American Society of Clinical Oncology Position Statement On Access to Investigational Drugs

Introduction

A vigorous public debate—in the courts, in state legislatures, in Congress, and in the media—is occurring regarding the ability of individual patients with terminal disease to obtain access to investigational drugs outside of clinical trials – known as "expanded access." Numerous state laws and a federal legislative proposal aim to bypass the existing expanded access program that has been characterized by some as excessively bureaucratic and difficult to navigate. A majority of states has passed right-to-try (RTT) laws allowing patients to seek access to investigational drug treatments without oversight of the Food and Drug Administration (FDA), and similar legislation is now under consideration by Congress.

As the leading medical society for physicians involved in cancer treatment and research, the American Society of Clinical Oncology (ASCO) supports access to investigational drugs outside of clinical trials when there are adequate patient protections in place. However, ASCO is concerned that existing and proposed RTT laws do not adequately protect patients, do little to facilitate patient access to such therapies, and potentially interfere with recent reforms that are already streamlining patients' access to investigational agents. In this statement, ASCO summarizes its concerns with RTT laws and recommends several strategies the Society believes will improve access to investigational drugs in a more optimal way.

Existing System for Access to Investigational Drugs Outside of Clinical Trials

The expanded access provisions of the U.S. Food, Drug and Cosmetic Act (21 U.S.C. 360) and associated regulations became law during the AIDS epidemic in 1987 to provide access to unapproved therapies outside of clinical trials. At the outset of the process, a manufacturer must be willing to provide the investigational product. The FDA mechanism for individual patients requires that:

- a patient's physician determines there is no comparable or satisfactory approved therapy available, and that the probable risk to the person from the investigational product is not greater than the probable risk from the disease or condition;
- the FDA determines there is sufficient evidence of the safety and effectiveness of the investigational product to support its use in the particular circumstance;
- the FDA determines the use will not interfere with clinical trials to support approval of the product; and

- the manufacturer or an investigator submit an individual clinical protocol for the use that is consistent with FDA regulations for use of investigational drugs, including oversight by an ethics board (institutional review board or IRB).

The FDA has approved the vast majority (approximately 99.5%) of applications for the use of investigational drugs under this mechanism. However, concerns have been raised about the efficiency and fairness of the existing system for the sickest patients. Chief among the concerns is a sense that the application process for expanded access is time consuming for both the patient and the requesting physician—and that the requirement for a full investigational new drug (IND) application and IRB oversight is a disadvantage to those patients who receive their care outside of major research institutions where these resources are more readily available.

In June 2016, the FDA finalized its guidance intended to address these concerns by streamlining the expanded access program forms and submission process, particularly for individual patient use.[1] The final guidance significantly shortens the form that physicians must submit and removes the requirement for filing a full IND application. Physicians can also submit the new form by phone, email, or fax. The FDA estimates that this new process could take as little as 45 minutes for a physician to complete, and is designed to be completed by clinicians who are not familiar with the full IND process.[2,3] Approximately 99.5% of requests were approved in fiscal year (FY) 2016 with a median of four days approval time for non-emergency cases.[4]

Although the FDA has streamlined its expanded access application process, patients and providers must complete certain steps before submitting their application and it is often in this stage that significant delays can occur. For example, applicants must determine a sponsor's willingness to provide the investigational drug. Providers and patients report difficulty locating information about drug manufacturer contacts for such requests, significant delays in response and even denial of the request altogether.

The recently passed provisions in the 21st Century Cures Act (Cures) contain language that specifies additional requirements aimed at improving the current FDA expanded access policy. ASCO supports these new provisions, which would require drug manufacturers to make their expanded access policies publicly available along with contact information; describe the process for making such requests; the general criteria considered for the request; and the length of time the manufacturer anticipates will be necessary to acknowledge receipt of the request. The

[1] Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers: Guidance for Industry, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf
[2] Yang YT, et al. "Right-to-try" legislation: progress or peril? J Clin Oncol. 2015;33:2597–9.
[3] Lurie P. A big step to help the patients most in need. U.S. Food and Drug Administration, available at http://blogs.fda.gov/fdavoice/index.php/tag/individual-patient-expanded-access-applications-form-fda-3926/
[4] Lurie P. Committee on Homeland Security and Government Affairs Hearing Testimony, U.S. Food and Drug Administration, available at https://www.fda.gov/NewsEvents/Testimony/ucm522044.htm

Cures language also acknowledges that the postings of policies by drug manufacturers do not serve as a guarantee of access to any unapproved investigational drug by a patient. These reforms will help standardize the expanded access process and require that manufacturers centralize access to information about their policies and processes.

