–This Clinical Resource gives subscribers
additional insight related to the Recommendations published in–

trc pharmacist's letter ™ trc prescriber's letter ™ trc pharmacy technician's letter ™ trc nurse's letter ™

December 2019 ~ Resource #351203

Vaccinating Immunocompromised Patients

Concerns are raised when a potentially immunocompromised (i.e., immunosuppressed) patient presents for vaccination. The concern with live vaccines is that the patient might contract the disease from the vaccine. Inactivated vaccines cannot cause disease, and some inactivated vaccines are especially recommended for immunocompromised patients. However, depending on the patient's degree of immunocompromise, response to some vaccines may be suboptimal. For some disease states/vaccinations, titers could be used to assess response. It is important to assess the patient's degree of immunocompromise when making vaccine decisions, especially for live vaccines. When in doubt, consult the specialist caring for the patient's immunocompromising condition.[3] If possible, ensure that patients are vaccinated with routine adult vaccinations (plus any others that are specific to their condition) **before** immunocompromise. And keep in mind that several live vaccines have inactivated alternatives (influenza, zoster, typhoid, polio).

--Information in chart may differ from product labeling.--

For help **identifying** which vaccines are **LIVE** and which are **INACTIVATED**, see:

- *Vaccines Licensed for Use in the United States* at https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states.
- *Types and Contents of Vaccines Available for Use in Canada* at https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-15-contents-immunizing-agents-available-use-canada.html#p1c14t1.

Abbreviations: BCG = bacilli Calmette-Guerin; DMARD = disease-modifying antirheumatic drugs; HCT = hematopoietic cell transplant; HPV = human papilloma virus; Hib = *Haemophilus influenzae* type b; IBD = inflammatory bowel disease; LAIV = live attenuated influenza virus; MMR = measles, mumps, rubella; MS = multiple sclerosis; TNF = tumor necrosis factor

Clinical Question	Pertinent Information of Resource
WHO is or might be immunocompromised in the context of vaccination?	• Patients with **cancer** (i.e., cancer affecting the bone marrow or lymphatics, solid tumors).[1,3] • Patients being treated with **chemo** (e.g., alkylating agents, antimetabolites) or **radiation**.[1,3] • Patients receiving certain **biologics** (i.e., ones that are immunosuppressive such as adalimumab or rituximab).[1,3] • **Transplant** patients.[2,3] • Patients with **congenital (primary) immunodeficiency**.[1,3] • Patients receiving large doses of **corticosteroids (see footnote a)**.[1] • HIV patients might be immunocompromised.[2] For help identifying these patients, see **footnote b** resources. • Patients taking **immunosuppressants** (e.g., high-dose methotrexate, azathioprine, or 6-mercaptopurine doses [see footnote a]; calcineurin inhibitors).[3] • Asplenia (increased risk of fulminant bacteremia).[2,4] • Chronic renal disease.[2]

More. . .

3120 W. March Lane, Stockton, CA 95219 ~ Phone: 209-472-2240 ~ Fax: 209-472-2249
pharmacist.therapeuticresearch.com ~ prescriber.therapeuticresearch.com ~ pharmacytech.therapeuticresearch.com ~ nursesletter.therapeuticresearch.com

Clinical Question	Pertinent Information of Resource

Can patients with immunocompromise receive **INACTIVATED** vaccines?	--Also see separate section on **immunosuppressive MEDICATIONS**, below.—
	
	• Because inactivated vaccines cannot replicate, they are safe for immunocompromised patients.[1] However, these patients may not respond as well as immunocompetent patients.[1] Consider the following:
	  • If risk of infectious exposure is low, consider delaying inactivated vaccines until the person is less immunosuppressed.[3]
	  • Review vaccination history and administer any needed vaccines **at least two weeks** before planned immunosuppression to optimize response.[3]
	  • All vaccines are likely effective in patients with asplenia, chronic renal disease, and complement deficiency.[2] For information on efficacy in other disease states, see reference 2.
	• Some inactivated vaccines are especially **encouraged** in immunocompromised patients. For recommendations for specific disease states or conditions (e.g., HCT, solid organ transplant, chronic renal disease, asplenia), see resources in **footnote b**.

