

## Update: Using rheumatology drugs for COVID-19

This is the lay version of the EULAR points to consider on the use of medicines traditionally used in rheumatology to treat the inflammation seen in people with severe COVID-19. The original publication can be downloaded from the EULAR website: [www.eular.org](http://www.eular.org).

Alunno A, et al. 2021 update of the EULAR points to consider on the use of immunomodulatory therapies in COVID-19. *Ann Rheum Dis* 2021;80:221–366. [doi:10.1136/annrheumdis-2021-221366](https://doi.org/10.1136/annrheumdis-2021-221366)

### Introduction

EULAR recommendations give advice to doctors, nurses and patients about the best way to treat and manage diseases. EULAR has updated the points on the pathophysiology of COVID-19 and the use of immunomodulatory therapies to treat it. Based on the low level of evidence available for this topic, it was not possible to develop full recommendations, and the work has been presented instead as ‘points to consider’.

Doctors, other health professionals and patients worked together to develop this advice. The patients in the team ensured that the patient point of view was included. The authors looked at the evidence on COVID-19 infection, and the use of different therapies that act on the immune system.

### What do we already know?

COVID-19 is the disease caused by infection with the SARS-CoV-2 virus. Since it emerged at the end of 2019, this virus has caused a global pandemic. COVID-19 can be mild, or even without symptoms at all. But it can also cause severe disease, leading to respiratory problems, organ failure, and death. Research on the immune mechanisms involved in people with severe COVID-19 has shown that they have widespread inflammation.

Many medicines used in rheumatology are anti-inflammatory or immunomodulatory drugs. They are designed to treat the inflammation caused by autoimmune diseases such as rheumatoid arthritis, where the body’s immune systems attacks its own tissues. New research is looking at how these medicines might be used to treat people with COVID-19. EULAR previously provided a framework to optimize the use of immunomodulatory therapies for the care of people with COVID-19. The first EULAR-endorsed points to consider on this topic were developed in 2020. Evidence is changing very quickly, and the points have been updated to include the most recent literature available.

These findings do not apply to people living with rheumatic and musculoskeletal diseases (RMDs) who are taking immunomodulatory treatments for their rheumatic disease. Separate recommendations are available for the management of people with RMDs in the context of the pandemic.

### What do the points say?

In total, there are two overarching principles and 12 points to consider. The principles are unchanged from the earlier publication, and stress that the picture of SARS-CoV-2 infection can be very different in different people. Infections range from asymptomatic or mild disease to severe or fatal. People with COVID-19 may need different treatment approaches, including antiviral medicines, oxygen therapy, anticoagulation and/or immunomodulatory treatment at different stages of the disease.

The 12 points to consider focus on immunomodulatory therapy, and how we might use existing medicines from the field of rheumatology to treat severe COVID-19. Overall, 4 of the 12 points are unchanged from the 2020 version, 4 are modified, and 4 are new. WHO has validated the use of two types of immunomodulators in severe and critical COVID-19: corticosteroids and anti-IL-6 receptor antibodies.

Each point is based on the best current knowledge and studies of scientific evidence or expert opinion. The more stars a point has the stronger the evidence is. However, points to consider with limited scientific evidence may still be important, because the experts can have a strong opinion even when the published evidence may be lacking.

One star (\*) means it is a point with limited scientific evidence.

Two stars (\*\*) means it is a point with some scientific evidence.

Three stars (\*\*\*) means it is a point with quite a lot of scientific evidence.

Four stars (\*\*\*\*) means it is a point supported with a lot of scientific evidence.

- **In people with COVID-19 who do not need hospitalisation, there is currently no evidence to support using an immunomodulatory therapy.\*\*\* (unchanged)**

Mild or moderate COVID-19 that does not require hospitalisation does not respond to immunomodulatory medicines. At the moment, the evidence suggests that these work only for severe COVID-19 where there is a severe systemic inflammatory state. Research is looking at anti-viral medicines to treat people outside the hospital setting.

- **In people hospitalised for COVID-19 who do not need oxygen therapy there is currently no evidence to support starting immunomodulatory therapy.\*\*\* (unchanged)**

There is no evidence to support using immunomodulatory drugs in people hospitalised for COVID-19 if they do not need oxygen therapy. For those who do need oxygen, there are specific guidelines below.

