Superior Health Council

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Vaccination of immunocompromised or chronically ill children and/or adults

In this scientific advisory report, which offers guidance to public health policy-makers, the Superior Health Council of Belgium provides recommendations on vaccination of immunocompromised individuals.

This report aims at providing clinicians of all specialities as well as the general practitioner with specific recommendations on vaccination of immunocompromised individuals.

This version was validated by the Board on
September 2019[1]

SUMMARY

Some medical conditions and immunosuppression increase the risk of acquiring certain infections or increase the risk of a complicated course of the disease. For these at-risk groups, standard vaccinations should be up to date in accordance with national recommendations, bearing in mind that live attenuated vaccines can be contra-indicated.
Additional vaccines or additional doses of vaccines are often required to offer the best possible protection.

This report aims to guide clinicians of all specialities as well as the general practitioner to plan the optimal vaccines, timing and the optimal schedule in order to acquire the best vaccine response and best protection for the patient.

This report includes recommendations on vaccinations in different situations: immunosuppressive treatment, underlying chronical diseases, close contacts of the patients and prenatal exposure to immunosuppression.

This fact sheet complements the Superior Health Council (SHC) vaccination guide and the additional SHC recommendations on specific vaccinations (https://www.health.belgium.be/nl/vaccinatie).

Therefore, also consult the vaccination guide and vaccination factsheets for the **standard recommendations** and contraindications for specific vaccines.
This text and the tables will be **reviewed** on a regular basis in order to keep them up to date with the latest findings, data and the consensus amongst international experts.

[1] The Council reserves the right to make minor typographical amendments to this document at any time. On the other hand, amendments that alter its content are automatically included in an erratum. In this case, a new version of the advisory report is issued.

CONTENTS

ABBREVIATIONS

A	Strongly Advised, given the additional risk posed by increased susceptibility and/or increased severity, and/or increase risk from complications
BCG	Bacille Calmette Guerin vaccine
cART	Combined antiretroviral therapy
CDC	Centers for Disease Control and Prevention, USA
CI	Contra-Indicated
DMARD	Disease Modifying Antirheumatic Drugs
DTPa	Vaccine against diphtheria, tetanus, and (acellular) pertussis,high dosage
dTpa	Vaccine against diphtheria, tetanus, and (acellular) pertussis,low dosage
GVHD	Graft Versus Host Disease
HSIL	High grade squamous intraepithelial lesion
Hib	Haemophilus influenzae b
HIV	Human Immunodeficiency Virus
HRIG	Human Rabies Immunoglobulins
HSCT	Hematopoietic Stem Cell Transplantation
HPV	Human Papilloma Virus
HSIL	High Grade Squamous Intraepithelial Lesion
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IIV	Inactivated influenza vaccine
IMD	Invasive Meningococcal Disease
IMID	Immune Mediated Inflammatory Diseases
ISD	Immunosuppressive drugs
IPV	Inactivated Polio Vaccine
ITMA	Institute Of Tropical Medicine Antwerp
IVDU	Intravenous Drug User
LAIV	Live-attenuated influenza vaccine
MMR	Measles, Mumps and Rubella
MS	Multiple Sclerosis
MSM	Men having Sex with Men
NA	Not applicable
Nab	Neutralizing antibodies
PCV	Pneumococcal Conjugated Vaccine
PCV13	13-valent Pneumococcal Conjugated Vaccine
PCV10	10-valent Pneumococcal Conjugated Vaccine
PEP	Post exposure prophylaxis
PID	Primary Immunodeficiency
PPV23	(Unconjugated) 23-valent Pneumococcal Polysaccharide Vaccine
PrEP	Pre exposure prophylaxis
R	To consider in case of epidemiological or personal Risk
RR	Relative risk

S	Standard indication for vaccination because this concerns routine vaccinations that are part of the basic vaccination schedule that holds for the general population
SHC	Superior Health Council
SOT	Solid Organ Transplantation
TBE	Tick Borne Encephalitis
VFR	Visiting friends and Relative
WHO	World Health Organisation

1. INTRODUCTION

Some medical conditions and immunosuppression increase the risk of acquiring certain infections or increase the risk of a complicated course of the disease. For these at-risk groups, standard vaccinations should be up to date in accordance with national recommendations, bearing in mind that live attenuated vaccines can be contra-indicated. Additional vaccines or additional doses of vaccines are often required to offer the best possible protection.

This guideline aims to guide clinicians of all specialities as well as general practitioners to plan the optimal vaccines, timing and the optimal schedule in order to acquire the best vaccine response and best protection for the patient.

This report includes recommendations on vaccinations in different situations: immunosuppressive treatment, underlying chronic diseases, close contacts of the immune deficient patients and prenatal exposure to immunosuppression.

1.1. Immunosuppression

Untreated chronic **inflammatory (auto) immune disorders**, also known as *Immune Mediated Inflammatory Diseases* **(IMID)** are usually not or not significantly immunosuppressive by themselves (except active lupus).
Immunosuppression caused by **immunosuppressive medications** can vary greatly depending on the type or combination of medications, dosage and total duration of treatment.

1.2. Vaccine safety and efficacy in immunosuppression

In general, **in patients with chronic diseases or inflammatory (auto) immune disorders who are not treated by immunosuppressive medication**, there are no contraindications for vaccination with the **inactivated nor live vaccines**. The same standard vaccines are recommended as for the general population. For recommendations: see the vaccination factsheets of the Superior Health Council (https://www.health.belgium.be/nl/vaccinatie).

In patients with a severe immune deficiency syndrome (due to primary immune deficiency or immunosuppressive medication):

- The administration of **inactivated vaccines** is safe, but immune response can be suboptimal (decreased immunogenicity and/or of shorter duration and/or taking longer to reach correlate of protection thresholds). It is therefore likely that the immune response after a first dose is not very good in patients and sometime extra doses are recommended. The immune response is probably less altered after a vaccine booster if the first dose was administered before the onset of immunosuppression.
- Administering **live vaccines is usually contra-indicated** as it can result in a replication and/or invasive infection with the vaccine micro-organism, persistence of the micro-organism in the patient and/or unwanted transmission.

The vaccinations themselves do not destabilise or exacerbate the **inflammatory (auto-) immune disorder**, nor are they responsible for causing inflammatory (auto-)immune disorders. If possible, it is advisable to wait until the disorder has reached a stable stage. If this is not possible and the vaccine is necessary, it can be administered in case of moderate or severe disease activity (on the basis of an individual assessment and after having consulted the treating specialist).

1.3. Serological monitoring

In general, there is no consensus concerning the use of serological titres to monitor the immunological status of immunocompromised patients. There are some recommendations in certain indications, see below. In the following table the correlates of protection are highlighted. Usefulness of monitoring of antibody titres against vaccine preventable diseases is debated. Nevertheless, they are mentioned in the table below if advised for certain patient groups or 'for information purpose'.

Table 1: Correlates of protection

Vaccination	Correlate of protection				Minimal timing after vaccination to measure correlate of protection	Remarks Reference centre
	Unit	No protection	Short-term protection	Long-term protection		
Tetanus	IU/L	< 100	100-999	> 1000	4 weeks	
Diphtheria	IU/L	< 100	100-999	> 1000	4 weeks	
Measles	IU/L	< 250	NA	> 500	4 weeks	
Rubella	IU/ml	< 10	NA	>20	4 weeks	
H. influenza type b	mg/L	< 0.15	0.15-0.99	> 1	4 weeks	
Hepatitis A	IU/L	< 20	NA	> 20	4 weeks	
Hepatitis B	IU/L	< 10	10-99	> 100	4 weeks	
S. pneumoniae	mg/L	< 0.3	0.3-0.9	> 1	4-6 weeks	
TBE Nab	IU/L	< 7	NA	> 10	4 weeks	ITMA (not reimbursed)
Rabies Nab	IU/mL	< 0.5	> 0.5	> 3.0	14 days	Sciensano (reimbursed for cat III lesion + HRIG)
Varicella	IU/L	< 50	50-200	> 200	4 weeks	
Yellow fever Nab	IU/L	< 10	NA	> 10	4 weeks	ITMA (reimbursed for Immunocompromised patients)

Adapted from Epéron G, Bühler S, Enriquez N, Vaudaux B. Voyageur immunosupprimé : recommendations vaccinales. Rev Méd Suisse 2018; 922-33.
TBE Tick Borne Encephalitis; Nab neutralizing antibodies; ITMA Institute of Tropical Medicine, Antwerp

Monitoring the antibody synthesis is currently recommended only for a limited number of vaccines:

a. Hepatitis B:
   - A control of serological antibodies once is systematically recommended for all immunocompromised patients following hepatitis B vaccinations (4 to 8 weeks after the last hepatitis B injection).
   - A systematic yearly control of antibodies is especially recommended in patients with a liver transplant and in patients with renal dialysis.
   - In immunocompetent people a serotiter above 10 IU/mL is enough for lifelong boostability. In contrast, in immune suppressed patients, it is preferable to achieve anti-HBs levels above 100 IU/ml, although levels of 10 IU/ml or more are generally accepted as enough to protect against infection. Serotiters above 100 IU/mL could be considered as long-lasting protection in immunosuppressed subjects, with a slower decrease of antibodies over time. Notably, in

immunosuppressed patients serotiters of 10 IU/mL could decrease fast over some months.
- When antibodies declined to or are lower than < 10 IU/mL a booster injection is strictly indicated in most immunocompromised patients. In HIV patients under cART a serotiter above 10 IU/mL once is considered boostable for lifelong.
- When antibody titers are between 10 and 100 IU/mL specialists have to decide for their individual immunosuppressed patient if a booster vaccination is indicated or not.
- In patients under renal dialysis an antibody titer of 100 IU/mL or more is recommended.

b. Rabies:
   - After post-exposure rabies vaccinations for category III lesions, the neutralizing antibody response is routinely evaluated in immunocompromised subjects, who received 5 intramuscular rabies vaccines with immunoglobulins (schedule 3), 10 to 14 days after the last vaccine dose). https://www.itg.be/Files/docs/Reisgeneeskunde/PEP_Rabies_ENG.pdf
   - We aim rabies neutralizing antibodies above 5.0 IU/mL if the patient is immunocompromised.

c. Yellow Fever:
   In people with a possibly impaired immune response a booster vaccination or testing of neutralising antibodies is recommended after 10 years:
   - Due to HIV (irrespective of the CD4 count): booster/testing is recommended (waiting for more data).
   - Due to medication that supresses the immune system (high dose of cortisone, certain treatments for autoimmune diseases): testing of neutralising antibodies is recommended.
   - Persons who received a vaccination against yellow fever before they had a bone marrow transplantation: revaccination is indicated, if no contra-indications.
   - The neutralizing antibody response to the yellow fever vaccine in immune compromised subjects can be measured at least 28 days after vaccination. This can be useful before travel to endemic regions. https://www.itg.be/E/Article/yellow-fever-vaccination

1.4. Practical considerations

Think of vaccinating patients with chronic medical conditions, those taking immunosuppressive treatments, or those who might require immunosuppressive treatment in the future even if at that time the patient is (not yet) immunocompromised.
For many (inactivated and live-attenuated) vaccines, the immunological response is better before immunosuppression. Notably vaccination with live-attenuated vaccines needs to be considered PRIOR to immunosuppression, because these vaccines are contra-indicated in immunocompromised patients. This includes patients who:

- will undergo a solid organ **transplantation;**
- **might be** treated with **immunosuppressive medication**;
- **are to** undergo an **elective splenectomy.**

Patients with chronic medical conditions also require extra vaccines. In these patients:

- check and update the standard vaccination schedule (in accordance with the national recommendations (https://www.health.belgium.be/nl/vaccinatie), bearing in mind the contra-indications for live attenuated vaccines in some cases;
- offer **additional disease-specific vaccinations**, when indicated;
- preferably and if feasible also administer inactivated vaccines (e.g. HPV vaccine) before onset of immunosuppression, as immune response might be blunted during immunosuppression;
- ask the patient with insistence about possible future travel wishes;
- respect a 4-week waiting period between administering **live vaccines** (including MMR, varicella and yellow fever) and initiating immunosuppressive medication. Inactivated vaccines are preferably administered at least two weeks before initiating immunosuppressive medication;
- in general, it is recommended for immunocompromised patients to plan a Travel consultation at least four months prior to travel, especially to a yellow fever endemic region**.**

The vaccination status of the chronically ill and immunocompromised patient has to be checked at least once a year. Once again, the general practitioner and the specialist in charge of the patient should communicate to state who will in charge of checking vaccination status every year.
Furthermore, think of vaccinating patients' close contacts as soon as there is confirmation that the patient must start immunosuppressive treatment (see chapter 7).
All treating specialists should provide the treating general practitioner or general paediatrician with clear information on the precise vaccination programme of the immunocompromised or chronically ill individual and his/her close contacts. Some yellow fever centres have programmed specific pretravel consultations for these vulnerable travellers.
Please check with the respective yellow fever centres. https://www.itg.be/Files/docs/Reisgeneeskunde/eADRVACC.pdf