Can patients with immunocompromise receive **LIVE** vaccines?	--Also see separate section on **immunosuppressive MEDICATIONS**, below.-- **General concepts**: Avoid live vaccines unless immunocompromise is mild, data supports use of the vaccine, and the risk of natural infection is greater than the risk of immunization.[3] Live vaccines should not be given to severely immunocompromised patients, or if immune status is uncertain.[1,3] The ultimate determination of severe immunocompromise should be made by the provider treating the patient's immunocompromising condition.[1] **Special disease-considerations (medications are discussed below)**: • Some patients with **B-cell deficiency** may receive certain live vaccines.[1,3] For details, see resources in **footnote b**. • Live vaccines are **not** contraindicated in patients with **complement deficiency**.[2,3] • **HCT**: Live vaccines should not be given within four weeks of the onset of the pre-transplant conditioning regimen.[3] BCG should never be given to any patient who may need an HCT.[3] MMR and varicella vaccines can be given to HCT recipients 24 months post-transplant, assuming immunocompetence.[1] • **Solid organ transplant**: live vaccines should be given at least four weeks prior to transplant.[3] Live vaccines are generally contraindicated post-transplant.[3] • **Asplenia**: only LAIV (e.g., *FluMist*) is contraindicated (U.S.).[2] • **Chronic renal disease**: only LAIV (e.g., *FluMist*) is contraindicated (U.S.).[2] • **HIV** patients who are **not** severely immunocompromised can get MMR, varicella, zoster, and rotavirus.[2,3] For help identifying these patients, see resources in **footnote b**.

More. . .

Clinical Question	Pertinent Information of Resource

Can patients receiving immunosuppressive **MEDICATIONS** receive vaccines?
 	
Continued…
	General concepts
	• Because **inactivated** vaccines cannot replicate, they are safe for immunocompromised patients.[1] However, these patients may not respond as well as immunocompetent patients.[1] Consider the following:
	  • Review vaccination history and administer any needed **inactivated** vaccines **at least two weeks** before planned immunosuppressive therapy to optimize response.[3]
	  • In addition to vaccines recommended as for immunocompetent patients, **pneumococcal** vaccines are recommended.[2,3] For patients ≥18 years of age (U.S., ≥19 years of age), give *Prevnar 13*, then *Pneumovax 23* at least 8 weeks later.[11,12]
	  • **Recombinant zoster vaccine** (e.g., *Shingrix*) is now recommended for all **psoriasis** and **psoriatic arthritis** patients, including those <50 years of age before (preferably) or during immunosuppressive therapy, especially systemic corticosteroids, tofacitinib, or combination systemic immunosuppressives.[10] Consider for **rheumatoid arthritis** patients.[5] It is also appropriate for patients receiving non-immunosuppressive corticosteroid doses (**see footnote a**), and other low-dose immunosuppression (see below).[7]
	  • For patients already on immunosuppressive therapy:
	  • Data suggests efficacy of influenza, pneumococcal, tetanus, hepatitis B, hepatitis A, HPV, and perhaps recombinant zoster vaccines (e.g., *Shingrix* [unknown for high-level immunosuppression]) given during immunosuppression.[5,8,10]
	  • If risk of infectious exposure is low, consider delaying inactivated vaccines until the person is less immunosuppressed.[3]
	  • If the patient is vaccinated during immunosuppression, consider checking titers once the drug is discontinued to guide whether vaccination requires repeating.[3]
	  • In chemo patients, expect vaccines to be held during chemo, although an inactivated vaccine (e.g., influenza) might be given between cycles. Patients might be revaccinated with vaccines given during chemo when chemo is over.[2] Each center will have protocols.
	  • Canada: double the usual hepatitis B vaccine dose, and use a 3- or 4-dose schedule.[3]
	  • HPV vaccine (e.g., *Gardasil 9*) should be given using a 3-dose schedule.[3,12]
	• In general, **live vaccines** should be avoided in patients receiving high-level immunosuppressive therapy (see **footnote a**).[1,3] Give any needed **live** vaccines **at least four weeks before** planned immunosuppressive therapy to reduce risk of acquiring an infection from the vaccine.[3]
	  • **Varicella** vaccination is recommended for susceptible patients before IBD immunosuppressive therapy is started.[8]
	
	Specific medications:
	• Consult prescribing information/product monographs for **MS** therapies for guidance. Also see below concerning use of alemtuzumab for cancer.

