



Pfizer's Position on Preapproval Access to Investigational Drugs

Preapproval access programs provide investigational drugs to patients diagnosed with a serious or immediately life-threatening disease or condition, who have exhausted approved treatment options, and who are not eligible for clinical trials. In these cases, companies may provide a not-yet-approved investigational drug to a patient through their treating physician. Companies carefully consider preapproval requests to ensure patient safety and that the potential medical benefits outweigh the risks. The 21st Century Cures Act requires companies to publicly post procedures and contact information for making requests, the general criteria, and length of time anticipated for acknowledgement of a request. Pfizer's overarching policy principle is to preserve the integrity of clinical trials and the regulatory oversight of preapproval access programs in order to protect the best interests of patients, with an emphasis on safety. At the same time, Pfizer supports efforts to provide rapid access to investigational drugs for patients diagnosed with a serious or life-threatening disease or condition, who have exhausted approved treatment options, and who are not eligible for clinical trials.

Background

Patients seeking preapproval access to investigational drugs often suffer from serious or immediately life-threatening diseases or conditions. These patients may be willing to try an experimental drug for which robust clinical information about efficacy is not yet available. These programs can be referred to by different names; two other common ones are "expanded access" and "compassionate use". The process for requesting preapproval access to an investigational drug requires several steps. Typically, the treating physician will make a request of the company developing the drug. If the company agrees to supply the investigational drug, the physician will initiate a request with the appropriate regulatory agency to approve the request. In most countries, companies are not allowed to distribute unapproved drugs without formal regulatory approval. In the U.S., a treating physician requests permission from the Food and Drug Administration (FDA). In the European Union, the European Medicines Agency (EMA) provides recommendations, but preapproval access programs are implemented by each member state with its own rules and procedures.

Pharmaceutical companies participate voluntarily in preapproval access programs and carefully consider each request. Considerations include: whether all other approved treatment options have failed; if enrollment in a clinical trial is possible; whether there is a scientific rationale to support that the requested experimental drug may provide benefit and that the potential benefits outweigh the potential risks; and if there is sufficient supply to make the investigational drug available to a patient outside the clinical trial setting.

Key Facts and Figures

- In the U.S., the FDA uses the term "expanded access" when referring to these programs. In 2018, the FDA reviewed 1,727 expanded access requests.¹
- FDA approved 99 percent of expanded access requests between 2012 and 2017. FDA typically responded to emergency single-patient requests within hours.²
- FDA made meaningful changes in approximately 10 percent of all expanded access applications. Modifications may be made to adjust dosing amounts, increase safety monitoring, and bolster informed consent. The changes are based on the scientific and medical expertise of FDA staff.³
- A July 2017 report examining the current FDA expanded access program found that substantial changes were not needed within the program, aside from greater clarity on the use of adverse event data.² FDA made updates to its expanded access guidance in October 2017 which included clarifying institutional review board (IRB) requirements, how FDA reviews adverse event data, and a reference to 21st Century Cures Act requirements that expanded access policies be publicly posted.⁴

¹ See: www.fda.gov/news-events/expanded-access/expanded-access-compassionate-use-submission-data#CBERCDCER.

² See: www.gao.gov/assets/690/685729.pdf.

³ See: www.hhs.gov/about/agencies/asl/testimony/2017-10/examining-patient-access-to-investigational-drugs.html.

⁴ See: www.fda.gov/downloads/drugs/guidances/ucm351261.pdf.





Pfizer's Position

Pfizer's overarching policy principle is to protect the best interests of patients by preserving the integrity of clinical trials and the regulatory oversight of preapproval access programs, with an emphasis on safety. Clinical trials follow strict scientific standards designed to produce reliable data and results. Where possible, use of an investigational drug within a clinical trial is preferable because clinical trials follow protocols designed to monitor and safeguard patient experiences with a drug, and because trials generate data that may lead to the approval of therapies so that they may be available for wider use. At the same time, Pfizer supports efforts to provide rapid access to investigational drugs for patients diagnosed with a serious or life-threatening disease or condition, who have exhausted approved treatment options, and who are not eligible for clinical trials.