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2. VACCINATING IMMUNOCOMPROMISED INDIVIDUALS

2.1. Children < 16 years

VACCINES	DISORDERS								
	IMID on ISD	PRIOR to SOT	AFTER SOT	Oncology	PRIOR to HSCT	AFTER HSCT	HIV CD4 < 15%	HIV CD4 ≥ 15%	Severe PID
INACTIVATED VACCINES									
DTPa dTpa	S	S	S	S	S	A DTPa only	S	S	S
IPV	S	S	S	S	S	A	S	S	S
Haemophilus influenzae b	S	S	S	S	S	A	S	S	S
Hepatitis A	R	A**	R	R	R	R	R	R	R
Hepatitis B	S	S	S	S	S	A	S	S	S
Influenza	A	A	A	A	A	A	A	A	A
Pneumococcal PCV13	S	S	S	S	S	A	S	S	S
Pneumococcal PPV23	A	A	A	A	A	A	A	A	A
Meningococcal ACWY (conjugate)	S	S	S	S	S	A	S	S	S
Men B	A	A	A	A	A	A	R	R	A
HPV	S	S	S	S	S	A	S	S	S

LEGEND:

S	**Standard** indication for vaccination because this concerns routine vaccinations that are part of the basic vaccination schedule that holds for the general population.
A	**Strongly Advised**, given the additional risk posed by increased susceptibility and/or increased severity, and/or increased risk from complications
R	To consider in case of **epidemiological or personal Risk**
CI	**Contra-Indicated**
NA	**Not Applicable**
*	> 24 months post HSCT in absence of immunosuppressive therapy and/or GVHD
**	Only in chronic liver disease
***	not available yet in Belgium (because available elsewhere)
#	after consultation with a specialist (in case of epidemiological or personal risk)

2.1. Children < 16 years

VACCINES	DISORDERS								
	IMID on ISD	PRIOR to SOT	AFTER SOT	Oncology	PRIOR to HSCT	AFTER HSCT	HIV CD4 < 15%	HIV CD4 ≥ 15%	Severe PID
Zoster (inactivated)* **	NA	NA	NA	NA	NA	NA	NA	NA	NA
LIVE VACCINES									
MMR	CI#	A	CI#	CI#	CI#	A*	CI#	S	CI
Rotavirus	NA	NA	NA	NA	NA	NA	NA	NA	NA
Varicella	CI#	A	CI#	CI#	CI#	A*	CI#	A	CI
Zoster	NA	NA	NA	NA	NA	NA	NA	NA	NA
INACTIVATED TRAVEL VACCINES									
Rabies	R	R	R	R	R	R	R	R	R
Japanese encephalitis	R	R	R	R	R	R	R	R	R
Typhoid fever-inactivated	R	R	R	R	R	R	R	R	R
TBE	R	R	R	R	R	R	R	R	R
Cholera	NA	NA	NA	NA	NA	NA	NA	NA	NA
LIVE TRAVEL VACCINES									
Yellow fever	CI#	R	CI	CI	CI	R*#	CI	R	CI
Typhoid fever - oral	CI	R	CI	CI	CI	CI*	CI	R	CI
BCG	CI#	R	CI	CI	CI	R*#	CI	CI	CI

LEGEND:

S	**Standard** indication for vaccination because this concerns routine vaccinations that are part of the basic vaccination schedule that holds for the general population.
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**	Only in chronic liver disease
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#	after consultation with a specialist (in case of epidemiological or personal risk)

2.2.0. General observations / recommendations for children < 16 years	
INACTIVATED VACCINES	
Tetanos-Diphtheria-Pertussis	• After HSCT, all patients should receive the hexavalent vaccine including DTPa according to the classical schedule (instead of the dTpa vaccine), regardless of their age, because DTPa provides a better immunological response than the dTpa vaccine against diphteria.
Hepatitis A	• For the at-risk groups, see the recommendations of the SHC on vaccinating against hepatitis A in the SHC vaccination guide (https://www.health.belgium.be/nl/vaccinatie) • In immunocompromised patients, at least 2 doses of hepatitis A vaccine (monovalent) should be given before departure (2 doses with 4 weeks in between). If there is little time, a double dose at D0 can be considered. The third dose needs to be scheduled after at least 6 months. • Once-only antibody testing can be indicated if travelling abroad. However, no recommendations can be made for non-responders.
Hepatitis B	• Since 1999, all infants, children and teenagers in Belgium have been systematically vaccinated. Hepatitis B vaccination is therefore a standard indication. • A control of serological antibodies once is systematically recommended for all immunocompromised patients following hepatitis B vaccinations (4 to 8 weeks after the last hepatitis B injection). • A systematic yearly control of antibodies is especially recommended in patients with a liver transplant and in patients with renal dialysis. • In immune suppressed patients, we aim to achieve titers above 100 IU/mL. Serotiters above 100 IU/mL could be considered as long-lasting protection in these immune suppressed patients. - When antibodies declined to or are lower than < 10 IU/mL a booster injection is strictly indicated in most immunocompromised patients. In HIV patients under cART a serotiter above 10 IU/mL once is considered boostable for lifelong. - When antibody titers are between 10 and 100 IU/mL specialists have to decide for their individual immunosuppressed patient if a booster vaccination is indicated or not. - Depending on the immune response, the antibodies need to be monitored on an annual basis. The antibody titre has to be kept > 100 IU/L by means of additional boosters in patients under renal dialysis.
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Influenza vaccine	• Vaccination schedule for children: see the recommendations of the SHC on the vaccination against seasonal influenza and the SHC vaccination guide (https://www.health.belgium.be/nl/vaccinatie). • The vaccination should be repeated each year annually in October/November. • For children younger than 9 years old who are vaccinated for the first time, a second dose 4 weeks later is recommended.

	• Two doses (with 1 month interval) may generate a better response in immunocompromised children, but confirmatory data is still lacking. • For most individuals with immune problems, there are no data available that show that there is a specific increase in mortality or an increased risk of complications as a result of influenza infections. However, according to the CDC, influenza does constitute a risk factor for secondary bacterial infections in immunocompromised individuals, which can result in severe disease. In some patients, the clearance of the influenza virus is disturbed, with sustained virus replication and possibly also longer disease duration and longer shedding as a consequence.
Pneumococcal	• See the recommendations of the SHC on pneumococcal vaccination and the SHC vaccination guide (https://www.health.belgium.be/nl/vaccinatie).
Meningococcal C (conjugate)	• See the recommendations of the SHC on meningococcal vaccination (https://www.health.belgium.be/nl/vaccinatie).
Meningococcal ACWY	• Use conjugated vaccine. • See the recommendations of the SHC on meningococcal vaccination and the SHC vaccination guide (https://www.health.belgium.be/nl/vaccinatie).
Meningococcal B	• See the recommendations of the SHC on meningococcal vaccination (https://www.health.belgium.be/nl/vaccinatie).
HPV	• See the recommendations of the SHC on vaccination against HPV (https://www.health.belgium.be/nl/vaccinatie).
LIVE VACCINES	
MMR	• Consider vaccination PRIOR to immunosuppression. These two doses of live attenuated vaccines should be administered at least 4 weeks before initiating an immunosuppressive treatment. • When necessary and when there are no contraindications, an accelerated schedule can be applied for MMR: – The MMR-vaccine should be administered from the age of 6 months in children; this early administration provides temporary immunization and needs to be followed by the recommended schedule (2 doses after 12 months of age). – The second doses MMR can already be administered after 4 weeks. – Both MMR and Varicella live vaccines can be administered simultaneously in different arms or with at least a 4 weeks interval between each other.
Rotavirus	• Should never be administered after the age of 6 months, and is contra indicated in immunosuppressed patients.

Varicella	• Consider vaccination PRIOR to immunosuppression. These two doses of (live attenuated) vaccines should be administered at least 4 weeks before initiating an immunosuppressive treatment. • When necessary and when there are no contraindications, an accelerated schedule can be applied for varicella: – The varicella-vaccine can be administered from the age of 9 months; this early administration provides temporary immunization and needs to be followed by the recommended schedule (2 doses after 12 months of age). – The second doses for varicella can already be administered after 4 to 6 weeks. – Both MMR and Varicella live vaccines can be administered simultaneously in different arms or with at least a 4 weeks interval between each other.
INACTIVATED TRAVEL VACCINES	
Rabies	• Rabies PrEP for immunocompromised patients consists of a three-visit schedule (Day 0, 7, 28). When exposed in endemic regions, it is strictly indicated to vaccinate immunocompromised patients against rabies before the risk (with a lower threshold than immunocompetent patient). Immune responses in these patients following booster doses (after the risk) are expected to be much better after previous priming than without priming. For further information see: https://www.itg.be/Files/docs/Reisgeneeskunde/PEP_Rabies_ENG.pdf • Immunocompromised patients should receive a rabies PEP schedule 3 (standard 5 vaccine dose regimen (Day 0, 3, 7, 14, 28) with immunoglobulins on day 0) - regardless of whether they have already been PrEP vaccinated - following a Category II or III risk (following the BE recommendation).
Japanese encephalitis	• Two doses over 28 days does give a sufficient protection in immunocompetent children. There are no data for immunosuppressed travellers. https://www.itg.be/Files/docs/Reisgeneeskunde/ejapenc.pdf
Typhoid fever	• In general, the use of the inactivated vaccine is recommended. The oral live attenuated vaccine is contraindicated in immunocompromised patients.
Tick-borne encephalitis	• In case of immunosuppression due to the use of DMARD and biologicals, the antibody response can be lower. Sometimes an extra priming third dose can be offered (limited data, see SHC recommendation on TBE vaccination). https://www.health.belgium.be/nl/advies-9435-tbe •
Cholera	• NA

LIVE TRAVEL VACCINES	
Yellow fever	• Consider vaccination PRIOR to immunosuppression, when traveling to yellow fever endemic regions in the future is not excluded. This avoids limiting the possible travel destinations in the future. In case of immunosuppression due to the use of ISD, interruption of the immunosuppressive medication can be discussed with the treating physician in some cases, in order to perform vaccination. Delays of interruption before and after vaccination have to be discussed with a specialist. For further information see: https://www.itg.be/E/Article/yellow-fever-vaccination • In children, it is recommended to wait at least 4 weeks between MMR vaccination and yellow fever vaccination. If this is not possible, it can be administered at the same moment, at two different sites.

2.2.1. Immune-mediated inflammatory diseases (IMID) & immunosuppressive drugs (ISD)

BEFORE INITIATING MEDICATION

- Determine the **vaccination status** of individuals (including the **hepatitis B** antibody titre) who might require immunosuppressive medication **BEFORE** initiating immunosuppressive treatment, and ensure that the basic vaccination schedule has been completed.
- If necessary, an accelerated schedule for **varicella** and for **MMR** may be used (see footnote: **2.2.0**).
- Strongly consider vaccinating against **yellow fever PRIOR** to initiating immunosuppressive medications, particularly if there is the likelihood that the patient travels to a yellow fever endemic region in the future.
- Strongly consider vaccinating against **HPV PRIOR** to initiating the immunosuppressive medication.
- Recommend vaccinating close contacts to the patient (see chapter 7).

LIVE VACCINES	
MMR	• Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • See **chapter 5** for a list of medications for which there is an absolute contraindication, or no contraindication at all to give these vaccines. When in doubt, consult a specialist. Also see **chapter 5** for the waiting periods that have to be observed (1) before administering the vaccine after having discontinued immunosuppressive medication and (2) before reinitiating immunosuppressive medication after vaccine administration.
Rotavirus	• Usually not applicable: should not be given after the age of 6 months.
Varicella	• Administering this vaccine is contraindicated for patients taking immunosuppressive medication.

	• See **chapter 5** for a list of medications for which there is an absolute contraindication, or no contraindication at all to give these vaccines. When in doubt, consult a specialist. Also see **chapter 5** for the waiting periods that have to be observed (1) before administering the vaccine after having discontinued immunosuppressive medication and (2) before reinitiating immunosuppressive medication after vaccine administration.
LIVE TRAVEL VACCINES	
Yellow fever	• Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • See **chapter 5** for a list of medications for which there is an absolute contraindication, or no contraindication at all to give this vaccine. When in doubt, consult a specialised "Travel clinic". Also see **chapter 5** for the waiting periods that have to be observed (1) before administering the vaccine after having discontinued immunosuppressive medication and (2) before reinitiating immunosuppressive medication after vaccine administration.
Typhoid fever Oral	• Do not use in patients with inflammatory bowel diseases. • Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • To be replaced by the inactivated typhoid fever vaccine.

2.2.2. Solid organ transplantation (SOT): Heart, liver, kidney, pancreas, lung, intestine

PRIOR TO SOT

- Remember to re-evaluate and, if required, complete the basic vaccination schedule PRIOR to transplantation. Serology can be checked for hepatitis A, hepatitis B, varicella zoster virus, measles-mumps-rubella. The vaccination history should be checked. Repeat booster vaccination must be administered at the same intervals as recommended for immunocompetent persons.
- Remember to complete the **basic vaccination schedule** PRIOR to transplantation. The **hepatitis B** vaccination should always be carried out prior to organ transplantation (also determine the antibody titre). It is also advisable to vaccinate against **hepatitis A** before a liver transplantation.
- Patients who have not yet contracted **varicella** should receive two varicella-vaccines with a minimal interval of 4 weeks, provided there is enough time (i.e. eight weeks prior to transplantation). If necessary, an accelerated schedule for **varicella** (and, if need be, for **MMR**) may be used (See footnote **2.2.0**).
- Timing of vaccination: Aim for vaccination prior to transplantation, at least 2 weeks before start of immunosuppressive medication for inactivated vaccines and at least 4 weeks before start of immunosuppressive medication for live-attenuated vaccines. In case of an urgent transplantation or in case of an incomplete vaccination schedule diagnosed after transplantation, additional inactivated vaccines can be administered from 6 months after transplantation, taking into account the current level of immunosuppression and the expected duration of intense immunosuppression in the following weeks.
- Strongly consider vaccinating against yellow fever PRIOR (> 4 weeks) to transplantation particularly if there is the likelihood that the patient travels to a yellow fever endemic region in the future.
- Recommend vaccinating people close contacts to the patient (see chapter 7).

