guidelines from the American Society of Transplantation ID Community of Practice. *Clin Transplant* 2019; 33e13529.
- 8. Danziger-Isakov L and Kumar D. ""Vaccination of solid organ Transplant candidates and recipients." Clin Transplant 2019; 33 (9) e13563.
- Patel RP, Liang SY, Koolwal P and Kulhmann FM. "Travel Advice for the Immunocompromised Traveler: Prophylaxis, Vaccination, and Other Preventive Measures." Therapeutics and Clinical Risk Management TCRM (2015): 217.
- 10. GlaxoSmithKline Inc. Product Monograph Havrix®. March 2021.
- 11. Sanofi Pasteur Ltd. Product Monograph Avaxim Pediatric®. June 2019.
- 12. GlaxoSmithKline Inc. Product Monograph Twinrix®. November 2018.

^t Ages for which the vaccine is approved.

^{*} Studies have shown that 720 ELISA units provides an effective booster dose in those over 19 yrs of age.

| | | | J.S HELAIIIS D - I | PRE-TRANSPLANT TRAVEL GU | | | |
|--|--|---|--|---|---|---|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL PRIOR TO TRAVEL | NUMBER OF DOSES REQUIRED | MINIMUM INTERVAL BETWEEN DOSES | INDICATION PRE-TRANSPLANT | SEROLOGY REQUIRED PRE/POST VACCINATION | COVERAGE IN ONTARIO |
| Hepatitis B RECOMBIVAX HB® OR ENGERIX® B (Interchangeable) IM inj For routine schedule refer to Publicly Funded Immunization Schedules for Ontario | Newborn ² | Accelerated schedule available given on Days 0, 7, 21 with booster at 6-12 mths (upon return from travel) ^{9, 10} | 3 dose schedule preferred (0, 1 and 6 mths) if travel not imminent ² (Various dosing schedules available, refer to dosing tables below) | 7 days after first dose, 14 days after second dose ^{2, 10} | YES If indicated If functionally immunosuppressed (asplenic, hypersplenic), receiving immunosuppressant for underlying condition or hyporesponsive (e.g. ESRD dialysis) consider double the microgram dose for age; use 3 or 4 dose schedule. ² Defer transplant for 2 wks following vaccine administration to ensure adequate response. | YES 6-8 wks post series* (range 1-6 mths)² Repeat series if antibody response is suboptimal (< 10 IU/L) (If higher dose used initially, ensure higher | Not covered routinely by ON MOHLTC except for HIGH RISK* individuals |
| Combination Hepatitis A+B Twinrix® Twinrix® Junior IM | 12 mth ¹² | If departing in <21 days and needing both HA & HB vaccines, use monovalent vaccines and complete the series after travel ² | Twinrix® 2 doses Twinrix® Junior 3 doses | Twinrix® 6 mths¹² Twinrix® Junior 1 mth between 1st and 2nd dose¹² 6 mths between 1st and 3rd dose¹² | NACI does not recommend the use of Twinrix® or Twinrix® Jr in immunosuppressed or hyporesponsive (e.g ESRD dialysis) patients² | dose used for repeat ²) If non-responsive to repeat series, consult ID | |

^{*} Expert Opinon

TABLE 1: CANADIAN IMMUNIZATION GUIDE (NACI)-HEPATITIS B STANDARD DOSING RECOMMENDATIONS1 FOR PAEDIATIC PATIENTS (3 OR 4 DOSE SCHEDULE ONLY):

| RECIPIENTS | RECOMBIVAX HB® | | | ENGERIX® B | | | |
|--|----------------|-----|-----------------|------------|-----|-------------------------------|--|
| | μg | mL | SCHEDULE (MTHS) | μg | mL | SCHEDULE (MTHS) | |
| Infants (regardless of mothers' HBV status) | 5 | 0.5 | 0, 1, 6** | 10 | 0.5 | 0, 1, 6 0R 0, 1, 2, 12 | |
| 12 mths- 19 yrs | 5 | 0.5 | 0, 1, 6** | 10 | 0.5 | 0, 1, 6 OR 0, 1, 2, 12 | |

^{*}Thimerosal preservative-free preparation is recommended.