More. . .

Clinical Question	Pertinent Information of Resource

Can patients receiving immunosuppressive **MEDICATIONS** receive vaccinations, continued	• **Low-level immunosuppression** (**see footnote a**): varicella can be given.[3] Other live vaccines can be given after a risk/benefit assessment (e.g., MMR before travel).[3,5] Consult an expert if immunosuppressants are used in combination.[3]
	• **High-level immunosuppression** (**see footnote a**): IBD guidelines recommend a three-month washout of immunosuppressive therapy before giving live vaccines (four months for the yellow fever vaccine).[8]
	• **Biologics**: Live vaccines should be avoided in patients receiving biologics (e.g., therapeutic monoclonal antibodies, [e.g., adalimumab, etanercept, infliximab, etc], lymphocyte-depleting agents).[1]
	  • Rheumatologic experts recommend a washout of two to three half-lives before giving live vaccines (at least four weeks) and restarting two to three half-lives after administration of live vaccines (at least one to two weeks).[6] Other experts specifically recommend waiting one month after discontinuing etanercept, and three months after discontinuing other anti-TNF agents before administering a live vaccine.[1] IBD guidelines recommend a three-month washout from high-level immunosuppressive therapy (**see footnote a**) (four months for the yellow fever vaccine).[8]
	  • **Rituximab** may cause prolonged immunosuppression.[1] Some experts advise waiting at least six to 12 months after treatment to vaccinate.[3,5] B cell enumeration is generally performed during rituximab therapy and should be reviewed prior to immunization.[3] Although data is lacking, some experts would recommend waiting at least four weeks after vaccination to restart rituximab.[1,5]
	• If a **cancer** patient is at least three months post-**chemo/radiation**,[1-3] cancer is in remission, and T cell function is normal, live vaccines can be given.[3] Alemtuzumab is an exception, it may cause prolonged immunosuppression.[1]
	• Live vaccines should be deferred for at least one month after stopping an **immunosuppressive corticosteroid** dose (**see footnote a**).[1,3] IBD and MS guidelines recommend a three-month washout.[8,9]

Can **HOUSEHOLD CONTACTS** of immunocompromised patients receive LIVE vaccines?	• Household contacts may receive MMR, varicella, rotavirus, and LAIV (e.g., *FluMist*).[1,3] See resources in **footnote b** for other vaccines recommended for contacts.
	  • If a recipient of the varicella or zoster vaccine develops a rash, they should keep the rash covered and avoid direct contact with the immunocompromised person until the rash has cleared.[3,5]
	  • LAIV (e.g., *FluMist*) is contraindicated in close contacts and caregivers of severely immunocompromised patients (e.g., HCT recipients requiring hospital isolation). Healthcare workers and visitors who have received LAIV should avoid contact with severely immunocompromised patients for seven days after vaccination.[13] Per Canadian guidance, recipients should avoid close contact with severely immunocompromised patients (e.g., HCT recipients requiring hospital isolation) for two weeks after vaccination.[3]
	  • Immunocompromised patients should avoid handling diapers of infants within the first month of infant rotavirus vaccination.[5]

More. . .

a. **Immunosuppressive steroid dose (i.e., high-level immunosuppression dose)**: prednisone ≥20 mg daily or ≥2 mg/kg daily (or equivalent) for ≥14 days.[1,3] This does **NOT** include alternate-day regimen; rapid tapers; short (<14 day) high-dose regimen; topicals; physiologic replacement doses; or intra-articular, bursal, or tendon injection.[1-3] Live vaccines can be given to patients receiving inhaled corticosteroids (Canada: with the exception of LAIV, which should not be given to patients with severe asthma receiving high-dose inhaled corticosteroids).[1,3]
Low-level immunosuppression examples: methotrexate ≤0.4 mg/kg/week, azathioprine ≤3 mg/kg/day, or 6-mercaptopurine ≤1.5 mg/kg/day).
High-level immunosuppression examples: immunosuppressive corticosteroid dose (see above), methotrexate >0.4 mg/kg/week, azathioprine >3 mg/kg/day, or 6-mercaptopurine >1.5 mg/kg/day; adalimumab, certolizumab, etanercept, golimumab, infliximab, natalizumab, vedolizumab.[1,3,8]