- **In people with COVID-19 who need supplemental oxygen or ventilation, systemic glucocorticoids should be used since they can decrease mortality.\*\*\* (unchanged)**

For people who are in hospital because of COVID-19 and need to be given oxygen – or need ventilation to help them breathe – there is evidence that using immunomodulatory glucocorticoids can reduce the number of people who die. The drug with the most evidence to support this is dexamethasone, which is a steroid that can help to reduce inflammation.

- **Hydroxychloroquine should be avoided for treating any stage of COVID-19.\*\*\* (unchanged)**

Early on in the pandemic, a rheumatology drug called hydroxychloroquine was proposed as a possible treatment. However, the evidence does not support this. It does not look like hydroxychloroquine provides any additional benefit to the standard of care, and could worsen the prognosis in more severe infections, particularly if given with azithromycin.

- **In people with COVID-19 who require oxygen or ventilation, combination treatment with glucocorticoids and tocilizumab should be considered.\*\*\* (modified)**

A combination of glucocorticoids and tocilizumab can reduce disease progression and mortality in COVID-19. More data are needed to fully appreciate the effect of other IL-6R inhibitors.

- **There is no robust evidence to support the use of anakinra at any disease stage.\*\*\* (modified)**  
There has been conflicting evidence about the use of anakinra for people with severe COVID-19, and nothing to support its use in any stage of COVID-19.
- **There is no robust evidence to support the use of low-dose colchicine at any disease stage.\*\*\* (new)**  
Since the 2020 publication, there has been new evidence from two trials, but the results were not solid enough to recommend in favour of colchicine.
- **In people with COVID-19 who need non-invasive ventilation or high-flow oxygen, the combination of glucocorticoids and baricitinib or tofacitinib could be considered.\*\*\* (modified)**  
Baricitinib or tofacitinib can decrease the time to recovery and speed up improvement, and can be considered in some people with severe COVID-19 who need non-invasive ventilation or high-flow oxygen to help them breathe.
- **Ongoing trials mean it is not possible to recommend the use of GM-CSF inhibitors in COVID-19.\*\*\* (new)**  
GM-CSF inhibitors (mavrilimumab, otilimab, and lenzilumab) are being investigated in clinical trials, but there is not yet enough evidence to recommend their use to treat COVID-19.
- **People without hypogammaglobulinaemia and with symptom onset more than 5 days ago should not be given convalescent plasma.\*\*\* (new)**  
Hypogammaglobulinaemia is a state where a person has low plasma gamma globulins and impaired antibody formation. For people whose COVID-19 symptoms started more than 5 days ago, and who do not have hypogammaglobulinaemia there is robust evidence against the use of convalescent plasma.
- **Monoclonal antibodies against antispikes protein should be considered in people at risk of severe COVID-19 who are seronegative or whose symptoms started less than 5 days ago.\*\*\* (new)**  
Some new drugs have been developed that target a particular protein on the virus called a spike protein. These include bamlanivimab, etesevimab, casirivimab and imdevimab. Trial data suggest these drugs can significantly reduce viral load, but efficacy depends on the virus variant, as well as how long ago symptoms started.
- **There is not enough evidence to recommend the use of other immunomodulators in COVID-19.\*\* (modified)**  
There currently not enough evidence to recommend the use of other immunomodulators to treat people with COVID-19. This includes interferon alpha, interferon beta, interferon kappa, interferon lambda, leflunomide, nonSARS CoV-2 IVIg, eculizumab and cyclosporine. No recommendation either in favour or against the use of these medicines can be made at this point. Other medicines are being investigated, but only those with published evidence are included here.

## Summary

Overall, the points give guidance on how to use existing anti-inflammatory, immunomodulatory therapies to treat COVID-19. EULAR hopes these will be a useful reference for health professionals involved in the care of people with SARS-CoV-2 infection. They should be used alongside local regulations and guidelines, and information from bodies such as the World Health Organization.

Points to consider with just one or two stars are based mainly on expert opinion and not backed up by studies, but these may be as important as those with three or four stars.

If you have any questions or concerns, you should speak to a health professional involved in your care.