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Guiding Principles from the American College of Rheumatology for Scarce Resource Allocation During the COVID-19 Pandemic: The Case of C5 Inhibitors

Background

Ethical principles must be balanced when making decisions about scarce resource allocation. In extreme circumstances, like the COVID-19 pandemic caused by the SARS-CoV-2 virus, the focus of medical care "shifts from the needs of the individual (ethical principle of autonomy) to the needs of the community as a whole (ethical principle of distributive justice)" (1) with the goal of achieving the greatest good for the greatest number of people.

Eculizumab is a complement inhibitor that blocks activation at the C5 convertase step and thus prevents formation of C5a and the membrane attack complex (2). Eculizumab is essential for patients with atypical hemolytic uremic syndrome (aHUS) (3), paroxysmal nocturnal hemoglobinuria (PNH) (4) and various types of thrombotic microangiopathies (TMA) such as that following hematopoietic stem cell transplantation. Eculizumab is used by rheumatologists and rheumatology health professionals to care for patients with systemic lupus erythematosus- and scleroderma-associated renal failure of the TMA type, as well as neuromyelitis optica, catastrophic anti-phospholipid syndrome, and complement-dependent hemolytic anemias. Ravulizumab, another C5 inhibitor, has been shown to be non-inferior to eculizumab in patients with PNH (5).

Clinical trials with eculizumab in COVID-19 patients have been initiated (6) based on a number of observations. SARS-related lung injury in animal models is causally linked to complement activation, and acute respiratory distress syndrome is clinically associated with complement activation. The efficacy of eculizumab for a number of conditions related to complement activation, especially aHUS, suggest that it might ameliorate pulmonary and systemic injury in COVID-19.

We offer the following recommendations regarding the allocation of C5 inhibitors during the COVID-19 pandemic. Clinical guidance from the American College of Rheumatology for the treatment of rheumatology patients during the COVID-19 pandemic are available here. All recommendations are based on current knowledge and are subject to revision as circumstances evolve.

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Recommendations:

- Every effort must be made to ensure an adequate supply of C5 inhibitors for all patients who need it. Efforts to increase production and distribution of C5 inhibitors for patients who take it for complementopathies, as well as patients with COVID-19 if indicated, should be supported. Protections on the supply of C5 inhibitors should include all aspects of the supply chain from manufacturer to wholesaler, wholesaler to pharmacy, and final distribution to patients.
- Adequate supplies of C5 inhibitors should be allocated for patients with complementopathies, especially those in whom even brief drug holidays would be reasonably expected to cause a flare of their disease or require a switch to an alternative regimen with less efficacy and/or safety.
- In the case of COVID-19, allocation of C5 inhibitors should be prioritized (but not limited) to support clinical trials designed to test the efficacy of C5 inhibitors as therapy for severe cases of COVID-19.
- The potential therapeutic benefits of C5 inhibitors in COVID-19, and the urgent need for effective therapy against SARS-CoV-2, justify expedited controlled trials in humans. Such trials should be carried out by experienced investigators equipped to generate and interpret reliable results while safeguarding patient safety and informed consent.
- Decisions about allocation of C5 inhibitors should be made locally, with input from experts, based on local conditions and calibrated over time as circumstances evolve. Decisions around allocation should not be made *ad hoc* by individual dispensing pharmacies acting in isolation.
- Decisions about allocation of C5 inhibitors should incorporate recommendations from rheumatologists, rheumatology health professionals and other experts in the management of these medicines.
- Rheumatologists and rheumatology health professionals, in shared decision making with a patient, may reasonably pursue C5 inhibitor dose reductions and extend dosing intervals tailored to an individual patient's needs when faced with shortages.
- During drug shortages we urge insurers to exempt patients from prior authorization, step therapy protocols, and other utilization management practices so that they may more readily gain access to appropriate alternatives as determined by their rheumatologist or rheumatology health professional.

To Be Avoided

- Pharmacy-level restrictions on new starts of C5 inhibitors for patients with appropriate rheumatologic conditions are inappropriate.
- Predatory price increases or cost-sharing requirements, especially during the COVID-19 pandemic, should be vigorously opposed by regulatory bodies.

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(6) https://clinicaltrials.gov/ct2/show/NCT04288713

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