Right-to-Try Legislation

Notwithstanding FDA's efforts to simplify the expanded access program and the new requirements of Cures to make the availability of such programs more apparent, the past three years have seen significant activity on RTT legislation. As of March 2017, 33 states have enacted RTT laws, and legislation has been proposed in a majority of states. Right-to-try laws allow patients to request access to investigational drugs directly from manufacturers without employing the EAP, if they meet certain conditions. These conditions vary somewhat by state, and in some states are even more detailed than existing FDA rules. The conditions generally include that the patient have a terminal disease; have considered, but not necessarily received, FDA approved options; have a prescription from a physician; and have signed an informed consent document. While conditions vary state-by-state, RTT laws generally are similar, based on model legislation from a national advocacy organization.

Proposed federal legislation, the Trickett Wendler Right to Try Act (H.R. 878/S. 204), would prohibit the FDA from preventing or restricting access to unapproved products when the patient has a terminal illness and lives in a state that has authorized RTT access.[5,6] The proposed legislation stipulates that a physician in good standing must certify that the patient has exhausted or does not have any other treatment options. It offers liability protections for producers, manufacturers, and prescribers who provide the treatment to the patient and prevents the FDA from using the outcome of such treatment "to delay or otherwise adversely impact review or approval" of the investigational product. Finally, the bill requires the FDA to report to Congress on the streamlining efforts made to ensure patient access to these treatments. Investigational products available under the bill must have successfully completed a phase I clinical investigation and remain under investigation in an FDA-approved trial. The bill offers no additional protections for patients.

ASCO Position on RTT Laws

ASCO is concerned that most RTT laws, while well intentioned, are not an effective mechanism for improving access to investigational drugs for terminally ill patients and may cause unintended harms, for the following reasons:

[5] Right to Try Act of 2017, H.R. 878, 115th Cong.), available at https://www.congress.gov/bill/115th-congress/housebill/878

[6] Trickett Wendler Right to Try Act of 2017, S. 204, 115th Cong., available at https://www.congress.gov/bill/115thcongress/senate-bill/204

- Right-to-try laws do not include an enforcement mechanism to provide access, since they do not require or compel drug manufacturers to provide investigational products. As such, these laws do not remove a frequent barrier to access.
- These laws place no legal obligations on insurers to pay for the routine care costs associated with delivery of treatment – unlike coverage requirements that do exist for patients who participate in clinical trials. As a result, RTT laws establish no new rights or protections for patients.
- Independent review of the potential safety and efficacy of investigational drugs is important for patient safety. Under the expanded access program, the FDA conducts a prompt review of the available data and makes an independent assessment on behalf of the patient. Such review is by-passed in RTT laws.

ASCO strongly supports actions aimed at increasing access to effective and safe new treatment options for all cancer patients. However, ASCO does not believe RTT laws will help patients achieve better access to investigational drugs. Moreover, these laws as currently envisioned and enacted will interfere with already-streamlined and effective protocols, potentially putting patients at high risk for unclear benefit. Specifically, these measures will:

- Jeopardize insurance coverage for the cost of patient care associated with the use of investigational drugs, particularly in the case of complications caused by these drugs;
- Circumvent the government's responsibility to monitor and protect the safety of patients seeking access to investigational products; and
- Fail to provide adequate transparency, in part due to a lack of reporting requirements, on how patients respond to investigational drugs under a right-to-try scenario.

In addition to their lack of patient protections, RTT laws do not mitigate the delays that can occur during the expanded access application process. For example, regardless of whether under RTT or the FDA process, applicants must determine a sponsor's willingness to provide the investigational drug. Providers and patients consistently report difficulty locating information about drug manufacturer contacts for such requests, significant delays in response and even denial of the request altogether.

Improving Access to Investigational Drugs: Needed Next Steps

ASCO supports improvements to existing FDA mechanisms for expanded access, a number of which are included in Cures as noted earlier. These mechanisms will broaden cancer patients' potential treatment options while monitoring and protecting their safety. Policy efforts should focus on greater transparency among pharmaceutical manufacturers' policies on expanded

access while ensuring that existing expanded access programs are timely and efficient for patients and their physicians.

To address concerns about delays in the process, ASCO supports improved facilitation and processing of expanded access applications. Ideally, an online portal or tool could provide patients and physicians seeking expanded access a universal point-of-entry to facilitate the step-by-step process for obtaining access to investigational agents from drug manufacturers.

ASCO believes that any expanded access framework should include continued FDA oversight that enables patients to access investigational drugs in appropriate circumstances as discussed above. ASCO urges all stakeholders to work together to support expanded access programs with FDA oversight and promote the optimal functioning of these programs.

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