- Pfizer supports policies that ensure transparency to patients and their physicians about how to make such requests so that every request is considered equally.
 - Pfizer supports industry guidelines for companies to post policies and provide a single point of contact to make requests.
 - The 21st Century Cures Act requires pharmaceutical companies to publicly provide the policies and procedures for processing requests for preapproval access. Pfizer follows these requirements and posts information on [Pfizer.com](https://www.pfizer.com).
- Pfizer supports efforts to streamline request processes and, to the extent possible, adopt standardized forms to lessen physician and patient burden.
 - FDA has made significant progress to streamline its application process; to simplify its website; provide factsheets; and streamline the IRB review process.
- Pfizer supports multiple-stakeholder educational efforts for physicians and patients to help them engage with the appropriate governing bodies and companies.
 - Pfizer sponsors the Expanded Access Navigator, a unique partnership between the Reagan-Udall Foundation for the FDA, patient advocacy organizations, the pharmaceutical industry, and the federal government. This website provides a consolidated directory of industry preapproval access programs and provides patients, caregivers, and physicians with information to guide them through the preapproval access request process.⁵

Preapproval Access to Gene Therapies

Pfizer believes that gene therapy has the potential to transform the treatment landscape and offer meaningful improvements in the lives of patients with certain rare diseases caused by genetic disorders. This new generation of medical research is highly specialized in many ways compared to traditional drug development. It offers potentially transformational opportunities to address the underlying causes of disease at the cellular level but requires finding answers to new and challenging research questions. The uniqueness of this treatment and challenges for development has led Pfizer to apply an additional level of vigilance to our current policy when considering preapproval access to gene therapies.

Clinical research offers the best approach to answer safety and efficacy questions about potential new treatments for diseases. Gene therapies, like all investigational treatments, must undergo rigorous benefit-risk assessments and are only approved by regulatory agencies once they have determined that the potential benefits exceed the potential risks. But, gene therapies, unlike traditional medicines, also need to address a unique set of challenges, including: concerns for immune-related side effects at administration, an understanding of the duration of treatment response, and the potential for loss of some or all treatment effects over time. In addition, because of the body's immune response, it may turn out that patients can receive only a single dose of gene therapy that has the potential to confer the desired degree or duration of benefit. Given the implications that a gene therapy may be limited to a single administration and may make it impossible for patients to receive another gene therapy in the future, it is particularly important that sufficient clinical trial data have been generated to support an assessment that the potential benefit of

⁵ See: navigator.reaganudall.org.





the therapy outweighs the potential risks of treatment prior to the therapy being made available outside the setting of a clinical trial.

For these reasons, Pfizer has decided not to provide preapproval access to gene therapy until there is clarity on these issues, a decision made after thorough consideration and in consultation with Pfizer's Bioethics Advisory Panel. We believe that our ability to address these challenging research questions is best accomplished through the conduct and completion of carefully designed clinical trials. Ensuring our research program can meet regulatory requirements as efficiently as possible will help the largest number of patients. We are committed to the patient communities that may benefit from these breakthrough treatments and will continue to review our policy.

Pfizer's Preapproval Access Activities

Pfizer has a record of providing preapproval access to Pfizer investigational medicines for qualifying patients via single patient or multi-patient protocols. In 2019, Pfizer received approximately 6,760 requests for preapproval access from 75 countries for 34 products, of which approximately 96 percent of requests were granted. Requests span the company's portfolio of products.

In December 2015, Pfizer launched a website, PfizerCAREs.com, where healthcare professionals can submit requests for access to Pfizer investigational drugs or unlicensed products on behalf of patients in their care.⁶ Patients and others may also use PfizerCAREs.com to submit questions about preapproval access. Pfizer's policy on preapproval access describes all the conditions that must be met for the review to proceed and describes the roles and responsibilities of the colleagues who plan, execute and manage these requests.⁷ Requests are reviewed by Pfizer medical experts dedicated to ensuring that requests are handled according to Pfizer policy in a timely manner. Pfizer strives to respond within five business days of receipt of the request and documentation required to evaluate the request. Preapproval requests from the U.S. then go to the FDA for review and approval. Requests originating in other countries are handled according to regulatory requirements and laws of the country where the request originates.

⁶ See: www.pfizercares.com.

⁷ See: www.pfizer.com/purpose/medicine-access/compassionate-use.