AFTER SOT • Depending on the recovery of cellular immunity, it is advised to wait for **6 to 12 months** after the transplantation before administering **inactivated vaccines**. • **Live vaccines** (against MMR, varicella, yellow fever) cannot be administered because of the obligatory mandatory continuous immunosuppression; only in extremely rare cases where the immunosuppressive medication can be discontinued after all, vaccination can be considered **as from 12 to 24 months** after the transplantation, depending on the degree of cellular immunosuppression (to be determined by a specialist).Yet there are a few studies in which live vaccines against MMR and varicella were administered to small numbers of paediatric patients after liver transplantation on immunosuppressive medication.	
INACTIVATED VACCINES	
Hepatitis B	• Hepatitis B vaccination should always be completed prior to organ transplantation (see footnote **2.2.0**).
LIVE VACCINES	
Rotavirus	• Usually not applicable: should not be given after the age of 6 months
Varicella	• In children who are treated with a low level of immunosuppression for a long period of time, varicella vaccination can be considered post-liver transplantation (to be discussed with a PID specialist). • In case of exposure of a naïve transplant patient to patient with varicella (with rash), administration of immunoglobulins is recommended, either polyclonal immunoglobulins (with confirmed high level of varicella IgG titers) or specific immunoglobulins. Specific immunoglobulins are currently not available in Belgium and are very expensive for the patient. In naïve exposed patient preventive treatment with (val-)acyclovir is given for 7 to 14 days.
LIVE TRAVEL VACCINES	
Yellow fever	• No vaccination as long as the state of immunosuppression persists after the transplantation (wait for at least three months after ending immunosuppressive therapy; yet it is usually impossible to discontinue the latter).

2.2.3. Haematological malignancies after receiving chemotherapy	
• For children **who are receiving chemotherapy, the basic vaccination schedules initiated prior to the disorder should be continued without extra booster** • Children who had **already received the full basic schedule** before the onset of the disease should **receive booster doses of all vaccines** (Haemophilus, MMR, Tetanus, Diphtheria, Polio, Hepatitis B, Meningocoque ACWY, Bordetella pertussis, and Pneumococcus).This vaccination needs to be planned 3 and 6 months after finalization of chemotherapy for inactive and live attenuated vaccines respectively. Antibodies can be checked against MMR and Hepatitis B. • **Inactivated vaccines** can be administered as of **3 months** after the end of chemotherapy. • **Live vaccines** can only be administered as of **6 months** after the end of chemotherapy. • After **extensive radiotherapy** (consult a specialist), there should be a **3-month waiting period** before administering **live vaccines**.	
LIVE VACCINES	
Rotavirus	There are no data available to date on the safety and efficacy of the vaccine in infants under the age of 6 months suffering from leukaemia, lymphoma or other oncological conditions.

2.2.4. Hematopoietic stem cell transplantation (HSCT)

PRIOR TO HSCT

- T cell memory of the patient is usually lost after HSCT. However, circulating antibodies will persist for several weeks to months post-transplant and will protect the patient during this very vulnerable early post-transplant period.
- Remember to complete the **basic vaccination schedule** PRIOR to the transplantation.
- **Vaccinating against hepatitis B** should always be done prior to transplantation (antibody titre should be > 100 IU).
- **A hepatitis B naïve patient receiving a graft from a hepatitis B positive donor (shown by hepatitis B surface antigen (HbsAg) positivity), should be vaccinated before transplantation.** Ideally, the two initial doses should be given prior to induction chemotherapy, as the response to vaccination is poor in patients immediately after therapy. A third dose should be given six months later, ideally also prior to transplantation, but only if it's safe to postpone it. Antibody titers should be measured 4-8 weeks after the last dose.
- **Influenza:** A recent Cochrane meta-analysis concluded that although the evidence is weak, it is in favour of vaccinating all patients with cancer, as well as their caregivers. As for allogeneic stem cell transplant recipients, a randomized controlled trial comparing no vaccination, recipient vaccination and donor vaccination pretransplant showed significantly improved antibody titers to H1 and H3 Ags if the patient was vaccinated pretransplant. The immunity however does wane over time. The authors concluded that in order to maintain the immune response, patients should receive a booster early after transplant (3 months) –see below. Of course, other measures should be taken to minimize the risk of influenza infection in transplant patients, by avoiding contact with possibly infected people and by vaccinating close contacts.
- **Recommend** vaccinating close contacts with the influenza, varicella, measles, mumps and rubella vaccines.
- The role of donor-vaccination is controversial because of ethical reasons. However, the benefit of donor vaccination has been shown and could/should be advised, especially in family donors, but of course never made compulsory. There is some evidence for a better immunity post-transplant in the recipient if the donor has been boosted with tetanus toxoid, pneumococcal vaccine (conjugated) and Hib before collection. If the recipient is both hepatitis B core antibody (HbcAb) and hepatitis B surface antibody (HbsAb) positive, vaccinating the donor will reduce the risk of reverse seroconversion. A recent study showed that the best hepatitis B control post-transplant in HBV-infected HSCT recipients was seen in donors who were vaccinated: the authors recommend to vaccinate the donor of a HBV-positive recipient or to apply a single booster immunization in pre-vaccinated donors.
- Influenza vaccination for donors: a randomized controlled trial comparing no vaccination, recipient vaccination and donor vaccination pretransplant showed no significant effect of donor pretransplant vaccination.

AFTER HSCT

- The same rules apply to **autologous**, and to **allogenic** HSCT.
- The full basic vaccination schedule has to be reinitiated with the **inactivated vaccines**, starting **3 to 12 months** after the transplantation, depending on the degree of cellular immunosuppression. Because of the risk of serious infections following HSCT, influenza and pneumococcal vaccinations should be initiated within the 3-6 months following HSCT. However, for vaccines against tetanus, diphteria, pertussis, HBV, and HPV, vaccination can be done at 6-12 months following HSCT, in order to obtain better immunological responses.
- Yearly influenza vaccination is recommended until complete immune recovery.

• **Live vaccines** (against MMR, varicella, yellow fever) **can only be administered in patients >24 months post HSCT who have discontinued all** immunosuppressive medication for at least 2 months, have a CD4 count > 200/ml and do not show any symptoms or signs of GVHD.	
INACTIVATED VACCINES	
DTPa - IPV - Hib - Hep B	**The hexavalent paediatric vaccine** should be used, even though it contains a higher dosage of **DTPa components**, because the immune system is once again "naïve", as is the case in children.
LIVE VACCINES	
Rotavirus	Usually not applicable: should not be given after the age of 6 months.

2.2.5. HIV

HIV infection in young children occurs almost exclusively through perinatal transmission: infants born to an HIV-infected mother should therefore be actively monitored from birth, and antiretroviral therapy should be initiated as soon as the diagnosis of HIV infection is established.
The basic vaccination schedule should be implemented before the onset of any significant immunodeficiency.
When assessing the efficacy of the vaccines that have already been administered and those that still have to be, the following factors need to be considered: age, degree of immunodeficiency, antiretroviral treatment, duration of treatment and immunological recovery in response to this treatment.

Severe immunosuppression is defined by CD4 cells <15% or:
<750/mm³ in children <1 year
<500/mm³ in children 1-5 years
<200/mm³ in children >5 years

* For attenuated live vaccines
(in addition to restrictions for general population):
• **Varicella, MMR (measles, mumps, rubella), yellow fever, oral polio vaccine and rotavirus**: contraindicated in case of severe immunosuppression.
• BCG: contraindicated in all HIV-infected children

Also see adult chapter on HIV.

INACTIVATED VACCINES	
Hepatitis A	• For the at-risk groups, see the recommendations of the SHC on vaccinating against hepatitis A in the SHC vaccination guide. (https://www.health.belgium.be/nl/vaccinatie). • Children of immigrants travelling to their country of origin form a substantial portion of these HIV-infected children and therefore qualify for vaccination. • Once-only antibody testing can be indicated if travelling abroad. Additional boosters have no proven efficacy in non-responders in the case of HIV-infection.

Hepatitis B	• Antibody monitoring once and non-responders: see footnote 2.2.0.
Influenza	• Inactivated influenza vaccine should be suggested annually to all HIV-infected children. (https://www.health.belgium.be/nl/vaccinatie). • LAIV has been proved to be superior to IIV but is no more available in Belgium.
Pneumococcal PCV13	• 2 doses of PCV13 (with at least 8-week interval) should be offered to all age groups if not previously immunized. • See the recommendations of the SHC on pneumococcal vaccination and the SHC vaccination guide (https://www.health.belgium.be/nl/vaccinatie).
Men ACWY (conjugated)	• See recommended schedule on https://www.health.belgium.be/fr/avis-9485-vaccination-contre-le-meningocoque
Men B	• See recommended schedule on https://www.health.belgium.be/fr/avis-9485-vaccination-contre-le-meningocoque
HPV	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie) • In immunocompromised children, always administer a three doses schedule whatever the age. • Indicated for teenage girls and boys and young women and men (aged 14 to 26). • Prevalence of HPV infections and progression of HPV infection to cancer are strongly increased in HIV-infected persons.
LIVE VACCINES	
MMR	• MMR vaccines should be administered to children 12 months or older who are stable clinically and who have low level of immunosuppression. Retesting for measles antibodies should be done on a regular basis (every 5 years) and seronegative patients should be revaccinated.
Rotavirus	• Vaccination is safe for HIV-positive infants under the age of 6 months: the immune response is efficient and there is no worsening of the HIV infection or immunosuppression.
Varicella	• MMR-V vaccine has not been studied in HIV-infected children and should not be substituted for single-antigen varicella vaccine. For varicella vaccine: eligible children aged more than 1 year should receive 2 doses at 8 weeks interval.
INACTIVATED TRAVEL VACCINES	

Rabies	• Studies are lacking in HIV-infected patients. Normal immune responses are expected in cART treated HIV patients.
	• Rabies pre-exposure prophylaxis.
	  ○ When patients with minor or moderate immunosuppression (treated with cART, VL < 20 copies/ml and CD4 > 350/mm3): consider a 2-visit schedule: day 0 – day 7.
	  ○ When major immunosuppression (not treated with cART, or VL > 20 copies/ml or CD4< 350/µl): wait or consider a 3-visit schedule: day 0 – day 7 – day 21/28 (with antibody testing at least 10 days following last dose).
	• Rabies post-exposure prophylaxis:
	  ○ When PrEP completed: 2 doses PEP + Nab testing.
	• When no PrEP was given before risk: 5 vaccine doses + Human Rabies Immunoglobulins + Nab testing.

Inactivated typhoid	• The inactivated typhoid fever vaccine should always be preferred if **the CD4 percentage is lower than 15%.**
TBE	• Standard schedule if recommended.
Cholera	• NA
LIVE TRAVEL VACCINES	
Yellow fever	• CD4 cells over 25% or 500/mm³: vaccination is allowed if necessary. • CD4 cells below 15% or 200/mm³ (**severe** immunosuppression): Vaccination is contra indicated. Travelling to a yellow fever endemic region should be discouraged. • CD4-cells between 200/mm³ (15%) and 500/mm³ (25%) (**moderate** immunosuppression): a specialised vaccination centre should balance the risk of infection with the yellow-fever virus against the risk of complications caused by the vaccine virus. If the patient is asymptomatic, the decision to administer the vaccine can still be fairly straightforward; in other cases, this decision will have to be made on an individual basis. In order to obtain the best possible immune response with a minimal risk of adverse effects, vaccination should be postponed until 3 to 6 months after the immunity has started to recover and the viral load is undetectable.
Live attenuated Typhoid fever	• The live, attenuated vaccine is contra-indicated if CD4 percentage is lower than 15%. The inactivated typhoid fever vaccine should always be preferred if the CD4 percentage is lower than 15%.

2.2.6. Primary immunodeficiency

Introduction

All patients with PID can safely receive **inactivated vaccines**. Although in most PID the immune response to vaccination is altered, only rarely the underlying immune deficiency is so pronounced that the vaccination will remain completely ineffective (eg SCID).
Use of **live vaccines** will depend on the severity of the underlying PID. In general, live vaccines are contra-indicated in patients with a severe lymphopenia or other cellular immunodeficiency. **Live vaccines** should also be avoided during diagnostic investigations when a cellular or combined immunodeficiency is suspected.

This simplified classification given here will help discerning patient categories. A detailed classification of PID can be consulted in "International Union of Immunological Societies: 2017 Primary Immunodeficiency Diseases Committee Report on Inborn Errors of Immunity".
As knowledge in PID is continuously evolving, cases (other than mild humoral immune deficiencies) can be discussed with PID specialists (www.bpidg.be → http://bpidg.be/nl/gemandateerde-bpidg-artsen-voor-de-terugbetaling-van-immunoglobulines-behandeling (NL) or http://bpidg.be/fr/mandates (FR).

