

Guidance from the EADV Task Force Autoimmune Blistering Diseases during the COVID-19 pandemic

The EADV Task Force Autoimmune Blistering Diseases supports patients and their families during this difficult period of COVID-19 pandemic and provides the following advices:

Follow carefully the general recommendations regularly updated by the governments of your country.

The following **Common Practical Advice** has been modified from the **European League Against Rheumatism (EULAR)**, the largest European Society for patients with autoimmune and inflammatory diseases. Regular updates can be found on:

www.eular.org/eular_guidance_for_patients_covid19_outbreak.cfm

Simple measures are likely to help to preserve your health and that of your family and friends:

- Regularly and thoroughly clean your hands with an alcohol-based hand rub or wash with soap and water for at least 20 seconds. Dry hands thoroughly afterwards.
- Try to avoid touching your face.
- Coughing or sneezing should be into an elbow or tissue paper and the latter should be discarded safely.
- Use disposable tissues.
- Wear a **mask** when
 - you are taking immunosuppressive drugs (see below) when being outside your flat/house
 - you are ill with coughing and sneezing
 - advised by national or local authorities

The mask cannot completely prevent virus transmission, but it reduces it and is a good reminder of not touching your face.

Details on how to put the mask on and how to dispose it can be found on the WHO website: www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/when-and-how-to-use-masks

- Practice sensible social distancing.
- We should greet each other without shaking hands and avoid hugs.
- Try to avoid busy public transport.
- Avoid receiving visits to your home from family or friends with respiratory symptoms
- Contact your doctor as soon as symptoms of respiratory tract infection appear (fever, cough, rhinitis)

- For contact with your doctor use, when possible, telemedicine or visits by phone except for clinical or therapeutic needs.
- Do not embark on unnecessary travel. Avoid travelling to certain geographical areas – please pay attention to public health advice to guide you in this.
- When you are taking immunosuppressive drugs (see below) reduce contact with others as much as possible (except household members and close family).

It has not (yet) been described that patients with an autoimmune blistering disease have a higher risk to be infected with SARS-CoV-2, the virus causing COVID-19, compared to healthy individuals. However, this is possible due to the immunosuppressive nature of the autoimmune disease itself.

Patients with the following **risk factors** are likely to be infected with SARS-CoV-2 and develop more severe COVID-19, in particular a more severe lung involvement:

- Cardiovascular illnesses including arterial hypertension
- Diabetics
- Renal failure
- Respiratory failure
- Pulmonary arterial hypertension
- Morbid obesity
- Patients over 70 years of age
- **Immunosuppressive drugs**

Immunosuppressive drugs that increase the risk for more severe COVID-19 are:

- Rituximab, within the last 1 year
- azathioprine
- mycophenolate mofetil
- mycophenolic acid
- methotrexate
- cyclosporine
- cyclophosphamide
- corticosteroids (prednis[ol]one > 10 mg/day)

Immunosuppressive drugs are useful to prevent a worsening of your autoimmune blistering disease. When you stop these drugs, you may experience a flare-up. **At present, we therefore advise you not to stop or reduce your medication at this time, unless your physician tells you otherwise for a specific reason.**

Some data in other autoimmune diseases do suggest that immunosuppressive drugs do not increase the risk for more severe COVID-19 diseases. In contrast, recent data about pemphigus patients indicate a more severe COVID-19 disease in patients with prednisolone >10 mg/d or after recent rituximab. During the pandemic, we therefore do not recommend the use of rituximab as maintenance therapy to prevent relapses.

If you have symptoms such as fever or persistent cough, you may need to be tested for coronavirus. If these symptoms are present, you should follow the national advice for access to health care, often via phoning to advice hotlines.

If you are positive for COVID-19, please discuss this with your doctor or dermatologist. Depending on the activity and severity of your autoimmune blistering disease it may be advisable to temporarily stop the following immunosuppressants during COVID-19:

- azathioprine
- mycophenolate mofetil
- mycophenolic acid
- methotrexate
- cyclosporine
- cyclophosphamide

In addition, your corticosteroid dose may be reduced.

The decision if and how to modify your immunosuppressive regimen depends on multiple factors including the severity of your autoimmune blistering diseases, your past medical history, your additional diseases (co-morbidities), age, and severity of COVID-19.

At the time being, no general guidance how your immunosuppressive regimen needs to be modified can be given. This decision needs to be taken in close cooperation between your treating physician/ dermatologist and the physician in charge of your COVID-19 infection.