TABLE 2: HEPATITIS B-REVISED DOSING GUIDELINES FOR TRANSPLANT (ADAPTED FROM CANADIAN IMMUNIZATION GUIDE-NACI) NOTE: DOSES LISTED ARE DOUBLE THE ROUTINE AGE RECOMMENDED DOSE

| RECIPIENTS | RECOMBIVAX HB® | | | ENGERIX® B | | | |
|--|----------------|----|--|------------|----|--|--|
| | μg | mL | SCHEDULE (MTHS) | μg | mL | SCHEDULE (MTHS) | |
| Infants (regardless of mothers' HBV status) | 10 | 1 | 0, 1, 6** | 20 | 1 | 0, 1, 6 OR 0, 1, 2, 12 | |
| 12 mths- 19 yrs | 10 | 1 | 0, 1, 6** OR 0, 1, 2, 12 for dialysis, chronic renal failure, and some immuno- compromised individuals | 20 | 1 | 0, 1, 6 OR 0, 1, 2, 12 | |
| 16 to <20 yrs | 10 | 1 | 0, 1, 6** OR 0, 1, 2, 12 for dialysis, chronic renal failure, and some immuno- compromised individuals | 40 | 2 | 0, 1, 2, 6 (CIG) particularly for ESRD/ dialysis patient | |

^{*}Thimerosal preservative-free preparation recommended;

^{**}Although a schedule of 0, 1 and >2 mths is approved, the preferred schedule is 0, 1, and 6.

^{**}Although schedule of 0, 1 and >2 mths is approved, the preferred schedule is 0, 1, and 6.

| TABLE 3: TWINRIX® AND TWINRIX JR® DOSING SCHEDULE ¹¹ | | | | | | | | | | |
|---|----------------------|----|-----------------|----|-----|-----------------|--|--|--|--|
| AGE | TWINRIX® TWINRIX® JR | | | | | | | | | |
| | μg | mL | SCHEDULE (MTHS) | μg | mL | SCHEDULE (MTHS) | | | | |
| 1 yr- <16 yrs | 20 | 1 | 0, 6-12 | 10 | 0.5 | 0, 1, 6 | | | | |
| 16- <19 yrs | - | - | - | 10 | 0.5 | 0, 1, 6 | | | | |

There are no data to support the use of Twinrix® and Twinrix® Jr on an accelerated schedule in children. 11

The manufacturer of Twinrix and Twinrix Jr has not authorized use of the combination products in children <1 yr of age.

- Publicly funded immunization schedules for Ontario-June 2022 Accessed September 29, 2022. http://www.health.gov.on.ca/en/pro/programs/immunization/docs/immunization schedule.pdf.
- National Advisory Committee on Immunization. (NACI). Canadian Immunization Guide.
 Nov 28, 2021 and June 17, 2022. http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php#toc.
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- 10. GlaxoSmithKline Inc. Product Monograph Engerix B®. October 2020.
- 11. Merck Canada Inc. Product Monograph Recombivax®. May 2012.
- 12. GlaxoSmithKline Inc. Product Monograph Twinrix®. November 2018.

| | 5.4 JAPANESE ENCEPHALITIS – PRE-TRANSPLANT TRAVEL GUIDELINES | | | | | | | | | |
|--|--|---|--|-----------------------------------|---|--|---------------------------------------|--|--|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL PRIOR TO TRAVEL | NUMBER OF DOSES REQUIRED | MINIMUM INTERVAL BETWEEN DOSES | INDICATION PRE-TRANSPLANT | SEROLOGY REQUIRED PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | |
| Japanese encephalitis IXIARO® (Inactivated) | 2 mths ^{3, 4, 7} | Consult travel clinic | 2 doses ^{3,7} Children younger than 3 yrs of age receive half of the adult dose ⁷ If primary series was administered ≥1 yr ago, a booster dose should be given prior to potential re-exposure or if there is a continued risk for JEV infection ^{2,7} | 28 days | YES If indicated ^{1, 4} | NO | Not covered routinely by ON-MOHLTC | | | |

Children receive 2 doses, 28 days apart⁷:

- · 2 mths-<3 yrs of age: 0.25 mL per single dose.
- · Refer to product monograph for Special Handling Instructions for preparing a 0.25 mL dose.
- · 3 yrs-<18 yrs of age: 0.5 mL per single dose.