1. **Combined immunodeficiencies affecting cellular and humoral immunity**
    a. **Severe Combined immunodeficiencies (SCID)** (e.g. T-B+ SCID, T-B- SCID, complete Di George syndrome)
        i. Contra-indication for live vaccines
        ii. Inactivated vaccines ineffective, no safety concern however

b. Other **combined immunodeficiencies (CID)** with or without syndromic features (eg CD40 (ligand) deficiency, MHC class I-II deficiency, Hyper IgE syndromes (HIES), Anhidrotic ectodermodysplasia with immunodeficiency (EDA-ID), Dyskeratosis congenita (DKC), Wiskott-Aldrich Syndrome, ataxia teleangiectasia, partial DiGeorge/velocardiofacial syndrome
    i. Contra indication for live vaccines, except for patients with milder forms of cellular deficiencies (eg. HIES, partial Di George). This will depend on total lymphocyte count and the results of lymphocyte proliferation test. This must be discussed with a PID specialist.
    ii. Inactivated vaccines can be safely given, but are probably less efficacious,
    iii. Annual inactivated influenza vaccine highly recommended, even in patients receiving IVIG/SCIG as immunoglobulin preparations may not contain antibodies to the circulating strains

2. **Predominantly Antibody deficiencies**
    a. Severe (e.g. X linked agammaglobulinemia, common variable immune deficiency (CVID), hyperIgM)
        i. Contra indication for live vaccines in XLA and patients with CVID and hyperIgM associated with severe lymphopenia.
        ii. Inactivated vaccines can be safely given, but probably less efficacious (not efficacious in XLA)
        iii. Annual influenza vaccine highly recommended, even in patients receiving IVIG/SCIG as immunoglobulin preparations may not contain antibodies to the circulating strains
    b. Mild (e.g. Isolated hypogammaglobulinemia, IgG subclass deficiency, specific antibody deficiency (SPAD), selective IgA deficiency, transient hypogammaglobulinemia of infancy)
        i. No contraindication for live vaccines (except for oral polio vaccine), actively recommended
        ii. No safety concern for inactivated vaccines, highly recommended
        iii. Annual inactivated influenza vaccine, highly recommended

3. **Diseases of immune dysregulation** (e.g. Familial hemophagocytic lymphohistiocytosis (HLH), Autoimmune lymphoproliferative syndrome (ALPS), Immunodysregulation, Polyendocrinopathy, Enteropathy, X Linked (IPEX) Syndrome, Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED)
    i. Contraindication for live vaccines in some cases, discuss with PID specialist
    ii. No safety concern for inactivated vaccines, highly recommended
    iii. Annual inactivated influenza vaccine, highly recommended

4. **Congenital defects of phagocyte number or function** (e.g. severe congenital neutropenia, leucocyte adhesion deficiency, chronic granulomatous disease)
    i. Contraindication for live bacterial vaccines, not for live viral vaccines (except for some forms of LAD affecting T cells)

ii. No safety concern for inactivated vaccines, highly recommended
iii. Annual influenza vaccine, highly recommended

5. **Complement deficiencies**
   i. No contraindication for both live and inactivated vaccines, they should be given
   ii. Annual influenza, highly recommended
   iii. Vaccination against all encapsulated bacteria, highly recommended
      1. H. *influenza type b* (no extra vaccine needed if already immunized according to routine schedule)
      2. S. *pneumoniae* (conjugated (PCV13)+ unconjugated vaccine (PPV 23) – see SHC guideline)
      3. N. *meningitidis* (conjugated men B + men ACWY vaccine – see SHC guideline)

6. Other PID: please refer to a PID specialist for advice on vaccination.

2.3. Adults and teenagers ≥ 16 years

VACCINES	DISORDERS								
	IMID on ISD	PRIOR to SOT	AFTER SOT	Oncology	PRIOR to HSCT	AFTER HSCT	HIV CD4 < 200	HIV CD4 > 200	PID
INACTIVATED VACCINES									
dTpa (or DTPa)	S	S	S	S	S	A (DTPa only)	S	S	S
IPV	R	R	R	R	R	A	R	R	S
Haemophilus influenzae b	NA	R	R	NA	S	A	NA	NA	S
Hepatitis A	R	R	R	R	R	R	R	R	R
Hepatitis B	R	A	A	R	A	A	A	A	S
Influenza	A	A	A	A	A	A	A	A	A
Pneumococcal PPV23	A	A	A	A	A	A	A	A	A
Pneumococcal PCV13	A	A	A	A	A	A	A	A	A
Men ACWY (conjugated)	R	R	R	R	R	A	R	R	A
Men B	R	R	R	R	R	A	R	R	A
HPV	R	R	R	R	R	A	A	A	A
Zoster (inactivated)***	NA	NA	NA	NA	NA	NA	NA	NA	NA
LIVE VACCINES									
MMR	CI#	A**	CI#	CI#	CI#	A*	CI#	A	CI
Varicella	CI	A**	CI#	CI	CI#	A*	CI#	A	CI

LEGEND

S	**Standard indication for vaccination because this concerns routine vaccinations that are part of the basic vaccination schedule that holds for the general population.**
A	**Strongly advised, given the additional risk posed by increased susceptibility and/or increased severity, and/or increased risk from complications**
R	**To consider in case of epidemiological or personal Risk**
CI	**Contra-Indicated**
NA	**Not Applicable**
*	> 24 months post HSCT in absence of immunosuppressive therapy and/or GVHD
**	> 4 weeks prior to activation transplant list
***	not available yet
#	after consultation with a specialist (in case of epidemiological or personal risk)

2.3. Adults and teenagers ≥ 16 years

VACCINES	DISORDERS								
	IMID on ISD	PRIOR to SOT	AFTER SOT	Oncology	PRIOR to HSCT	AFTER HSCT	HIV CD4 < 200	HIV CD4 > 200	PID
Zoster (live)	CI	R**	CI	CI	CI	A*	CI	A	CI
INACTIVATED VACCINES FOR TRAVEL-RELATED EXPOSURES									
Rabies	R	R	R	R	R	R	R	R	R
Japanese encephalitis	R	R	R	R	R	R	R	R	R
Typhoid fever - inactivated	R	R	R	R	R	R	R	R	R
TBE	R	R	R	R	R	R	R	R	R
Cholera	NA	NA	NA	NA	NA	NA	NA	NA	NA
LIVE VACCINES FOR TRAVEL-RELATED EXPOSURES									
Yellow fever	CI#	R**	CI	CI	CI	R*#	CI	R	CI
Typhoid fever - oral	CI	R**	CI	CI	CI	R*	CI	R	CI

LEGEND

S	**Standard indication for vaccination because this concerns routine vaccinations that are part of the basic vaccination schedule that holds for the general population.**
A	**Strongly advised, given the additional risk posed by increased susceptibility and/or increased severity, and/or increased risk from complications**
R	**To consider in case of epidemiological or personal Risk**
CI	**Contra-Indicated**
NA	**Not Applicable**
*	> 24 months post HSCT in absence of immunosuppressive therapy and/or GVHD
**	> 4 weeks prior to activation transplant list
***	not available yet
#	after consultation with a specialist (in case of epidemiological or personal risk)

2.3.0. General recommendations	
INACTIVATED VACCINES	
DTPa and dTPa	• Generally the use of the hexavalent child vaccine (including DTPa and others antigens instead of dTPa) should be favoured due to higher antigen dose of diphteria. However, it has not been licenced for adults.
Hepatitis A	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie) • In case of immunosupressive medication, 2 doses should be given prior to departure and serological response should be measured. If there is no time to do so, a double dose at day 0 or 2 vaccines with a 4 weeks interval, followed by the third one at least 6 months later (data known from studies in subjects under MTX and aTNF). • Once-only antibody testing can be indicated if travelling abroad. However, no recommendations can be made for non-responders.
Hepatitis B	• For the at-risk groups, see the recommendations of the SHC on vaccinating against hepatitis B in the SHC vaccination guide. (https://www.health.belgium.be/nl/vaccinatie). • Since 1999, all infants, children and teenagers in Belgium have been systematically vaccinated. Hepatitis B vaccination is therefore a standard indication. • A control of serological antibodies once is systematically recommended for all immunocompromised patients following hepatitis B vaccinations (4 to 8 weeks after the last hepatitis B injection). • A systematic yearly control of antibodies is especially recommended in patients with a liver transplant and in patients with renal dialysis. • In immune suppressed patients, we aim to achieve titers above 100 IU/mL. Serotiters above 100 IU/mL could be considered as long-lasting protection. - When antibodies declined to or are lower than < 10 IU/mL a booster injection is strictly indicated. In HIV patients under cART a serotiter above 10 IU/mL once is considered boostable for lifelong. - When antibody titers are between 10 and 100 IU/mL specialists have to decide for their individual immunosuppressed patient if a booster vaccination is indicated or not. - Depending on the immune response, the antibodies need to be monitored on an annual basis. The antibody titre has to be kept > 100 IU/L by means of additional boosters in patients under renal dialysis.
Influenza	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie) • Repeat the vaccination each year. Two doses (together or with 1 month interval) may generate a better response, but confirmatory data is still lacking. • Concerning most individuals with immune dysfunction, there are no data that show that there is a specific increase in mortality or an increased risk of complications as a result of influenza infections. Conversely, according to the CDC, influenza does constitute a risk factor for secondary bacterial infections in immunocompromised individuals, which can result in severe

	disease. In some patients, the clearance of the influenza virus is particularly slow, with sustained virus replication and possibly also longer-lasting disease as a consequence.
Pneumococcal **PCV13** **PPV23**	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie). • The conjugate vaccine (PCV13) is a mix of capsular polysaccharides of 13 serotypes. The immune response to the conjugated vaccine is significantly greater than the response to the polysaccharide vaccine (PPV23), in immunocompromised patients. • A first dose of PCV13 should be given, followed by a dose of PPV23 at least 8 weeks later. • If the patient has already been vaccinated by the PPV23 in the past, then there should be at least a 1 year interval before administering the PCV13 vaccine.
Men ACWY	• Use conjugated vaccine: 2 doses are recommended in the immune suppressed patient. • See the recommendations of the SHC on meningococcal vaccination (https://www.health.belgium.be/fr/avis-9485-vaccination-contre-le-meningocoque).
Men B	• See the recommendations of the SHC on meningococcal vaccination (https://www.health.belgium.be/fr/avis-9485-vaccination-contre-le-meningocoque).
HPV	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie). • In immunocompromised, always administer a three doses schedule. • Indicated for teenage girls and boys and young women and men (aged 14 to 26) who have not yet had sexual intercourse; the treating physician decides on an individual basis whether or not it is useful to vaccinate teenage girls and boys and young women and men (aged 14 to 26) who have already had sexual intercourse.
LIVE VACCINES	
MMR	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie). Consider vaccination PRIOR to immunosuppression. These (live attenuated) vaccines (2 doses) should be administered at least 4 weeks before initiating an immunosuppressive treatment. Individuals born in Belgium before 1970 are considered immune against measles. • When necessary and when there are no contraindications, an accelerated schedule can be applied for MMR and varicella. The second dose for varicella and MMR can already be administered after 4 to 6 weeks. Both live vaccines can be administered simultaneously or with at least one month of interval.
Varicella	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie). • Consider vaccination PRIOR to immunosuppression. These (live attenuated) vaccines (2 doses) should be administered at least 4 weeks before initiating an immunosuppressive treatment.

	• When necessary and when there are no contraindications, an accelerated schedule (SHC 9212) can be applied for MMR and varicella. The second dose for varicella and MMR can already be administered after 4 to 6 weeks. Both live vaccines can be administered simultaneously or with at least a 4 weeks interval.
Zoster	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie).
INACTIVATED TRAVEL VACCINES	
Rabies	• Immunocompromised patients should receive a rabies PEP schedule 3 (standard 5 vaccine dose regimen (Day 0, 3, 7, 14, 28) with immunoglobulins on day 0) - regardless of whether they have already been PrEP vaccinated - following a Category II or III risk (according to the BE recommendation). • Rabies PrEP for immunocompromised patients consists of a three-visit schedule (Day 0, 7, 28). When exposed in endemic regions, it is strictly indicated to vaccinate immunocompromised patients against rabies before the risk (with a lower threshold than immunocompetent patient). Immune responses in these patients following booster doses (after the risk) are expected to be much better after previous priming than without priming. For further information see https://www.itg.be/Files/docs/Reisgeneeskunde/PEP_Rabies_ENG.pdf
Japanese encephalitis	• Two doses over 28 days does give a sufficient protection in immunocompetent adults. No data is existing for immunosuppressed travellers. For further information see https://www.itg.be/Files/docs/Reisgeneeskunde/ejapenc.pdf
Typhoid fever	• In general, the use of the inactivated vaccine (instead of the oral live attenuated vaccine) is recommended.
Tick borne encephalitis	• In case of immunosuppression due to the use of DMARD and biologicals, the antibody response can be lower. An extra (3rd) priming dose can be offered. https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/shc_9435_tbe.pdf
LIVE TRAVEL VACCINES	
Yellow fever	• Consider vaccination PRIOR to immunosuppression, when traveling to yellow fever endemic regions in the future is not excluded. This avoids limiting the possible travel destinations in the future. For further information see https://www.itg.be/E/Article/yellow-fever-vaccination

2.3.1. Immune-mediated inflammatory diseases (IMID) & immunosuppressive drugs (ISD)
BEFORE INITIATING MEDICATION • Determine the **vaccination status** of individuals who will require immunosuppressive medication BEFOREHAND, and ensure that the basic vaccination schedule has been completed. Determine **the hepatitis B** antibody titre. • Patients who have not yet contracted **varicella** should receive the varicella vaccine, provided there is enough time. If necessary, an accelerated schedule for **varicella** and for **MMR** may be used: See footnote **2.4.0**. • If appropriate, consider vaccinating against **yellow fever** PRIOR to initiating the medication when travelling to a yellow fever endemic region in the future is not excluded.

