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Cite this as: *BMJ* 2021;375:n2700

<http://dx.doi.org/10.1136/bmj.n2700>

Published: 12 November 2021

Covid-19: surging demand for some arthritis drugs

Patients with rheumatic diseases face serious shortages of vital medicines

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Over the past 18 months, shortages have emerged for several medications used to control inflammatory rheumatological diseases, the highest profile of which is tocilizumab.

Early in the pandemic, there was considerable interest in hydroxychloroquine—a drug for rheumatoid arthritis and systemic lupus erythematosus—as a possible treatment for covid-19.¹ A surge in demand led to concerns about shortages and a warning from the US Food and Drug Administration in April 2020.² Demand abated after studies showed it was ineffective in preventing and treating covid-19.^{3–5}

The UK Department of Health and Social Care then issued a medicine supply notification for sulfasalazine in October 2020, one of the most commonly prescribed treatments for rheumatoid arthritis. A serious shortage protocol was issued,⁶ and supply problems continue, with potentially serious implications for several thousand patients in the UK alone. The manufacturer, Pfizer, is reported to be out of stock.

The importance of systemic inflammation in covid-19 morbidity and mortality drove interest in other immunomodulatory medications. Tocilizumab is a monoclonal antibody that inhibits interleukin-6 (IL-6) and is used to reduce symptoms and prevent disease progression in moderate-to-severe rheumatoid arthritis.^{7,8} In 2018, tocilizumab became the first targeted therapy licensed for giant cell arteritis, providing a much needed treatment option for patients with steroid refractory disease.⁹ It is also licensed to treat systemic and polyarticular juvenile idiopathic arthritis and cytokine release syndrome after chimeric antigen receptor T cell (CAR-T) therapy. The NHS in England spent an estimated £55m on tocilizumab in 2017–18.¹⁰

In November 2020, NHS England and the devolved administrations issued an interim statement permitting use of tocilizumab for patients with severe covid-19 pneumonia who require respiratory support or intensive care.¹¹ This followed publication of data showing improvements in survival and other outcomes after treatment with IL-6 inhibitors.^{12,13} The US FDA granted emergency use authorisation for tocilizumab for severe covid-19 in June 2021,¹⁴ and in July the World Health Organization added tocilizumab for severely or critically ill patients to its covid-19 patient care guidelines.¹⁵

Demand for tocilizumab has subsequently increased substantially worldwide. Roche, the manufacturer, issued a statement in August 2021 highlighting a global surge in demand, which had increased by over 400% in the US alone since the start of the pandemic.¹⁶

The manufacturing processes for biological drugs such as tocilizumab are complex, and the capacity to rapidly scale up production is more limited than for other drugs. The unprecedented increase in demand for tocilizumab has resulted in global supply shortages.¹⁷ In September, the Australian Therapeutic Goods Administration warned that intravenous tocilizumab stocks would run out unless usage was reduced by 75%.¹⁸ And shortages in the subcutaneous formulation of tocilizumab mean that patients in the UK are now restricted to no more than four weeks' supply at a time.

Global shortages raise important questions around how to prioritise and conserve the use of potentially life saving medications such as tocilizumab. Patients with some rheumatic diseases have few other treatment options (for example, those with giant cell arteritis or systemic juvenile idiopathic arthritis), and some countries have prioritised these patients for treatment with IL-6 inhibitors.¹⁸ Patients with other diseases such as rheumatoid arthritis have alternative options, including tumour necrosis factor- α inhibitors, Janus kinase inhibitors, B cell depletion therapy, and T cell co-stimulatory blockade. However, not all options are available or effective for everyone. Furthermore, changes to treatment increase the risk of disease flares, which in turn increase the risk of severe covid-19. Reducing the dose of IL-6 inhibitors may be another option for patients who are in remission,¹⁹ but again this increases the risk of disease flares.

Shortages of hydroxychloroquine, sulfasalazine, and tocilizumab have understandably caused anxiety and stress for patients. Many have been taking these treatments for a long time, having struggled to find alternatives that adequately control their disease. These stresses have added to anxiety about covid-19 among people with rheumatic diseases, especially those who are immunosuppressed.²⁰ Rheumatology departments have seen substantial increases in calls to their advice lines throughout the pandemic. The National Rheumatoid Arthritis Society recorded a 600% increase in calls (unpublished data). Medication shortages increased the workloads of rheumatology departments just when many staff were being redeployed to cover inpatient wards. Workload pressures continue with covid-19 recovery activity.

As the pandemic continues globally, shortages of some medications are likely to remain. Clinicians, patient organisations, manufacturers, and policy makers must now work together to agree a plan of action to ensure that patients with rheumatic diseases don't face the double jeopardy of covid-19 combined with lack of access to vital medicines for their high risk underlying condition.

Competing interests: *The BMJ* has judged that there are no disqualifying financial ties to commercial companies. The authors declare no other interests. Further details of *The BMJ* policy on financial interests is here: <https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-col-form.pdf>.

Provenance and peer review: Commissioned; not externally peer reviewed.

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