Vaccinations
and Tocilizumab Therapy

Evidence Based Medicine | Official recommendations | Expert opinion

Rheumatoid arthritis (RA) does not contraindicate vaccinations and, in the absence of immunosuppressive therapy, the response to vaccines is adequate [84]. If a potentially immunosuppressive agent is used, potential safety issues raised by vaccines should be discussed.

As with all biological therapies, the immunisation history of patients given tocilizumab therapy should be checked at several points in time, as indicated below.

- before tocilizumab therapy initiation (more specifically, routinely check whether the **mandatory immunisations**, are up to date, particularly those against tetanus and poliomyelitis, and whether the **recommended immunisations** have been performed as appropriate given the patient's characteristics);
- when changing from one biological agent to another;
- every year in late summer;
- and in the event of travel abroad.

Vaccines that should be recommended prior to tocilizumab initiation

Always check that the mandatory immunisations (particularly those against tetanus and poliomyelitis) are up to date and that recommended immunisations have been performed as appropriate given the patient's characteristics. The appropriate vaccines should be administered if needed (according to the modalities described in "Vaccination with a live attenuated vaccine" and "Vaccination with an inactivated vaccine").

In the fall, when tocilizumab therapy is considered, the influenza vaccine is recommended.

Administration of the pneumococcal vaccine is recommended every 3 to 5 years, particularly in patients with risk factors for lung infections. Pneumococcal vaccination is not contraindicated in patients who have a history of confirmed or unconfirmed pneumococcal infection. The pneumococcal vaccine can be administered at the same time as the influenza vaccine (if appropriate), at a different injection site.

Which immunisations should be performed in patients who are switched from another biological agent to tocilizumab?

The recommendations about immunisations are similar across biological agents. Therefore, the immunisation strategy used when continuing the same biological agent applies also to switching from one biological agent to another.

Which immunisations should be performed in patients on long-term tocilizumab therapy?

Check regularly that the mandatory immunisations (particularly those against tetanus and poliomyelitis) are up to date, as well as the immunisations that are appropriate to the patient's history.

Administration of the influenza vaccine should be recommended in the fall and of the pneumococcal vaccine every 3-5 years.

Should immunisations be offered to close contacts of the patient?

Immunisation of close contacts (children and grandchildren) may be considered (particularly the influenza vaccine) to diminish the risk of contamination of the patient on tocilizumab therapy.

Immunisation with live attenuated vaccines

The live attenuated vaccines are listed below.

- BCG
- Yellow fever
- Measles-Mumps-Rubella (MMR)
- Oral polio (reserved for outbreaks)
- Varicella

Modalities of immunisation with live attenuated vaccines before tocilizumab initiation

Live attenuated vaccines that need to be administered prior to tocilizumab therapy initiation should be given at a time when the patient has no immune deficiency (i.e., is no longer under the effect of any prior biological treatments). The immunisation should be performed **at least 2 weeks, and ideally 4 weeks,** before tocilizumab initiation.

In practice, the issue of greatest concern is yellow fever immunisation. Always ask the patient about trips to areas of yellow fever endemicity, before and during tocilizumab therapy. In patients who are likely to travel in the near- or mid-term

to countries where yellow fever immunisation is mandatory, the vaccine (which is effective for 10 years) should be given after the immunosuppressive effects of any prior treatments have worn off, **at least 2 weeks, and ideally 4 weeks,** before starting tocilizumab therapy.

If the patient is taking methotrexate therapy, the yellow fever vaccine can be given provided the CD4+ cell count is higher than 250/mm3. Otherwise, methotrexate therapy should be discontinued before administering the vaccine.

● Can live attenuated vaccines be given to patients on tocilizumab therapy?

Both the safety and the efficacy of live attenuated vaccines are of concern in patients who are receiving biological agents.

As with other biotherapies, live attenuated vaccines are contraindicated in tocilizumab-treated patients, given the risk of treatment-related loss of attenuation of the vaccine micro-organism, which warrants the utmost caution.

Live attenuated vaccines should not be given concomitantly with tocilizumab therapy, as no clinical safety data are available for this combination. There are no available data on secondary transmission of the vaccine microorganism from patients immunised with live attenuated vaccines to tocilizumab-treated patients. Neither are any reliable data available about potential effects of tocilizumab on viraemia levels or reactions to live vaccines. Antibody production in response to prophylactic immunisation may be altered. However, any effects on antibody production do not seem greater with tocilizumab than with conventional DMARDs or TNF antagonists [85, 86].

● What are the modalities for administering live attenuated vaccines in tocilizumab-treated patients?

When a live attenuated vaccine is required in a tocilizumab-treated patient, **the treatment should be stopped at least 70 days (5 times the half-life) before administration of the vaccine.** The recommended interval **from vaccine administration to tocilizumab re-treatment is 2 weeks at least and 4 weeks ideally.**

Immunisation with inactivated vaccines

The main inactivated and component vaccines are listed below.

- Influenza
- Pneumococcus
- Meningococcus
- Haemophilus influenza
- Hepatitis A and hepatitis B
- Combined Diphtheria-Tetanus-Polio-Pertussis-*Haemophilus influenza* b,
- Typhoid fever
- Injectable polio

● What are the modalities for administering inactivated vaccines in tocilizumab-treated patients?

The concern with inactivated vaccines is effectiveness. Therefore, inactivated vaccines and component vaccines can be administered during tocilizumab therapy (the worst-case scenario is a decrease in vaccine effectiveness).

When an inactivated vaccine is required in a tocilizumab-treated patient (e.g., the influenza vaccine in the fall), the vaccine can be given at any time, and there is no need to postpone the next tocilizumab infusion.

Although the effectiveness of inactivated vaccines in tocilizumab-treated patients is somewhat uncertain, studies with other biological agents have established that these vaccines can induce an immune response. Thus, the risk/benefit ratio is in favour of administering inactivated vaccines if needed.