• Recommend vaccinating close contacts of the patient (chapter 7).	
LIVE VACCINES	
MMR	• Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • See **chapter 5** for a list of the medication for which there is an absolute contraindication or no contraindication at all. When in doubt, consult a specialist. Also see **chapter 5** for the waiting periods that have to be observed (1) before administering the vaccine after having discontinued immunosuppressive medication and (2) before reinitiating immunosuppressive medication after vaccine administration.
Varicella	• Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • See **chapter 5** for a list of the medication for which there is an absolute contraindication or no contraindication at all. When in doubt, consult a specialist. Also see **chapter 5** for the waiting periods that have to be observed (1) before administering the vaccine after having discontinued immunosuppressive medication and (2) before reinitiating immunosuppressive medication after vaccine administration.
Live attenuated zoster	• For adults aged 60 and up. Definitive recommendations will be issued when there are enough scientific data available for immunocompromised adults (https://www.health.belgium.be/nl/vaccinatie). • Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • See **chapter 5** for a list of the medication for which there is an absolute contraindication or no contraindication at all (e.g. low-dose corticosteroids). When in doubt, consult a specialist. Also see **chapter 5** for the waiting periods that have to be observed (1) before administering the vaccine after having discontinued immunosuppressive medication and (2) before reinitiating immunosuppressive medication after vaccine administration. • Exception: Treatment with low doses of immunosuppressive medication such as methotrexate (≤0.4 mg/kg/week), azathioprine (<3.0 mg/kg/day) or 6-mercaptopurine (<1.5 mg/kg/day) to treat rheumatoid arthritis, polymyositis, sarcoidosis, IBD, etc. is not considered to be sufficiently immunosuppressive to affect the safety **of this vaccine**, and therefore does not constitute a contraindication for administering the zoster vaccine (which is not the case for other live vaccines) (MMWR RR-5June 6, 2008 / Vol 57).
LIVE TRAVEL VACCINES	
Yellow fever	• Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • See **chapter 5** for a list with the medication for which there is an absolute contraindication and no contraindication at all. When in doubt, consult a specialised "Travel clinic". Also see **chapter 5** for the waiting periods that have to be observed (1) before administering the vaccine after having discontinued immunosuppressive medication and (2) before reinitiating immunosuppressive medication after vaccine administration.
Typhoid fever - oral	• Do not use in patients with inflammatory bowel diseases. • Administering this vaccine is contraindicated for patients taking immunosuppressive medication. • To be replaced by the inactivated typhoid fever vaccine.

2.3.2. Solid organ transplantation (SOT): Heart, liver, kidney, pancreas, lung, intestine

PRIOR TO SOT

- Remember to re-evaluate and, if required, complete the **basic vaccination schedule** PRIOR to transplantation. Serology can be checked for hepatitis A, hepatitis B, varicella zoster virus, measles-mumps-rubella. The vaccination history must be checked for those vaccines that lack serological confirmation (e.g. tetanus-diphtheria-pertussis, pneumococcal vaccine, etc.). Repeat booster vaccination must be administered at the same intervals as recommended for immunocompetent persons.
- See also footnote **2.3.0.**
- It is advisable to vaccinate liver transplant candidates against **hepatitis A**. **Vaccinating against hepatitis B** should always be performed prior to organ transplantation (determine the antibody titre).
- Consider **vaccinating against yellow fever** PRIOR to transplantation when travelling to a yellow fever endemic region in the future is not excluded.
- Timing of vaccination: Aim for vaccination prior to transplantation, at least 2 weeks before start of immunosuppressive medication for inactivated vaccines and at least 4 weeks before start of immunosuppressive medication for live-attenuated vaccines. In case of an urgent transplantation or in case of an incomplete vaccination schedule diagnosed after transplantation, additional inactivated vaccines can be administered from 6 months after transplantation, taking into account the current level of immunosuppression and the expected duration of intense immunosuppression in the following weeks.
- In patient who may travel in the post-transplant years, administer yellow fever vaccine pre-transplant if activation of the transplantation waiting list can be postponed for at least 4 weeks. In case of an urgent transplantation, vaccination is contraindicated.

AFTER SOT

- Depending on the recovery of cellular immunity, it is advised to wait for 6 to 12 months after the transplantation before administering inactivated vaccines.
- Live vaccines (against MMR, varicella, yellow fever) cannot be administered because of the obligatory mandatory continuous immunosuppression; only in extremely rare cases where the immunosuppressive medication can be discontinued after all, vaccination can be considered as from 12 to 24 months after the transplantation, depending on the degree of cellular immunosuppression (to be determined by a specialist).Yet there are a few studies in which live vaccines against MMR and varicella were administered to small numbers of paediatric patients after liver transplantation on immunosuppressive medication.

INACTIVATED VACCINES

Hepatitis B	• The vaccination should be performed prior to organ transplantation (footnote **2.4.0**). Serology is checked annually for those patients at higher risk of exposure. If the antibody titer is below 100 IU/l a booster dose must be given and antibody titer must be checked after 4 weeks Hepatitis B naïve transplant patients must receive the standard vaccination schedule.
Influenza	• During an influenza epidemic, vaccination can be given as early as **one month** post-transplantation. In other circumstances vaccination is preferably given at 3 months or later post-transplantation, at a lower level of immunosuppression. A quadrivalent vaccine is recommended.
Pneumococcal	• Patients who have received organ transplantation should be vaccinated with the PCV13 and 23-valent pneumococcal polysaccharide vaccine for the indications mentioned according to the SHC recommendations (PCV13 followed by PPV23). After 5 years a revaccination with PPV23 is recommended once. If the patient already received PPV23 it is recommended to administer PCV13 after an interval of at least one year, followed by a revaccination with PPV23 after 5 years. • SHC recommendation on pneumococcal vaccination (www.health.belgium.be)
Meningococcal	• A 4-valent conjugate vaccine (A-C-W135-Y) is preferred in organ transplant patients. Concerning meningococcus type B, further advice by SHC is awaited. See the recommendations of the SHC on meningococcal vaccination. https://www.health.belgium.be/nl/vaccinatie
Inactivated Zoster (not available in BE yet)	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie)
LIVE VACCINES	
General remark	• Live attenuated vaccines must be given at least 4 weeks before activation of the waiting list, which means that following vaccination the patient must wait at least 4 weeks before active search for a transplant organ can be launched. In case of an urgent need for transplantation, live attenuated vaccines are contraindicated.
MMR	• As the immunosuppressive medication cannot be discontinued in nearly all patients, vaccination is contraindicated.
Varicella	• As the immunosuppressive medication cannot be discontinued in nearly all patients, vaccination is contraindicated.... Check serostatus before transplantation. If negative, start vaccination if activation of the transplantation waiting list can be postponed for at least 4 weeks. In case of an urgent transplantation, vaccination is contraindicated. • In case of exposure of a naïve transplant patient to an active varicella patient with rash, administration of immunoglobulins is recommended, either polyclonal immunoglobulins (with confirmed high level of varicella IgG titers) or specific immunoglobulins (600 units for a person of > 30 kg). Specific immunoglobulins are currently not available in Belgium and very expensive for the patient. In naïve exposed patient preventive treatment with (val-)acyclovir should be given for 7 to 14 days.
Live attenuated Zoster	As the immunosuppressive medication cannot be discontinued in nearly all patients, vaccination is contraindicated.

LIVE TRAVEL VACCINES	
Yellow fever	In patient who may travel in the post-transplant years, administer yellow fever vaccine pre-transplant if activation of the transplantation waiting list can be postponed for at least 4 weeks. In case of an urgent transplantation, vaccination is contraindicated.

2.3.3. Haematological malignancies after receiving chemotherapy	
• Concerning patients receiving **immunosuppressive chemotherapy**, **inactivated vaccines** should be postponed until at least **3 months** after the end of treatment, depending on the recovery of the immune system. **Live vaccines** can only be administered **6 months** after the end of treatment. • After **extensive radiotherapy** (consult a specialist), there should be **a 6-month waiting period** before administering **live vaccines**.	
INACTIVATED VACCINES	
Influenza	• Vaccination prevents influenza-induced interruptions in the chemotherapy.
LIVE VACCINES	
MMR	• Live vaccine. Administering this vaccine is contraindicated for patients taking immunosuppressive medication. Wait for **6 months** after having discontinued this medication.
Varicella	• Live vaccine. Administering this vaccine is contraindicated for patients taking immunosuppressive medication. Wait for **6 months** after having discontinued this medication.
LIVE TRAVEL VACCINES	
Yellow fever	• Can be administered as from **6 months** after the last chemotherapy session.
Typhoid fever - oral	• Can be administered as from **6 months** after the last chemotherapy session.

2.3.4. Hematopoeitic stem cell transplantation (HSCT)
PRIOR TO HSCT • T cell memory of the patient is usually lost after HSCT. However, circulating antibodies will persist for several weeks to months post transplant and will protect the patient during this very vulnerable early post transplant period. • Booster of dTpa PRIOR to the transplantation if the last vaccine is > 10 years ago. • **Vaccinating against hepatitis B** should always be done prior to transplantation. If vaccination already performed, then antibody titers should be determined.

- **A hepatitis B naïve patient receiving a graft from a hepatitis B positive donor (evidenced by hepatitis B surface antigen (HbsAg) positivity), should be vaccinated pretransplant:** the vaccination should start before the transplant, and preferably prior to induction chemotherapy, at least for the two initial doses, as the response to vaccination is poor in patients immediately after therapy. A third dose should be given six months later, ideally also prior to transplantation, but only if it's safe to postpone it. Antibody titers should be measured 4 weeks after the last dose.
- **Influenza:** A recent Cochrane meta-analysis concludes that although the evidence is weak, it is in favour of vaccinating all patients with cancer, as well as their caregivers in general As for allogenic HSCT recipients, a randomized controlled trial comparing no vaccination, recipient vaccination and donor vaccination pretransplant showed significantly improved antibiody titers to H1 and H3 antigens if the patient was vaccinated pretransplant. However, the immunity wanes over time. The authors concluded that in order to maintain the immune response, patients should receive a booster early after transplant (3 months). Of course, other measures should be taken to minimize the risk of influenza infection in transplant patients, by avoiding contact with possibly infected people and by vaccinating close contacts.
- **Recommend** vaccinating close contacts of the patient, living in the same house, and those having daily contact with the patient (Influenza, Measles, Mumps, and Rubella, and Varicella vaccines) (see chapter 7)
- The role of donor-vaccination is controversial because of ethical reasons. However, for several vaccines, the benefit of donor vaccination has been shown and could/should be advised, especially in family donors, but of course never forced. There is some evidence for a better immunity post transplant in the recipient if the donor has been vaccinated with tetanus toxoid, pneumococcal vaccine (conjugated) and Hib before collection If the recipient is both hepatitis B core antibody (HbcAb) and hepatitis B surface antibody (HbsAb) positive, vaccinating the donor will reduce the risk of reverse seroconversion). A recent study showed that the best hepatitis B control post transplant in HBV-infected HSCT was seen if donors were vaccinated: the authors recommend to completely vaccinate the donor of a HBV-positive recipient or to apply a single booster immunization in pre-vaccinated donors.
- Influenza vaccination for donors: no studies available; a randomized controlled trial comparing no vaccination, recipient vaccination and donor vaccination pretransplant showed no significant effect of donor pretransplant vaccination.

AFTER HSCT

- The same rules that apply to **allogenic** HSCT also hold for **autologous** HSCT.
- The full basic vaccination schedule has to be reinitiated with the **inactivated vaccines**, starting **3 to 6 months** after the transplantation, depending on the degree of cellular immunosuppression. Because of the risk of serious infections following HSCT, influenza and pneumococcal vaccines should be given within the 3-6 months following HSCT. However, for vaccines against tetanus, diphteria, pertussis, HBV, and HPV, vaccination can be done at 6-12 months following HSCT, in order to obtain better immunological responses.