- NACI: Japanese Encephalitis.Canadian Immunization Guide. Accessed September 29, 2022 https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-11-japanese-encephalitis-vaccine.html
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- 7. Valneva Austria. Product Monograph. Ixiaro. March 2018.

| | 5.5 RABIES – PRE-TRANSPLANT TRAVEL GUIDELINES | | | | | | | | | |
|---|---|--|--|---|---|---|--|--|--|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL PRIOR TO EXPOSURE OR TRAVEL | NUMBER OF DOSES REQUIRED | MINIMUM INTERVAL BETWEEN DOSES | INDICATION PRE-TRANSPLANT | SEROLOGY REQUIRED PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | |
| Rabies IMOVAX® RabAvert® (inactivated vaccine) (Can be used interchangeably) IM 1 mL | Newborn ¹ | 7 days | Pre-Exposure Prophylaxis 3 doses Day 0, 7 and between day 21 to 28 ² Post-Exposure prophylaxis Day 0, 3, 7 and 14 (immunocompromised patients should receive 5th dose on Day 28) ^{2,3,8} | Interval varies depending on prescribed prophylaxis | Pre-Exposure No; unless immunocompromised and expecting intense animal exposure or who will be distant from medical care Post-Exposure Prophylaxis Yes, if indicated ² | Pre Exposure NO Post Exposure Consider serology 7 to 14 days post- completion of series ^{2,3} If titre <0.5 re-vaccinate with 2nd series | Pre-exposure prophylaxis is not routinely covered by ON MOHLTC Post-exposure immunization is covered by OHIP for exposures in Ontario | | | |
| Rabies Pasteurized immune globulin IMOGAM® (rabies immune globulin) | | | Recommended dose of Rablg: 20 IU/kg body weight for all age groups ² Given on Day 0 ² | N/A | | | | | | |

Whenever possible, the complete complement of vaccines should be administered before transplantation. Vaccines noted to be safe for administration after transplantation may not be sufficiently immunogenic after transplantation.

Persons with egg allergies are not necessarily at increased risk of a hypersensitivity reaction to RabAvert®. However, for pre-exposure vaccination, an alternative vaccine, Imovax®, should be used in patients with a history of hypersensitivity reactions to egg or egg products. If an alternative vaccine is not available, post-exposure prophylaxis using RabAvert should be administered with strict medical monitoring. Facilities for emergency treatment of anaphylactic reactions should be available.²

- 1. Kumar D and Humar A (eds). The AST Handbook of Transplant Infections: Immunizations after pediatric solid organ transplant and hematopoetic stem cell transplant (2011).
- NACI: Rabies Vaccine. Canadian Immunization Guide. Accessed November 28, 2021 and September 29, 2022. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-18-rabies-vaccine.html#p4c17t2.
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- 7. Cramer CH, Shleck V, Thomas SE, Kershaw DB et al. "Immune Response to Rabies Vaccination in Pediatric Transplant Patients." *Pediatric Transplantation* 2008; 12 (8): 874-77.
- 8. Sanofi Pasteur. Product Monograph. Imovax. March 2021.
- 9. Bavarian Nordic. Product Monograph. RabAvert. July 2021.
- 10. Sanofi Pasteur. Product Monograph. IMOGAM. December 2015.

| | 5.6 TYPHOID (SALMONELLA TYPHI) – PRE-TRANSPLANT TRAVEL GUIDELINES | | | | | | | | | |
|--|---|--|--|-----------------------------------|---|--|---------------------------------------|--|--|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL PRIOR TO TRAVEL | NUMBER OF Doses required | MINIMUM INTERVAL BETWEEN DOSES | INDICATION PRE-TRANSPLANT | SEROLOGY REQUIRED PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | |
| Salmonella Typhi (parenteral inactivated) TYPHIM Vi® | 2 yrs ^{1, 2} | 14 days prior to travel ^{1, 2} | 1 dose | N/A | YES If indicated ^{2,3} Immunosuppressed transplant candidates should only receive | | Not covered routinely by ON MOHLTC | | | |
| Oral, LIVE attenuated Vivotif® | 5 yrs ⁸ | 7 days following last dose of capsules | 4 enteric-coated capsules* taken on alternate days (7-day course) ⁸ | | inactivated vaccine Re-immunize by IM route every 3 yrs if ongoing risk ^{1, 2, 3} Re-immunization by PO route every 7 yrs if ongoing risk ^{2, 8} | Not required ² | Not covered routinely by ON MOHLTC | | | |

Whenever possible, the complete complement of vaccines should be administered before transplantation. Vaccines noted to be safe for administration after transplantation may not be sufficiently immunogenic after transplantation.

