In ordinary clinical circumstances, the process of identifying and prescribing a medication to meet a patient’s needs is fairly straightforward. But for physicians caring for patients seriously ill with COVID-19, the urgency to act combined with the lack of approved therapies for the disease has made prescribing far more clinically and ethically challenging.

The AMA has created an ethics resource page, “Prescribing medications responsibly in a pandemic,” that offers expert ethical advice on off-label prescribing for seriously ill patients with COVID-19. Citing numerous opinions from the AMA Code of Medical Ethics, the page provides a comprehensive guide to help physicians understand when off-label prescribing is appropriate, how to initiate it and how to follow-up on treatment.

The AMA and the Centers for Disease Control and Prevention are closely monitoring the COVID-19 pandemic. Learn more at the AMA COVID-19 resource center. Also check out pandemic resources available from the AMA Code of Medical Ethics, JAMA Network™ and AMA Journal of Ethics®, and consult the AMA’s physician guide to COVID-19.

Guidance to minimize stress

Drawing on opinion 9.6.6, “Prescribing and Dispensing Drugs and Devices,” the resource page quotes the Code as saying that physicians should prescribe drugs “based solely on medical considerations, patient need and reasonable expectations of effectiveness for the particular patient.”

Of course, there may be situations when approved therapies have proven ineffective in treating a serious medical condition or when there simply are no approved therapies for a condition, which are legitimate reasons to consider off-label drug use.
“The big difference in a pandemic is the time frame and the sense of urgency,” said Elliott Crigger, PhD, director of ethics policy at the AMA. “Ordinarily, a physician would say to a patient, ‘This medication isn’t approved for your medical condition, but I think it will work for you for the following reasons. Would you be willing to try it as an off-label medication?’ That’s a much calmer conversation than physicians can have in the heat of the pandemic.”

First steps

Citing opinion 1.2.11, “Ethically Sound Innovation in Medical Practice,” the resource page notes that responsibly prescribing an approved medication for a novel use requires that the physician do so:

- On the basis of sound scientific evidence and appropriate clinical expertise.
- With input from colleagues or other medical professionals in advance or as early as possible in the course of innovation.
- In ways that minimize the risks to individual patients and maximize the likelihood of application and benefit for populations of patients.

Referring to opinion 5.5, “Medically Ineffective Interventions,” the page adds that—regarding both approved and off-label uses—physicians should not provide therapy that, in their best medical judgment, “cannot reasonably be expected to yield the intended clinical benefit or achieve agreed on goals of care.”

Obtaining informed consent

As always, the ethical principles of autonomy, justice, beneficence and nonmaleficence apply. The resource page notes that physicians must seek the patient’s explicit consent to off-label use by disclosing:

- How the diagnostic or therapeutic service differs from the standard therapeutic approach (when there is one).
- Why the physician is recommending the innovative modality.
- The known or anticipated risks, benefits and burdens of the recommended therapy and any alternatives.
- Experience with the innovative use in the professional community in general and the physician’s individual experience with the innovative use.
- Any conflicts of interest the physician may have with respect to the therapy.


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Following up

“Having prescribed an innovative therapy, physicians must monitor and discontinue any therapy that is not benefitting the patient,” the page notes. “To promote patient safety and quality of care, physicians should also share their findings with peers, including both positive and negative outcomes. “

The AMA has also developed an ethics resource page on conducting clinical trials in a pandemic.

In addition, check out the ethics resource page on access to experimental treatments by individuals who are unable or unwilling to participate in clinical trials.