b. **Additional resources**:
   - **U.S.**: Altered immunocompetence. General best practice guidelines for immunization: best practices guidance of the Advisory Committee on Immunization Practices (ACIP). (https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html).
   - **U.S.**: CDC Recommended Adult Immunization Schedule (https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf).
   - **Canada**: Canadian Immunization Guide, Immunization of Immunocompromised Persons (https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html#t5).

More. . .

Project Leader in preparation of this clinical resource (351203): *Melanie Cupp, Pharm.D., BCPS; Last modified September 2021.*

References

1. CDC. Epidemiology and prevention of vaccine-preventable disease (The Pink Book). 13th edition (2015). Chapter 2: General recommendations on immunization. April 15, 2019. https://www.cdc.gov/vaccines/pubs/pinkbook/genrec.html#contraindications. (Accessed October 1, 2019).
2. CDC. Altered immunocompetence. General best practice guidelines for immunization: best practices guidance of the Advisory Committee on Immunization Practices (ACIP). Last reviewed August 20, 2019. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html. (Accessed October 2, 2019).
3. Public Health Agency of Canada. Canadian Immunization Guide: Part 3-vaccination of specific populations. Immunization of immunocompromised persons. May 2018. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-8-immunization-immunocompromised-persons.html. (Accessed September 10, 2021).
4. Public Health Agency of Canada. Canadian Immunization Guide: Part 3-vaccination of specific populations. Immunization of persons with chronic diseases. July 2015. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations/page-7-immunization-persons-with-chronic-diseases.html#p3c6a11. (Accessed October 2, 2019).
5. Furer V, Rondaan C, Heijstek MW, et al. 2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis* 2019 Aug 14. doi: 10.1136/annrheumdis-2019-215882.
6. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol* 2019;80:1029-72.
7. Dooling KL, Guo A, Patel M, et al. Recommendations of the Advisory Committee on Immunization Practices for use of herpes zoster vaccines. *MMWR Morbid Mortal Wkly Rep* 2018;67:103-8.
8. Farshidpour M, Charabaty A, Mattar MC. Improving immunization strategies in patients with inflammatory bowel disease. *Ann Gastroenterol* 2019;32:247-56.
9. Farez M, Correale J, Armstrong MJ, et al. Practice guideline update summary: vaccine-preventable infections and immunization in multiple sclerosis: report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. *Neurology* 2019;93:584-94.
10. Baumrin E, Van Voorhees A, Garg A, et al. A systematic review of herpes zoster incidence and consensus recommendation on vaccination in adult patients on systemic therapy for psoriasis or psoriatic arthritis: from the Medical Board of the National Psoriasis Foundation. *J Am Acad Dermatol* 2019;81;102-10.
11. Public Health Agency of Canada. Canadian Immunization Guide: Part 4-Acitve Vaccines. Pneumococcal vaccine. October 2016. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-16-pneumococcal-vaccine.html#tb3. (Accessed October 2, 2019).
12. CDC. Recommended adult immunization schedule for ages 19 years or older. 2019. https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf. (October 2, 2019).
13. CDC. Prevention and control of seasonal influenza with vaccines: recommendations of the advisory committee on immunization practices, United States, 2021-22 influenza season. August 27, 2021. https://www.cdc.gov/mmwr/volumes/70/rr/rr7005a1.htm. (Accessed September 10, 2021).

Cite this document as follows: **Clinical Resource,** ***Vaccinating Immunocompromised Patients. Pharmacist's Letter/Prescriber's Letter.*** **December 2019.**

trc pharmacist's letter ™ trc prescriber's letter ™

Evidence and Recommendations You Can Trust…

trc pharmacy technician's letter ™ trc nurse's letter ™

3120 West March Lane, Stockton, CA 95219 ~ TEL (209) 472-2240 ~ FAX (209) 472-2249