ACI NSW Agency for Clinical Innovation

CLINICAL GUIDELINES

Vaccination Guidelines

Post Blood and Marrow Transplant

Blood and Marrow Transplant Network NSW

1. Introduction

These post blood and marrow transplant vaccination guidelines are derived from the *Australian Immunisation Handbook*[1]. This, in turn, is based on the *Vaccination of hematopoietic cell transplant recipients* (Ljungman *et al*, 2009[2]). The 2009 international guidelines represent joint recommendations from:

- European Group of Blood and Marrow Transplantation (EBMT)
- Centres for Disease Control and Prevention (CDC)
- Infectious Diseases Society of America (IDSA)
- American Society for Blood and Marrow Transplantation (ASBMT)

This schedule is an extract from the BMT Network's Post-Transplant Vaccination Guidelines v3 (TX-BMT-X4).

2. Application of guidelines

These ACI BMT Network guidelines are recommended for all allogeneic HPCT recipients. It is recognised internationally that there is currently insufficient data to definitively inform whether all autologous HPC recipients require the same extensive vaccination regimen as allogeneic HPCT recipients. Current international consensus recommends the same vaccination schedule for both allogeneic and autologous HPC recipients in the interim until further evidence is available.

References

1. Commonwealth of Australia (2015). *The Australian Immunisation Handbook* (10th ed.) Canberra

2. Ljungman, P., Cordonnier, C., Einsele, H., Englund, J., Machado, C. M., Storek, J., & Small, T. (2009). Vaccination of hematopoietic cell transplant recipients. *Bone marrow transplantation*, *44*, 521.

TABLE 1: Recommended vaccination schedule for HPCT recipients ≥ 10 years

Section A) Vaccinations during first 12 months post HPCT

Disease & vaccine preparations	Months post HPCT				Additional considerations
	6	7	8	12	
Influenza Per recommended annual seasonal formulation	●	●			2 doses at least 4 weeks apart required in first year. Annual single dose influenza vaccination after first year post HPCT.
***S. pneumoniae* (pneumococcal disease) – 13v PCV** 13-valent conjugate vaccine *e.g.* Prevenar13 ® IM	●		●	●	Requires further vaccination with 23-valent polysaccharide (23vPPV) vaccine at 24 months & beyond – see Section B
***Haemophilus influenzae* type b (Hib)** e.g. ACT-HIB ® IM Hiberix ® IM Liquid Pedvax HIB ® IM	●		●	●	The same brand of Hib vaccine should be used for all primary doses. If different Hib-containing vaccines (i.e. a mix of PRP-OMP & PRP-T vaccines) are used in the primary series, then give a HiB booster dose at 24 months post-transplant.
***Neisseria meningitis* (meningococcal disease)** **Quadrivalent meningococcal conjugate vaccine (4vMenCV)** e.g. Menactra ® IM, Menveo ® IM Nimenrix ® IM	●		●		Requires ongoing 5 yearly boosters for life - see Section B
Meningococcal B (MenBV) *e.g. Bexsero ® IM*	●		●		
Diphtheria, Tetanus & Pertussis* **dTpa** *e.g. Adacel ® IM, Boostrix ® IM*	●				dT is preferred for booster doses at 8 and 12 months.
dT *e.g. ADT Booster ® IM*			●	●	If dT unavailable, complete the vaccination course with dTpa.
Poliomyelitis* **Inactivated polio vaccine** e.g. IPOL (inactivated polio vaccine) SC	●		●	●	Please note IPOL® is given subcutaneously. ***Combination dTpa & polio vaccines can be used if desired:** *e.g. Adacel Polio ® IM* *Boostrix-IPV ® IM*
Hepatitis B **10 to < 20 yrs** *e.g. H-B-Vax II ® (dialysis formulation)* *H-B-Vax II ® (paediatric formulation)* *Engerix B ® (paediatric formulation)* **≥ 20 yrs** *e.g. H-B-Vax II ® (dialysis formulation)* *H-B-Vax II ® (adult formulation)* *Engerix B ® (adult formulation)*	●		●	●	High-dose formulation (H-B-Vax II dialysis formulation) preferred. Alternatives: ⇒ Give single strength Hep B vaccine in each arm at each dosing interval ⇒ Standard vaccination course Check Hep B serology 4-8 weeks after last dose. If HepB sAb <10 mIU/mL, seek further advice.