INACTIVATED VACCINES

DTPa – IPV-Hib - Hep B	**It is recommended to use the hexavalent paediatric vaccine, with a higher dosage of diphtheria and tetanus toxoids and acellular pertussis components (DTPa) than the dTpa vaccine. Indeed, the immune system is once again "naïve", as is the case in unvaccinated children.**
Separate components:	
dTpa – IPV	Initiate the basic vaccination schedule **as from 6 months** after the transplantation (3 doses at a 1-month interval and a booster after 1 year).
Haemophilus influenzae b	Initiate the basic vaccination schedule **as from 6 months** after the transplantation (3 doses at a 1-month interval and a booster after 1 year). NB: patients with chronic GVHD are at risk of developing functional hyposplenism.
Hepatitis B	Initiate the basic vaccination schedule or catch-up vaccination schedule **as from 6 months to 1 year** after HSCT 2 doses at a 1-month interval and a booster after 4-12 months. If not enough antibodies a second 3-dose scheduled needs to be performed. See also 2.2.0
Influenza	Initiate vaccination **as from 3 months to 1 year** after the transplantation (**annually**).
Pneumococcal	• Pneumococcal conjugate (PCV13) at 3 to 6 months after transplantation, 3 doses in monthly doses. Following the primary series of three PCV doses, a dose of the PPV23 to broaden the immune response should be given at least 8 weeks later.
Meningococcal ACWY (conjugate)	• SHC factsheet "Catch-up vaccinations" (https://www.health.belgium.be/nl/vaccinatie) for individuals up to the age of 18. If this vaccination was not yet carried out, 1 dose may be administered immediately. • Provide an additional dose after the transplantation.
Inactivated zoster Not available in BE yet	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie)
LIVE VACCINES	
MMR	• Can be administered as **from 24 months** after the transplantation, provided there is no "graft-versus-host" disease and the patient does not receive any immunosuppressive medication (stopped for at least 2 months), and CD4 count of 200/mm3).
Varicella	• can be administered as **from 24 months** after the transplantation, provided there is no "graft-versus-host" disease and the patient does not receive any immunosuppressive medication(stopped for at least 2 months), and CD4 count of 200/mm3).
Live attenuated zoster	• See the recommendations of the SHC on vaccination (https://www.health.belgium.be/nl/vaccinatie)

LIVE TRAVEL VACCINES	
Yellow fever	• If indicated, **as from 24 months** after stem cell transplantation, for patients with no "graft-versus-host-disease" and who are not on any immunosuppressive medication (stopped for at least 2 months), and CD4 count of 200/µl)

2.3.5. HIV

Immune depression depending among others on CD4 T-cell counts:

- **Above 500/mm³** : **minor**
- Between **200 and 499/mm³** : **moderate**
- Below **200/mm³**: **severe**

The immunity is assumed to have sufficiently recovered after the initiation of cART, if the CD4 count has risen over 500/mm³, unless on antiretroviral therapy for less than 3 to 6 months. We advise to administrate vaccines in HIV positive subjects with suppressed viral load.

For live attenuated vaccines (in addition to restrictions for general population):

- **Varicella, measles, mumps, rubella, yellow fever, live zoster**

Contraindicated if CD4 count <200 cells/µL (<15%) and/or AIDS, because of impaired protection after vaccination with unsuppressed viraemia and risk of replication of the vaccine strain.

- **Oral live typhoid**

Contraindicated if CD4 count <200 cells/µL (< 15%): give inactivated parenteral polysaccharide vaccine. The inactivated parenteral polysaccharide vaccine is also preferred if CD4 count > 200 cells/µL (≥ 15%).

INACTIVATED VACCINES	
Pertussis	• No data in HIV+ pregnant women, clinical trial pending. Few data on pertussis vaccination efficacy in HIV infected patients
Polio	• One study found a 78–100% serologic response rate, with the best responses among those with CD4 counts >300 cells/mm3 - lack of data on the durability of protection and no current evidence-based recommendations regarding boosters for HIV-infected persons
Hepatitis A	• For the at-risk groups, see the recommendations of the SHC on the vaccination against hepatitis A in the SHC vaccination guide (https://www.health.belgium.be/nl/vaccinatie). Among others, it is advisable to immunize MSM, IVDU, travelers, close contact with children, food handlers and patients with liver diseases. • Seroconversion rate after 2 doses is 48-94% depending on CD4 and HIV viral load control. Antibodies persist in 75-85% of patients for > 5 years after vaccination, depending on HIV control. We recommended to control antibodies of hepatitis A after primary vaccination in patients immunized when CD4 <200/µl, and also 2 to 5 years after primary immunization (2 doses) because cases of hepatitis A infection have been reported in fully vaccinated HIV-patients.

	• Additional boosters have no proven efficacy in non-responders in the case of HIV-infection.
Hepatitis B	• Shared routes of transmission, increased severity of HBV in HIV patients. • For the at-risk groups, see the recommendations of the SHC (https://www.health.belgium.be/nl/vaccinatie)on the vaccination against hepatitis B in the SHC vaccination guide. Among others, it is advisable to vaccinate the following individuals against hepatitis B: MSM, sex workers, IVDU, patients who have been diagnosed with a sexually transmittable infection and those with multiple sexual partners. • Lower response rates to vaccination has been reported in HIV patients compared to the general population (33-88% versus 90%) linked to immunovirological status, HCV coinfection, age > 40 years, male sex and being an active smoker. Patients present lower Ab titers and quicker decline than HIV negative individuals. Prefer vaccination when HIV VL is controlled and CD4 are above 350/µl to enhance immune response. Consider HIV patients under cART to be protected lifelong once Ab titers has been demonstrated. • Non-responders: see footnote **2.3.0.** The use of cART containing TDF or TAF is recommended (whenever possible) in non-responders to vaccination.
Influenza	• There are no recent data on increased mortality in HIV patients, but in theory they have a higher risk for (post-influenza) pneumonia. Therefore, yearly vaccination against influenza is advised. There are no data on quadrivalent vaccine. • No clinical data available on high doses or booster (double) dose of vaccine in HIV patients. Immunogenicity of 65-85% depending on CD4 and HIV control but no data concerning durability of protection.
Pneumococcal PCV13 PPV23	• Increased frequency and severity of pneumococcal infections in HIV patients: combination of- conjugated vaccine followed by the polysaccharidic vaccine is recommended > 8 weeks later. No boosters are needed. A weak immunological response is seen when the 23-valent polysaccharide vaccine is given alone.
Men ACWY (conjugated)	• Discrepant data about RR (relative risk) of IMD in HIV patients. • Vaccination is advised for MSM attending crowded gay events (higher RR of IMD). • There is a lack of data on immunogenicity. However, some small studies show lower seroconversion rate in HIV patients, when CD4 counts are <200/µl, the CDC recommends 2 doses for HIV patients at ≥ 8 weeks interval). • No data on long-term duration of protection; boost every 5 years if risk persists.
Men B	• Discrepant data about relative risks in HIV patients. There is a lack of data concerning pharyngeal carriage in Belgium especially in MSM.

HPV	• Shared route of transmission- increased risk of anal, cervical and oropharyngal neoplasia, increased risk of condylomas (incidence and recurrence), vaccinate adolescents, men and women: recommended until 26 years old and until 40 for MSM The vaccines needs to be considered between 26 and 40 years for others. • Always prefer 9-valent vaccine. • Consider also in secondary prevention after treatment of high grade squamous intraepithelial lesion (HSIL). • Always try to vaccinate when HIV is controlled, always 3 doses even in adolescents. (no data with less than 3 doses).
Inactivated Zoster (not available in BE yet)	• See the recommendations of the SHC on zoster vaccination: https://www.health.belgium.be/nl/advies-9209-vaccinatie-tegen-herpes-zoster-virus-zona • Increased risk of shingles (incidence, recurrence, severity, sequelae), particularly when aged >50 years old: give 3 doses at 0-2-6 months. • Duration of protection at least 18 months. • There are currently no data on HIV-infected patients formerly vaccinated with live attenuated vaccine.
LIVE VACCINES	
MMR	• Check the immune status for measles (and for rubella in child-bearing age women) at baseline once. In case of doubt or incomplete vaccination and no history of measles, revaccinate when possible or test immune status - if (re)vaccinated during adulthood, check antibodies once. • HIV vertical transmission is a risk factor for seronegativity for measles and rubella. • HIV is a risk factor for measles complications (data from pre-cART era).
Varicella	• HIV-positive adults with a negative or uncertain history of chickenpox or shingles need to undergo VZV IgG testing (especially important for women of childbearing age) to determine susceptibility to primary infection and reactivation. • Vaccinate if seronegative and no severe immunosuppression (CD4 should be >200/mm^3). • There is an increased severity of chickenpox in HIV-infected patients. • There are little data on vaccine immunogenicity, but data in HIV positive children suggest lower vaccine immunogenicity. • Vaccinate patients in case of post-exposition after exposure if seronegative and CD4 >200/mm^3.
Live attenuated Zoster	• Prefer inactivated zoster vaccine if available, if not, give only 1 dose of the live attenuated vaccine. • Safe and immunogenic in adults with controlled HIV VL and CD4 >200/mm^3 in a small study with 2 doses (6 weeks interval).

INACTIVATED TRAVEL VACCINES	

Rabies	• Studies are lacking in HIV-infected patients. We expect normal immune responses in HIV patients under cART.
	• Rabies pre-exposure prophylaxis.
	  ○ When patients with minor or moderate immunosuppression (treated with cART, VL <20 copies/ml and CD4 > 350 cells/mm³): consider a 2-visit schedule: day 0 – day 7.
	  ○ When major immunosuppression (not treated with cART, or VL >20 copies/ml or CD4 <350 cells/mm³): wait or consider a 3-visit schedule: day 0 – day 7 – day 21/28 (with antibody testing at least 10 days following last dose).
	• Rabies post-exposure prophylaxis:
	  ○ When PrEP completed and minor or moderate immunosuppression: 2 doses PEP + Nab testing.
	  ○ When no PrEP was given before risk: 5 vaccine doses + Human Rabies Immunoglobulins + Nab testing.

Japanese encephalitis	• Use classical schedule- rapid schedule is generally not recommended for HIV-infected persons. • Immunogenicity and clinical efficacy of JE vaccination in HIV-infected adults are unknown. • No efficacy or safety data in HIV patients for JE live attenuated vaccine (not available in Belgium).
Inactivated typhoid	• HIV-infected patients have an increased risk of Salmonella spp. infections including complicated disease with bacteremia and relapsing and/or persistent infection. Care providers should have a low threshold to immunize, especially Visiting Friends and Relatives (VFR) travelers. • Lower post-vaccination responses to typhoid vaccination have been described among HIV-infected persons, and poorer responses are correlated with low CD4 counts- • There are no data on durability of protection.
Tick-borne encephalitis	• Consider a 4-dose series (0, 1, 2, and 9–12 months) for HIV-infected adults given concerns about lower vaccine response in this group. • There are no data on accelerated schedule and therefore it should be avoided in HIV infected patients. • Regarding immunogenicity, HIV patients (especially those with a CD4 count <400 cells/mm³) have poorer responses compared with HIV-uninfected persons and protection durability is unknown. • Boosters are recommended at 3–5 years, with the shorter interval among those with CD4 counts <400 cells/mm³.
Cholera	• Almost never given to travelers. Contra indicated in case of severe immunosuppression.

LIVE TRAVEL VACCINES	
Yellow fever	• CD4+ cells >500/mm³: No contra-indication. • CD4+ below 200/mm³ (**severe** immunosuppression): The vaccine should not be administered, and the patient should be advised against travelling to a yellow fever endemic region. • CD4+ between 200 and 500 /mm³ (**moderate** immunosuppression): The specialised vaccination centre should balance the risk of infection with the yellow-fever virus against the risk of complications caused by the vaccine virus. If the patient is asymptomatic, the decision to administer the vaccine can still be fairly straightforward. In other cases, this will be a decision that will have to be made on an individual basis. You may consider having an "informed consent" form signed if the patient decides to have the vaccine administered, or if he/she decides to travel without having received it. In order to obtain the best possible immune response with a minimal risk of adverse effects, administering this vaccine should be deferred until 3 to 6 months after the immunity has started to recover. • There is decreased seroconversion and duration of protection. It is currently recommended to revaccinate patients every 10 years. We are waiting for more data.
Live attenuated Typhoid fever - oral	• In patients CD4 <200 cells/mm³ there is a theoretical contraindication. HIV-infected persons have an increased risk of Salmonella infections including complicated disease with bacteremia and relapsing and/or persistent infection. Lower post-vaccination responses to typhoid vaccination have been described among HIV-infected persons, and poorer responses are correlated with low CD4 counts- no data on durability of protection. • The inactivated typhoid fever vaccine should also be preferred if **the CD4 count is >200/mm³.**

3. REVACCINATION SCHEDULE AFTER HSCT

3.1 Standard vaccination for all HSCT recipients (auto/allo)

Organism	Type of vaccine	Schedule	Time after HSCT	Comments
INACTIVATED VACCINES				
Diphteria **Tetanos** **Pertussis** **Polio** **Hib**	Combined vaccine DTPa-IPV-Hib	4 doses schedule 0 – 1 – 2 – 12 months	6 months	• Regardless of the age, paediatric formulation is mandatory because of higher antigen concentration • Tetanus Ab titer may be checked after vaccination if poor response is suspected
Hepatitis B	Inactivate vaccine	3 doses schedule 0 – 1 – 6 months	6 – 12 months	• Antigen concentration may be adapt regarding the patient age • Hexavalent vaccine could be used • HBsAb may be measured 1 month after 3d dose
Influenza	Tetravalent inactivated vaccine	Age < 9 years 2 doses (1 month interval) Age > 9y and delay from HSCT more than 6 months 1 dose (2 doses if delay < 6 months)	3 – 6 months	• During the flu season
Pneumococcal	Inactivated conjugate vaccine 13-valent (PCV13)	3 doses schedule 0 – 1 – 2 months	3 – 6 months	
Pneumococcal	Inactivated polysaccharide vaccine (PPV23)	1 doses schedule (at least 6 months after the last PCV13 vaccine)	6 months	• In case of chronic GVHD, replace PPV23 vaccine with a fourth dose of PCV13 (poor response to PPV23)
LIVE VACCINES				
MMR	Live-attenuated vaccine	2 doses schedule 0 – 1 month	Min 24 months*	In seronegative patients and min 8 to 11 months after last IVIG injection * Contra-indicated if

