



Management of vaccinations

Evidence-based Medicine

Official Recommendations

Expert opinion

RA does not contraindicate the administration of vaccines, and the response to vaccines is adequate in the absence of immunosuppressive treatment (86).

According to most of national guidelines, live attenuated vaccines are contraindicated during abatacept therapy (20).

● **The available live attenuated vaccines are listed below.**

- BCG
- Measles-mumps-rubella (MMR)
- Varicella
- Yellow fever
- Oral polio (reserved for outbreaks)

Live attenuated vaccines against herpes zoster and influenza administered via the nasal route will be available in the near future.

Inactivated vaccines can be administered to patients on abatacept therapy. The available inactivated vaccines are listed below:

- Injectable flu vaccine
- Hepatitis A and B
- Combined diphtheria-tetanus-polio-pertussis-*Haemophilus influenzae* b (used in pediatric patients)
- Combined diphtheria-tetanus-polio-acellular pertussis vaccine (used in adults),
- Invasive meningococcal disease
- Pneumococcus
- Typhoid fever
- Injectable polio vaccine

Vaccines that should be given before initiation of abatacept therapy

- The patient's immunization history should be reviewed to ensure that all necessary vaccines are given before initiation of abatacept therapy, particularly the MMR vaccine in pediatric patients (and the varicella vaccine in children who have not had the disease). The MMR and varicella vaccines are also recommended in patients with negative serological tests for these diseases.
- If the intradermal tuberculin test is negative, the BCG vaccine is formally contraindicated before starting the biological agent (risk of local or systemic BCG dissemination).
- The pneumococcal vaccine should be offered routinely, particularly in high-risk patients (e.g., splenectomy, chronic lower respiratory tract disease, diabetes, elderly institutionalized patients) in whom biological therapy has been deemed appropriate after a careful evaluation. A new conjugate 3-valent vaccine has been licensed for use in pediatric patients younger than 2 years of age and is

being evaluated in adults.

- The hepatitis B vaccine has been recommended by the European Association for the Study of the Liver (87) in patients who require immunosuppressant therapy. This recommendation can be applied to patients scheduled for abatacept therapy, most notably in the presence of risk factors.
- The patient should be asked about possible trips planned for the short or medium term to countries where the yellow fever vaccine is mandatory. In this case, the yellow fever vaccine, which is effective for 10 years, should be given at an accredited center at least 3 weeks before starting abatacept therapy. However, no studies have specifically addressed this issue.
- The annual flu vaccine should be offered routinely.
- To date, the available information is not sufficient to support the administration of the *Haemophilus influenzae* type b vaccine, which may, however, be considered in the patients at highest risk.

Vaccines that should be offered during long-term abatacept therapy

- Inactivated vaccines can be administered.

During abatacept therapy, the antibody response is slightly blunted but inactivated vaccines nevertheless seem to be effective in most cases in terms of antibody production (21, 88-92). Boosters of inactivated vaccines should therefore be given at the scheduled dates without discontinuing abatacept therapy.

- The annual flu vaccine should be offered routinely.
- To date, the available information is not sufficient to support the administration of the *Haemophilus influenzae* type b vaccine, which may, however, be considered in the patients at highest risk.
- **Live vaccines are contraindicated.**

Yellow fever raises the most challenging vaccination problems. The experts made the following recommendations:

- Patients should ask whether the yellow fever vaccine is mandatory before planning trips to foreign countries
- In the event of a trip to countries where the yellow fever vaccine is mandatory, the risk/benefit ratio should be evaluated carefully by a physician who is specialized in immunization issues.

This physician may recommend an interruption in the abatacept schedule:

- For instance, after at least 5 times the abatacept half-life, i.e., about 3 months, administration of the yellow fever vaccine can be considered
- Followed by a waiting period of at least 3 weeks and preferably 4 weeks (the duration of viral replication) before re-starting abatacept therapy

Similarly, when the yellow fever vaccine must be administered to a patient on methotrexate therapy, an interruption of methotrexate should be considered:

- For instance, the vaccine can be given after a treatment-free period that allows clearance of methotrexate from the body. There is no consensus on the optimal duration of this treatment-free

period. It ranges from 1 to 3 months, depending on the situation and most notably on the degree of immunosuppression in the individual patient

- Followed by a waiting period of at least 3 weeks and preferably 4 weeks (the duration of viral replication) before re-starting methotrexate therapy

In case of an emergency requiring immediate travel to an area where yellow fever is endemic, a certificate indicating that the yellow fever vaccine is contraindicated can be established in accredited centers; this measure will avoid denial of entry into the country or vaccination at the border (which is useless, as 10 days are required to achieve immunization). In this extremely rare situation, prophylaxis is based on protection from the vector (mosquito nets, effective repellants). The patient must be clearly informed of the risk, given the high mortality rate of yellow fever, around 30% to 40%.

Vaccines that should be offered when switching from a TNF antagonist to abatacept

The advice regarding vaccines is the same for abatacept and TNF antagonists. Consequently, the management in the event of a switch is identical to that in the event of continued treatment with the same drug.