Section B) Vaccinations beyond 12 months post HPCT

Vaccine & preparations	Dose No.	Timing	Additional considerations
Human Papilloma Virus (4vHPV)[#]			
e.g. Gardasil ®	Dose 1:	At least 12 months post-transplant	Recommended age range for administration is 9-18 years old (optimal timing is between **11-13 years old.)** [#]Individual recommendations for HPV vaccination in those > 9 years of age should be determined by an individual risk assessment (see Section 4.6 'Human papillomavirus' of the *Australian Immunisation Handbook*).
	Dose 2:	2 months after last dose	
	Dose 3:	4 months after last dose	
Streptococcus pneumoniae (pneumococcal disease) – 23vPPV			
e.g. Pneumovax 23 ®	Dose 1:	24 months	If ongoing active immunosuppression for cGVHD, also requires prophylaxis with phenoxymethylpenicillin 250mg PO bd
	Dose 2:	5 years after last dose	
	Dose 3:	65 yo (non-indigenous) / 50 yo (indigenous) OR 5 years after last dose whichever is later	
***Neisseria meningitidis* (meningococcal disease) – 4vMenCV**			
e.g. Menactra ® IM Menveo ® IM Nimenrix ® IM	Indefinite	Booster every 5 years	Note: No booster dose is currently recommended for MenBV.
Influenza			
Following ecommended annual seasonal formulation	Indefinite	Annual vaccination	

Section B) Vaccinations beyond 12 months post HPCT

LIVE ATTENUATED VACCINES
Consider at 24 months post-transplant

Can only be given if

- **Off immunosuppression**
- **No Chronic Graft Versus Host Disease (cGvHD)**
- **Cell-mediated immunity has reconstituted**

Measles, Mumps & Rubella (MMR)			
e.g. M-M-R II ® Priorix ®	Dose 1:	≥ 24 months post-transplant	Check serology 4 weeks after first dose. **Repeat dose** if no seroconversion
Varicella zoster (VZV)			
e.g. Varilrix ® Varivax Refrigerated®	Dose 1:	Check serology prior to administration. If seropositive, no need for vaccination.	**DO NOT USE** Herpes zoster vaccine (e.g. Zostavax®) which contains 14x the amount of live attenuated virus
	Dose 2:	At least 4 weeks after dose 1	

IVIG and other transfusion products can interfere with immune response to live vaccines. Therefore a decent interval should be therefore allowed between administration of the two product types to optimise the response to vaccination. Recommended waiting intervals varies, e.g.

IVIg – dose dependent, ranges from 8-11 months

Blood, plasma, platelets – ranges from 3-7 months

Please refer to *Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and measles-mumps-rubella (MMR), measles-mumps-rubella-varicella (MMRV) or varicella vaccination* *The Australian Immunisation Handbook* or more detailed information on recommended intervals between the administration of live attenuated vaccines and transfusion products.