				• GVHD • Immunosuppressive therapy (until 2 months before vaccination) • CD4 < 200/μl
Varicella	Live-attenuated vaccine	2 doses schedule 0 – 1 month	Min 24 months*	In seronegative patients and min 8 to 11 months after last IVIG injection * Contra-indicated if • GVHD • Immunosuppressive therapy (until 2 months before vaccination) • CD4 < 200/μl

3.2 Vaccination for specific risk group HSCT recipients (auto/allo)

Organism	Type of Vaccine	Risk group	Timing after HSCT	Schedule
INACTIVATED VACCINES				
Hepatitis A	Inactivated conjugate vaccine	See SHC recommendations	6–12 months	2 doses schedule 0 - 6 months
Meningococcus C	Inactivated vaccine	If no previous vaccination and age < 18 years	6–12 months	1 dose schedule
Meningococcus A-C-W-Y	Inactivated vaccine	• Before travelling to endemic area • Eculizumab use • Hyposplenism	6–12 months	2 doses schedule 0-2 months
Meningococcus B	Inactivated vaccine	No specific recommendation	No data	No data available 2 doses schedule 0 – 1 month
HPV	Inactivated vaccine 9-valent	See SHC recommendations	6–12 months	3 doses schedule 0 – 2 – 6 months
INACTIVATED TRAVEL VACCINES				
Rabies	See SHC recommendations			

Japanese encephalitis	Inactivated vaccine	Before travelling to endemic area	12–24 months	2 doses schedule 0 – 1 month
Typhoid fever	Inactivated vaccine	Before travelling to endemic area	6–12 months	1 dose schedule
Tick-borne encephalitis	Inactivated vaccine	Before travelling to endemic area	6–12 months	3 doses schedule 0 – 1 – 6 months
LIVE TRAVEL VACCINES				
Yellow Fever	Live-attenued vaccine	Before travelling to endemic area	> 24 months	1 dose schedule

4. VACCINATING INDIVIDUALS WITH A CHRONIC CONDITION

- **Routine basic vaccinations, including live vaccines** should be given (see individual SHC factsheets and "catch up vaccinations" (https://www.health.belgium.be/nl/vaccinatie).
- Often, extra disease- specific vaccines are recommended
- There are usually no contraindications against proceeding with the **vaccinations for travel-related exposures**, including the **live vaccines**.

	Children < 16 years	**Adults and teenagers ≥ 16 years**
1. Diabetes mellitus	Recommended: • **Influenza vaccine** (annually); • **Pneumococcal vaccination (PCV13 + PPV23).**	Recommended: • **Influenza vaccine** (annually); • **Pneumococcal vaccination (PCV13 + PPV23).**
2. Metabolic disorders, including morbid obesity with BMI > 35	Recommended: • **Influenza vaccine** (annually)	Recommended: • **Influenza vaccine** (annually)
3. Chronic renal disease including chronic renal failure, nephrotic syndrome and renal dialysis	Recommended: • **Influenza vaccine** (annually); • **Hepatitis B vaccine**; • **Pneumococcal vaccination (PCV13 + PPV23).** In renal dialysis: an AcHBs antibody titer of 100 IU/mL is recommended. Remember to administer live vaccines timely if possible evolution towards transplantation (see introduction)	Recommended: • **Influenza** (annually); • **Hepatitis B vaccine** (in adults double dosage or adjuvant hepatitis B vaccine (from the age of 15); • **Pneumococcal vaccination (PCV13 + PPV23).** In renal dialysis: an AcHBs antibody titer of 100 IU/mL is recommended. Remember to administer live vaccines timely if possible evolution towards transplantation (see introduction)
4. Chronic liver disease including chronic hepatitis, cirrhosis, biliary atresis, auto-immune hepatitis	Recommended: • **Influenza vaccine** (annually); • **Hepatitis A & B vaccine;** • **Pneumococcal vaccination (PCV13 + PPV23)** Remember to administer live vaccines timely if possible evolution towards transplantation (see introduction)	Recommended: • **Influenza vaccine** (annually); • **Hepatitis A & B vaccine**; • **Pneumococcal vaccination (PCV13 + PPV23)** Remember to administer live vaccines timely if possible evolution towards transplantation (see introduction)

	Children < 16 years	Adults and teenagers ≥ 16 years
5. Chronic cardiopulmonary conditions (including heart failure, congenital heart disease, ischemic heart disease, hypertension with cardiac complications, bronchopulmonary disease, COPD, interstitial lung disease, severe asthma, bronchiectasis)	Recommended: • **Influenza vaccine** (annually); • **Pneumococcal vaccination (PCV13 + PPV23).**	Recommended: • **Influenza vaccine** (annually); • **Pneumococcal vaccination (PCV13 + PPV23).**
6. Cystic fibrosis	Recommended: • **Influenza vaccine** (annually); • **Hepatitis A & B vaccine;** • **Pneumococcal vaccination (PCV13 + PPV23).** Remember to administer live vaccines timely if possible evolution towards transplantation (see introduction)	Recommended: • **Influenza vaccine** (annually); • **Hepatitis A & B vaccine;** • **Pneumococcal vaccination (PCV13 + PPV23).** Remember to administer live vaccines timely if possible evolution towards transplantation (see introduction)
7. Chronic aspirin treatment	Recommended: • **Influenza vaccine** (annually)	Not applicable
8. Chronic neurological disease including cerebral, neuromuscular disease*	Recommended • **Influenza vaccine** (annually); • **Pneumococcal vaccination PCV13 + PPV23** (if risk of aspiration).	Recommended • **Influenza vaccine** (annually); • **Pneumococcal vaccination PCV13 + PPV23** (if risk of aspiration).
9. Bleeding disorders including haemophilia and Von Willebrand disease	Recommended: • **Hepatitis A & B vaccines in patients receiving plasma- derived concentrates, not in patients only receiving recombinant concentrates.**	Recommended: • **Hepatitis A & B vaccines in patients receiving plasma- derived concentrates, not in patients only receiving recombinant concentrates.**
10. Anatomic or functional asplenia/hyposplenia including sickle cell disease	Recommended: • **Men B, ACWY** (conjugate vaccine); • **Influenza vaccine** (annually); • **Pneumococcal vaccination (PCV13 + PPV23);** • **Haemophilus influenzae b** (no supplementary doses if already vaccinated).	Recommended: • **Men B, ACWY** (conjugate vaccine); • **Influenza** (annually); • **Pneumococcal vaccination (PCV13 + PPV23);** • **Haemophilus influenzae b** (no supplementary doses if already vaccinated).

	Children < 16 years	Adults and teenagers ≥ 16 years
11. Cerebrospinal fluid leak, (including CSF shunts), cochlear implant	Recommended: • **Influenza vaccine** (annually); • **Pneumococcal vaccination (PCV13 + PPV23);** • **Meningococcal vaccination (men ACWY + men B).**	Recommended: • **Influenza vaccine** (annually); • **Pneumococcal vaccination (PCV13 + PPV23);** • **Meningococcal vaccination (men ACWY + men B).**
12. Extensive radiotherapy	Recommended: • **Influenza vaccine** (annually). Vaccination with **live vaccines** -if indicated- as from 3 months after the end of radiotherapy (to discuss with the specialist).	Recommended: • **Influenza vaccine** (annually). Vaccination with **live vaccines** - if indicated- as from 3 months after the end of radiotherapy (to discuss with the specialist).
13. Thymus dysfunction or thymectomy for reasons linked to thymus dysfunction (eg for thymoma or in case of mantle field radiation therapy). This does not includes incidental thymectomy	Recommended: • **Influenza vaccine** (yearly); • **Pneumococcal vaccination (PCV13 + PPV23).** Contra-indication: Yellow Fever vaccine	Recommended: • **Influenza vaccine** (yearly); • **Pneumococcal vaccination (PCV13 + PPV23).** Contra-indication: Yellow Fever vaccine

	Children < 16 years	Adults and teenagers ≥ 16 years
Patients on intravenous / subcutaneous immunoglobulin replacement therapy (IVIG/SCIG)	Recommended • **Influenza vaccine** (annually); • No contra-indication for administration of inactivated vaccines. • Possible interference of immune response after vaccination with some live vaccines (varicella, measles and rubella). • No interference with yellow fever vaccine. When administering IVIG/SCIG, there should, if possible, be a 6 to 8 month waiting period (after ending IVIG/SCIG treatment) before offering these live, vaccines in order to obtain a proper immune response. If persistent replacement is required for the patient, a 6 month waiting period is not possible. In addition, these patients will always develop but a weak antibody response themselves. In such cases, a waiting period of 3-4 weeks may be applied.	Recommended • **Influenza vaccine** (annually) • No contra-indication for administration of inactivated vaccines. • Possible interference of immune response after vaccination with some live vaccines (varicella, measles and rubella). • No interference with yellow fever vaccine. When administering IVIG/SCIG, there should, if possible, be a 6 to 8 month waiting period (after ending IVIG/SCIG treatment) before offering these live, vaccines in order to obtain a proper immune response. If persistent replacement is required for the patient, a 6 month waiting period is not possible. In addition, these patients will always develop but a weak antibody response themselves. In such cases, a waiting period of 3-4 weeks may be applied.

* *a small risk of relapse of MS after a yellow fever vaccination can't be ruled out.*

5. LIST OF (POTENTIALLY) IMMUNOSUPPRESSIVE MEDICATIONS

In order to find the brand names of the various medications, see:
Gecommentarieerd Geneesmiddelen Repertorium *(Belgisch Centrum voor Farmacotherapeutische informatie; www.bcfi.be)*
Répertoire Commenté des Médicaments *(Centre Belge d'Information Pharmaco thérapeutique; www.cbip.be)*

The list of immunosuppressive medication is long. There is a continuous introduction of new monoclonal antibodies. The best moment for vaccination is **before** the start of immunosuppressive medication. At that moment, the function of the immune system is still intact and there will be an optimal response to vaccination. In addition, live-attenuated vaccines (Yellow Fever, Varicella-Zoster, Measles-Mumps-Rubella) are contra-indicated during immunosuppressive therapy. The interval after which a live-attenuated vaccine can safely be given after cessation of immunosuppressive therapy is dependent on pharmacokinetic and pharmacodynamics characteristics of the medication in question.

Pharmacokinetics: As a rule of thumb there are no significant concentrations of a medication present after five times the elimination half-life.
Pharmacodynamics: The suppressive effect on the immune system can last longer than the presence of detectable concentrations in the blood. In anti-cytokine drugs the immunosuppressive effects after clearance in the serum will be of shorter duration than in drugs that inhibit cell division and cell function. As a rule of thumb the immunosuppressive effect after stopping a drug will be waned 2 weeks after elimination of anti-cytokine drugs and 4 week after elimination of other drugs, unless there are other data found in the literature.

Table 2 summarizes the safe interval after which a live-attenuated vaccine can safely be given, taken the above considerations into account,

There are several drugs known that can lead to prolonged suppression of T and B lymphocytes: Obinutuzumab, Rituximab, Alemtuzumab. In the table there is a minimum duration indicated before a live-attenuated vaccine can be given, provided that the absolute CD4+ T-lymphocytes, CD8+ T-lymphocytes and B-lymphocytes are within the normal range.