- 1. Sanofi Pasteur Ltd. Product Monograph Typhim Vi®. June 2021.
- NACI: Typhoid-I Vaccine. Canadian Immunization Guide. Accessed September 29, 2022 https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-23-typhoid-vaccine.html
- 3. NACI: Immunization of Immunocompromised Persons: Vaccination of solid organ transplant candidates and recipients. Accessed September 29, 2022
- Buchan C, Kotton C. Travel medicine, transplant tourism, and the solid organ transplant recipient-guidelines from the American Society of Transplantation Infectious Diseases Comunity of Practice. Clin Transplant 2019; 33 e13529.
- Abuali M, Arnon R and Posada R. "An Update on Immunizations before and after Transplantation in the Pediatric Solid Organ Transplant Recipient." *Pediatric Transplant*ation 15.8 (2011): 770-77.
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- 7. Patel R, Liang S, Koolwal P and Kulhmann F. "Travel Advice for the Immunocompromised Traveler: Prophylaxis, Vaccination, and Other Preventive Measures." Therapeutics and Clinical Risk Management TCRM (2015): 217.
- 8. Emergent Travel Health Inc. Product Monograph Vivotif®. November 2020.

^{*}Vivotif capsules MUST be swallowed whole, 1 hour before or 2 hours after a meal.8

| | 5.7 YELLOW FEVER – PRE-TRANSPLANT TRAVEL GUIDELINES | | | | | | | | | |
|--|---|--|--|-----------------------------------|---|---|------------------------------------|--|--|--|
| NAME OF VACCINE PRODUCTS AVAILABLE IN CANADA | MINIMUM AGE FOR 1 ST DOSE | MINIMUM INTERVAL PRIOR TO TRAVEL | NUMBER OF DOSES REQUIRED | MINIMUM INTERVAL BETWEEN DOSES | INDICATION PRE-TRANSPLANT | SEROLOGY REQUIRED PRE/POST VACCINATION | COVERAGE IN ONTARIO | | | |
| Yellow Fever YF-VAX® (LIVE attenuated) SC inj | 9* mths ^{1,9} | 10 days ^{2,9} (Neutralizing antibodies develop 10 days after vaccination in 80% of immunized persons ²) | 1 dose ^{1, 2, 9} Booster only required every 10 yrs ^{1, 2} if patient meets certain criteria | N/A | YES If indicated based on travel destination ¹ In general, not recommended for transplant candidates who are receiving immunosuppressive medications ² | For patients who become immunocompromised following immunization, serologic testing should be considered two to five yrs post-immunization ² | Not routinely covered by MOHLTC | | | |

Whenever possible, the complete complement of vaccines should be administered before transplantation.²

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- CATMAT: Statement on the use of booster doses of yellow fever vaccine. Accessed May 19, 2021 and September 22, 2022. https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/mthly-issue/2018-44/issue-5-may-3-2018/article-6-catmat-yellow-fever-guidelines-update.html
- 3. Buchan C, Kotton C. Travel medicine, transplant tourism and the solid organ transplant recipient. Guidelines from the AST Infectious Diseases Community of Practice. *Clin Transplant* 2019; 33 (9).

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- 8. Azevedo L, Lasmar E, Contieri I, Boin L et al. "Yellow Fever Vaccination in Organ Transplanted Patients: Is It Safe? A Multicenter Study." Transplant Infectious Disease Transpl Infect Dis 14.3 (2011): 237-41. Web. Sanofi Pasteur Limited. *Product Monograph YF-Vax®*, April 2019.

^{*}If travel is unavoidable, the decision to vaccinate infant between 6 to <9 mths needs to balance the risk of YF exposure with the risks of vaccination (increased risk of encephalitis) in this age group.²

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