TABLE 1: Recommended vaccination schedule for HPCT recipients ≤ 10 years

Schedule A) Vaccinations during first 12 months post HPCT

Vaccine & preparations	Months post HPCT				Additional considerations
	6	7	8	12	
Influenza Per recommended annual seasonal formulation	●	●			2 doses at least 4 weeks apart required in first year. Annual single dose influenza vaccination after first year post HPCT.
Pneumococcal (13v PCV) 13-valent conjugate vaccine *e.g.* Prevenar13 ® IM	●		●	●	Requires further vaccination with 23-valent polysaccharide (23vPPV) vaccine at 24 months & beyond – see next section
Combination vaccine for immunisation against 6 vaccine preventable diseases: Diptheria Tetanus Pertussis Poliomyelitis *Haemophilus influenza* Hepatitis B *e.g.* Hexaxim ® Infanrix Hexa ® IM	●		●	●	**Hepatitis B:** Check Hep B serology 4-8 weeks after last dose. If HepB sAb <10 mIU/mL, seek further advice. **Hib:** The same brand of Hib-containing vaccine should be used for all primary doses. If different Hib-containing vaccines (i.e. a mix of PRP-OMP & PRP-T vaccines) are used in the primary series, then give a Hib booster dose at 24 months post-transplant.
Neisseria meningitis Quadrivalent meningococcal conjugate vaccine (4vMenCV) *e.g.* Menveo ® IM (only brand that should be used in infants <12m) Menactra ® IM Nimenrix ® IM	●	Total number of primary doses & intervals are age dependent - see Table 4.10.2 *The Australian Immunisation Handbook*			Different brands of 4vMenCV are not Interchangeable. However, for infants ≥ 12 months old, if the brand of vaccines for previous doses are not known then the use of another brand for the subsequent dose(s) is acceptable.
Meningococcal B vaccine (MenBV) *e.g.* Bexsero ® IM	●		●		If vaccination course commenced between the age of 6–11 months, a booster dose is required at either: ⇒ 8 weeks after last dose OR ⇒ 12 months of age, whichever is later.

Schedule B) Vaccinations beyond 12 months post HPCT

Vaccine & preparations	Dose No.	Timing	Additional considerations
Human Papilloma Virus (4vHPV)			
e.g. Gardasil ®	Dose 1:	At least 12 months post-transplant	Recommended age range for administration is 9-18 years old; optimal timing is between 11-13 years old.
	Dose 2:	2 months after last dose	
	Dose 3:	4 months after last dose	
Pneumococcal vaccination (23vPPV)			
e.g. Pneumovax 23 ®	Dose 1:	24 months	If ongoing active Immunosuppression for Chronic Graft Versus Host Disease (cGvHD), also requires prophylaxis with phenoxymethylpenicillin 250mg PO bd
	Dose 2:	5 years after last dose	
	Dose 3:	65yo (non-indigenous) / 50yo (indigenous) OR 5 years after last dose whichever is later	
Meningococcal vaccination (4vMenCV)			
e.g. Menactra ® IM *Menveo ® IM* *Nimenrix ® IM*	Indefinite	Booster every 5 years	Note: No booster dose is currently recommended for MenBV.
Influenza			
Per recommended annual seasonal formulation	Indefinite	Annual vaccination	

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Consider at 24 months post-transplant

Can only be given if

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- **Cell-mediated immunity has reconstituted**

Measles, Mumps & Rubella (MMR)			
e.g. M-M-R II ® *Priorix ®*	Dose 1:	≥ 24 months post-transplant	Check serology 4 weeks after first dose. Repeat dose if no seroconversion
Varicella zoster (VZV)			
e.g. Varilrix ® *Varivax Refridgerated®*	Dose 1: Dose 2:	Check serology prior to administration. If seropositive, no need for vaccination. At least 4 weeks after dose 1	**DO NOT USE** Herpes zoster vaccine (e.g. Zostavax®) which contains 14x the amount of live attenuated virus

IVIG and other transfusion products can interfere with immune response to live vaccines.
Therefore a decent interval should be therefore allowed between administration of the two product types to optimise the response to vaccination. Recommended waiting intervals varies, e.g.

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Please refer to *Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and measles-mumps-rubella (MMR), measles-mumps-rubella-varicella (MMRV) or varicella vaccination*

The Australian Immunisation Handbook for more detailed information on recommended intervals between the administration of live attenuated vaccines and transfusion products.