Table: Safe interval of live-attenuated vaccines

Medication	Elimination half-life	Safety margin (in weeks)	**Recommended interval: 5 xt 1/2 + safety margin before vaccination**
high dose prednisone > 1mg/kg/d, > 14 days (children) > 20 mg/d, > 14 days (adults)	6 hours	4	**1 month**
Methotrexate low dose: ≤0.4 mg/kg/week or ≤20 mg (adults)	3-17 hours		**Individual assessment***
Methotrexate high dose >0.4 mg/kg/week or >20 mg (adults)	3-17 hours	4 4	**1 month** **1 month**
6-mercaptopurine	5 hours	4	**1 month**

Medication	Elimination half-life	Safety margin (in weeks)	**Recommended interval: 5 xt 1/2 + safety margin before vaccination**
Azathioprine	5 days	4	**2 month¶**
Basiliximab	4-10 days	4	**3 month**
Belatacept	8-10 days	4	**3 month**
Cyclosporine	6 hours	4	**1 month**
Everomilus	30 hours	4	**6 weeks**
Fotemustine	83 hours	4	**6 weeks**
Leflunomide			**2 years****
Mitotranxone	12 days	4	**3 month**
Mycophenolate mofenil	12-18 hours	4	**1 month**
Sirolimus	50-70 hours	4	**6 weeks**
Tacrolimus	12-15 hours	4	**1 month**
Medications for IMID			
Abatacept	13 (8-25) days	2	**3-4 months**
Alemtuzumab			**6 months‡**
Anakinra	6 hours	2	**2 weeks**
Apremilast	9 hours	2	**2 weeks**
Baricitinib	12,5 hours	2	**2 weeks**
Belimumab	19 days	4	**4 months**
Canakinumab	26 days	2	**5 months**
Daclizumab	21 days	4	**6 months**
Eculizumab	8-20 days	4	**6 months°**
Fingolimod	6-9 days	4	**3 months**
Ixekizumab	13 days	4	**3 months**
Natalizumab	16 days	4	**3 months**
Secukinumab	27 (18-46) days	4	**9 months**
Siltuximab	16 days	2	**4 months**
Teriflunomide	19 days	4	**6 months**
Tocilizumab	6-23 days	4	**3 months**
Tofacitinib	3 hours	4	**1 month**
Ustekinumab	15-32 days	4	**4 months**
Vedolizumab	25 days	4	**5 months**
TNF inhibitors			
Adalimumab	2 weeks	2	**3 months**
Certolizumab	14 days	2	**3 months**
Golimumab	12 days	2	**3 months**
Etanercept	70 hours	2	**1 month**
Infliximab	12 weeks	2	**4 months**
Alkylating medication			
Melfalan	1 hours	4	**1 month**
Busulfan	3 hours	4	**1 month**

Medication	Elimination half-life	Safety margin (in weeks)	**Recommended interval: 5 xt 1/2 + safety margin before vaccination**
Cyclophosphamide	9 hours	4	**1 month**
Ifosfamide	22 hours	4	**6 weeks**
Chloorambucil	2 hours	4	**1 month**
Other alkylating medication			
Bendamustine	0,5 h	4	**1 month**
Dacarbazine	5 h	4	**1 month**
Estramustine	110 h#	4	**2 months**
Temozolomide	1,8 h	4	**1 month**
Thiotepa	4 h	4	**1 month**
Monoclonal antibodies / cytokines			
Brentuximab	5d		**3 months**
Elotuzumab	8d	4	**3 months**
Ipilimumab	15d	4	**4 months**
Obinutuzumab	37 d	4	**6 months****
Rituximab			**1 year****
Treatment for MS			
Alemtuzumab			**6 month‡**
Daclizumab	21d	4	**6 month**
Dimethyl fumaraat	1 h	2	**2 weeks‡**
Fingolimod	6-9d	4	**3 month**
Glatiramer acetate	21d	4	**6 month**
Natalizumab	16d	4	**3 month**
Teriflunomide	19d	4	**4 month**

**Live attenuated vaccines are probably safe in low dose methotrexate. Decision to vaccinate should be guided by individual risk assessment,* ¶ varicella vaccination possible in low dose azathioprine : >3 mg/kg/day
*** therapeutic drug monitoring Possibility for ´wash-out´ procedure; ‡ decision guided by measuring lymphocyte count; °TDM possible; # active metabolite*

5.2. List of medication not considered immunosuppressive

- **Paracetamol, NSAID, Sulphasalazine, (hydroxy) chloroquine**
- **Corticosteroids**
  - Short treatment with corticosteroids (< 14 days) or long-term treatment with a daily dose
    - of < 10 mg prednisone (8 mg methyprednisolone) or equivalent in adults
    - < 0.3 mg/kg/d prednisone or equivalent in children
  - Physiological doses (substitution treatment)
  - Inhalation steroids
    Topical steroids (skin, ears, eyes)
  - Intra-articular, bursal, or intra-tendon injection of steroids
  - Budesonide enteric coating (Entocort®, etc.)

- **Glatiramer acetate Copaxone**® (Sanofi-Aventis) (MS) (www.bcfi.be/www.cbip.be)
- **Selective Estrogen-receptor modulators** (treatment of hormone responsive breast cancer) Clomifen, tamoxifen, toremifen, raloxifen, fulvestrant (www.bcfi.be/http://www.cbip.be)
- **Aromatase-Inhibitors** (estrogen synthesis inhibitors; treatment of hormone responsive breast cancer) Anastrozol, exemestan, letrozol (www.bcfi.be/www.cbip.be)
- **Growth factors** Hematopoietic growth factors (Granulocyte colony- stimulating factors,G-CSF)
- **Antiviral therapy: HIV-drugs, ribavirin, interferon, inosine pranobex**.

  Treatment with interferons can weaken the efficacy of some live-attenuated vaccines (because of the mode of action), but there is no increase in side effects.

5.3 List of medication probably not immunosuppressive

- Hydroxycarbamide (Hydrea®)*
- Monoclonal antibodies against:
  - VEGF (vascular endothelial growth factor)
  - EGFR (epidermal growth factor)
  - Growth factor HER-2

  Anti GD2, AntiPD1, IL2 analogon
- Aflibercep (Eylea®, Zaltrap®)
- Aldesleukine (Proleukin®)
- Bevacizumab (Avastin®)
  Cetuximab (Erbitux®)
  Dinutuximab
- Nivolumab (Opdivo®)
- Panitumumab (Vectibix®)
- Pembrolizumab (Keytruda®)
- Ramucirumab (Cyramza®)
  Trastuzumab (Herceptin®)

** the underlying condition necessitating treatment with Hydroxycarbamide (Hydrea®) can be immunosuppressive.*

6. INFANTS BORN TO A MOTHER WHO RECEIVED IMMUNOSUPPRESSIVE TREATMENT DURING PREGNANCY

Women with IMID need to continue long-term immunosuppressive treatment, even during pregnancy.

Some of these molecules, as well as their metabolites, pass the placental barrier and can be found in newborns for 6-8 months, especially when these medications were administered towards the end of pregnancy. The effects of such prenatal exposure on the development of the newborn's immune system as well as his/her vaccine response need to be taken into account when administering a vaccine. Cheent et al. have described a case in which BCG vaccination resulted in a fatal outcome in a 3-month old infant whose mother had been treated with infliximab during her pregnancy. This case report raised concerns over the potential effects of in utero exposure to biological agents on the development of the immune system in newborns.

Some of the medications used to treat inflammatory autoimmune diseases are contra-indicated during pregnancy due to the risk of teratogenicity. These include methotrexate, mycophenolate mofetil and cyclophosphamide. These molecules will not be discussed in this chapter.
Other medications, such as azathioprine, cyclosporine and dexamethasone, don't induce immunosuppression in newborns.

The active transplacental transfer of immunoglobulins, and, consequently, of biological agents derived from immunoglobulins, begins at around the 13th week of gestation and increases progressively during pregnancy. This transfer peaks during the last 4 weeks of pregnancy, resulting in blood levels in full-term newborns that are equal to 120-130 % of the maternal blood levels. There is strong evidence that the half-life of these biological agents is extended in newborns (infliximab can be found for up to 6-12 months in infants, adalimumab for 3-6 months).

There are currently few data available on the administration of certolizumab, golimumab, abatacept, tocilizumab, rituximab and belimumab to pregnant women.

According to the EULAR (European League Against Rheumatism) recommendations, it is advised to vaccinate infants according to the regular vaccination schedule, including the use of live vaccines, when biological agent treatment was discontinued before the 22nd week of gestation.
If the treatment is continued past the 22nd week, vaccinating with live-attenuated vaccines (BCG, rotavirus, oral polio and MMR) should be postponed until after the age of 6 months (alternatively, medication dosages should be calculated for the newborn if available). Inactivated vaccines can be administered according to the usual vaccination schedule.

ECCO (European Crohn’s and colitis organisation) and WCOG (World congress in gastroenterology) advise to postpone vaccination with live-attenuated vaccines (BCG, rotavirus, oral polio and MMR) for 6 months. Inactivated vaccines can be administered according to the regular vaccination schedule.

Recent research seems to show that children exposed in utero to infliximab or adalimumab treatment develop vaccine responses to tetanus, Hib and pneumococci that are comparable to those in non-exposed children.

Introducing biological treatment of the monoclonal antibody type during breastfeeding has little impact on the newborn as well as his/her vaccine response. In fact, only a few molecules pass into the breastmilk and the low amount that does end up being ingested by the newborn is destroyed by his/her digestive system. As a result, children who are exclusively exposed to biological agents during breastfeeding can be vaccinated with inactivated vaccines and live-attenuated vaccines according to the regular vaccination schedule.

7. VACCINATION OF HOUSEHOLD MEMBERS AND CLOSE CONTACTS OF IMMUNOCOMPROMISED PATIENTS

7.1 Vaccination of household members for better protection of the immunocompromised patients

Household members and healthcare professionals should be vaccinated yearly against **influenza** for protection of the immunocompromised patients. Other vaccines to reduce household transmission include **MMR, pertussis and varicella** vaccines. Vaccination schedule (MMR, pertussis) and a history of varicella should be checked in the household members and vaccination updated if incomplete.

7.2 Safety of administration of live vaccines to close contacts of immunocompromised patients

Except for oral polio, all other **live vaccines** are allowed to **those living under the same roof of the immunocompromised patients**:

Following **precautions** should be taken:

- The vaccinated close contact needs to temporarily avoid contact with the immunocompromised patient if he/she develops a rash after having been vaccinated against measles and/or varicella until the rash disappears.
- It is advisable for the immunocompromised patient to take the appropriate hygienic measures (avoid contact with faeces of infants who have been vaccinated with the rotavirus vaccine) for 4 weeks after vaccine administration.

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9. COMPOSITION OF THE WORKING GROUP

The composition of the Committee and that of the Board as well as the list of experts appointed by Royal Decree are available on the following website: About us.

All experts joined the working group ***in a private capacity***. Their general declarations of interests as well as those of the members of the Committee and the Board can be viewed on the SHC website (site: conflicts of interest).

The following experts were involved in drawing up and endorsing this advisory report. They attended multiple meetings face-to-face during the whole project. The working group was chaired by **Patrick SOENTJENS**; the scientific secretary was Veerle MERTENS.

CHATZIS Olga	Pediatrics	UCLouvain, Brussels
HITES Maya	Internal Medicine, Infectiology, Travel clinic	ULB Erasmus, Brussels
MANIEWSKI Ula	Internal Medicine, Infectiology, Tropical Medicine, Travel Clinic	ITM Antwerp
MARTIN Charlotte	Internal Medicine, Infectiology, Tropical Medicine, Travel Clinic	CHU Saint-Pierre Brussels
PEETERMANS Willy	Internal Medicine, Infectiology, Travel Clinic	University Hospital Leuven
SCHELSTRAETE Petra	Pediatrics, pneumology, vaccinology	University Hospital Ghent
SOENTJENS Patrick	Internal Medicine, Infectiology, Tropical Medicine, Travel Clinic	ITM Antwerp – Defense Brussels
VAN DER HILST Jeroen	Infectiology, Internal Medicine, Travel Clinic	Jessa Hospital Hasselt
VAN DER LINDEN Dimitri	Pediatrics, Infectiology	Saint-Luc Brussels

The following experts were involved in drawing up and reviewing this advisory report.

AERSSENS Annelies	Travel Clinic, Infection Control	University Hospital Ghent
CALLENS Steven	Infectiology	University Hospital Ghent
GOFFARD Christophe		ULB Erasmus
KERRE Tessa	Hematology	University Hospital Ghent
KNOOP Christiane	Pneumology	ULB Erasmus Brussels
LERUT Jan	Abdominal and Transplantation Surgery	UCLouvain Brussels
NAESENS Maarten	Nephrology	University Hospital Leuven
SCHOEMANS Helene	Hematology	University Hospital Leuven

VAN DE VELDE Ann	Hematology	University Hospital Antwerp

The standing working group Vaccination (NITAG) has endorsed the advisory report. The standing working group was chaired by **Yves VAN LAETHEM**; the scientific secretary was Veerle MERTENS.

About the Superior Health Council (SHC)

The Superior Health Council is a federal body that is part of the Federal Public Service Health, Food Chain Safety and Environment. It was founded in 1849 and provides scientific advisory reports on public health issues to the Ministers of Public Health and the Environment, their administration, and a few agencies. These advisory reports are drawn up on request or on the SHC's own initiative. The SHC takes no decisions on the policies to follow, nor does it implement them. It does, however, aim at giving guidance to political decision-makers on public health matters. It does this on the basis of the most recent scientific knowledge

Apart from its 25-member internal secretariat, the Council draws upon a vast network of over 500 experts (university professors, members of scientific institutions), 200 of whom are appointed experts of the Council. These experts meet in multidisciplinary working groups in order to write the advisory reports.

As an official body, the Superior Health Council takes the view that it is of key importance to guarantee that the scientific advisory reports it issues are neutral and impartial. In order to do so, it has provided itself with a structure, rules and procedures with which these requirements can be met efficiently at each stage of the coming into being of the advisory reports. The key stages in the latter process are: 1) the preliminary analysis of the request, 2) the appointing of the experts within the working groups, 3) the implementation of the procedures for managing potential conflicts of interest (based on the declaration of interest, the analysis of possible conflicts of interest, and a Committee on Professional Conduct) as well as the final endorsement of the advisory reports by the Board (ultimate decision-making body of the SHC, which consists of 30 members from the pool of appointed experts). This coherent set of procedures aims at allowing the SHC to issue advisory reports that are based on the highest level of scientific expertise available whilst maintaining all possible impartiality.

The advisory reports drawn up by the working groups are submitted to the Board. Once they have been endorsed, they are sent to those who requested them as well as to the Minister of Public Health and are subsequently published on the SHC website (www.shc-belgium.be), except as regards confidential advisory reports. Some of them are also communicated to the press and to target groups among healthcare professionals.

The SHC is also an active partner in developing the EuSANH network (European Science Advisory Network for Health), which aims at drawing up advisory reports at the European level.

In order to receive notification about the activities and publications of the SHC, you can send a mail to info.hgr-css@health.belgium.be .