The following medication for autoimmune blistering diseases is unlikely to increase your risk for infection or more severe COVID-19:

- dapsone
- sulfapyridine
- antibiotics (e.g. doxycycline, tetracycline)
- antihistamine

Meantime, if not already done, it would be wise to undertake or complete vaccination protection according to national guidelines, at present with priority against influenza and pneumococcus.

Preliminary communications made by Chinese and European colleagues report cases of purpura, erythema multiforme, erythema nodosum, chilblain-like lesions, urticarial, chickenpox-like vesicles, and rashes affecting predominantly the face in patients with COVID-19. The overall incidence of cutaneous manifestation was around 5% in China, while in Italy up to 20% of hospitalized cases appear to show some cutaneous, often nonspecific, skin rashes.

Vaccination against SARS-CoV2

Two SARS-CoV-2 vaccines have been approved by European Medicines Agency (EMA) so far, the vaccine from Biontech/Pfizer and from Moderna. Both vaccines are based on the mRNA technology. By this technology, the genetic information to produce the coronavirus spike (S) protein, that is important for the entry of the coronavirus to human cells, i.e. the infection, is coded on small parts of genetic molecules, the so-called messenger ribonucleic acid (mRNA). During the vaccination mRNA with the genetic information of the coronavirus S protein is provided to the person to be vaccinated. The vaccinated individual will produce for some time the coronavirus S protein which is then recognized by the immune system. Subsequently, immune cells and neutralizing antibodies are produced that can immediately attack the SARS-CoV2 virus in case of contact with the virus. In this case, COVID-19 disease is prevented or the COVID-19 disease is much milder than without vaccination.

Both vaccines are so called non-live vaccines, which mean that they cannot transfer you COVID-19 since only a single protein of the coronavirus is injected. The vaccines also will not change your genetic information nor is the genetic information for the coronavirus S protein integrated in your genes.

Both vaccines can be used safely in patients with AIBD also when under treatment with immunomodulating or immunosuppressive drugs (see above). **Vaccinations should preferably be given when the AIBD disease is in a quiet phase; it is also preferred to vaccinate before planned immunosuppression if feasible.** A vaccination is most effective when the amount of, or level of immunosuppression is low; however, the risk of a flare of the AIBD disease is real, and therefore it is not advised to decrease your immunomodulating or immunosuppressive drugs before being vaccinated.

Provisional observations may disfavour vaccination within three months after application of rituximab since earlier vaccination may not be fully effective.

At present, it is still advised for vaccinated individuals to adhere to all above mentioned preventive measures until more information are available if the vaccinated person can still transfer the SARS-CoV2 virus to non-immune individuals.

In summary, **it is recommended that every AIBD patient from an EU country is vaccinated with one of the EMA-approved vaccines** to prevent COVID-19.

Online registry for patients with COVID-19

The EADV task force has initiated a registry for AIBD patients that suffered from confirmed COVID-19. The aim of the registry is to gather epidemiological information about patients that became infected, determine whether certain medication or co-morbidities are associated with the infection, and record the severity of the COVID-19 disease. These data will be valuable in estimating the risk of our patients and may advise us on future recommendations.

We would like to encourage every dermatologist/physician to include these patients online (<https://recovab.umcg.nl>). The registry is hosted and managed in Groningen, The Netherlands (Barbara Horvath, Joost Meijer) and **open to every physician worldwide**.

Knowledges concerning COVID-19 are in constant progression, and information concerning treatments will have to be updated according to international research.

Summary

The EADV Task Force *Autoimmune Blistering Diseases* recommends the following:

- Look for, and abide by, the advice offered by your **national public health care system**, as they will have the most up to date information that is tailored for the circumstances in different regions.
- Adhere to the advices given for every individual shown above (**simple measures**)
- **Do NOT stop or modify by yourself your treatment: a relapse of your disease can be more severe than an infection with COVID-19**
- In case of COVID-19 infection modification of your treatment needs to be done in close collaboration between the physician/dermatologist managing your autoimmune blistering disease and the physician treating COVID-19.
- **It is recommended that every AIBD patient from an EU country is vaccinated with one of the EMA-approved vaccines**
- We recommend including all AIBD patients with confirmed COVID-19 in the **online registry** (<https://recovab.umcg.nl>) initiated by the EADV task force.