AstraZeneca Policy on Early Access to Investigational Medicines

Purpose & Scope

AstraZeneca's purpose is to discover and develop new medicines that make a meaningful difference to patient's lives, primarily for the treatment of diseases in three main therapy areas: oncology, cardiovascular and metabolic disease, and respiratory. We are also selectively active in the fields of autoimmunity, neuroscience and infection.

In our endeavor to bring innovative medicines to patients as fast and safely as possible, we conduct clinical trials to establish the safety and efficacy of an 'Investigational Medicine', which is a potential medicine that is in active clinical development but has not yet received marketing approval by health authorities.

The clinical trials and the subsequent generation of safety and efficacy data are the most effective way of ensuring timely review and decision making by Health Authorities on a given medicine. This will ultimately result in access to new, safe and effective approved medicines for the broadest patient population. For this reason, AstraZeneca prioritizes access to an investigational medicine through clinical trials and encourages patients to be enrolled in such studies. For information on available clinical trials visit: www.ClinicalTrials.gov.

However, we recognize that there are circumstances wherein patients with serious or life-threatening diseases have exhausted other comparable or satisfactory alternative therapeutic options and may not be eligible for, or otherwise unable to participate in one of our trials. In such circumstances, subject to the criteria set forth below and country specific regulations, patients may be eligible for Early Access to AstraZeneca's investigational medicines.

This document summarizes our policy on access to our investigational medicines outside of a clinical trial, which AstraZeneca refers to as Early Access. The information on our Early Access Policy is applicable to all requests.

Outside of a clinical trial, any use of an AstraZeneca investigational medicine must be overseen by a licensed and appropriately qualified physician, in accordance with local laws and regulations governing such programs, as well as AstraZeneca policies and procedures.

The Early Access program does not apply to the use of an approved medicine for an indication beyond the authorized prescribing information (often referred to as "off-label use").

Acquisition and use of marketed medicines outside of approved indications is at the discretion of the treating physician and the patient and is neither facilitated nor endorsed by AstraZeneca.

Early Access programs will terminate around the time of the investigational medicine receiving regulatory (i.e., marketing) approval authorizing its general availability for physicians and patients.

Types of Early Access Programs

AstraZeneca operates two distinct types of Early Access programs – Individual Named Patient Supply (NPS) and Multiple Patient Early Access Programs (MPEAP). It is important to note that terminology used can vary from country to country and in some instances different countries use identical terminology to describe different approaches.

Multiple Patient Early Access Programs (MPEAP)

Multiple Patient Early Access programs (MPEAP) known as Expanded Access Programs in the US or Compassionate Use in Europe, describes the process by which an investigational medicine is made available to a group of patients under a specific treatment protocol. This may be undertaken on AstraZeneca's initiative and conducted following discussions with and approval by the relevant regulatory authorities in a given country. These programs are conducted in accordance with the proposed prescribing information for the investigational medicine. These programs may begin enrollment only after sufficient data are available to support the benefit/risk profile and the regulatory submission for marketing approval.

Individual Named Patient Supply (NPS)

Where there is no MPEAP, AstraZeneca may make an investigational medicine available to a single patient in accordance with country-specific regulations. Terminology and requirements of named patient access schemes vary globally; in the US, for instance this includes the FDA's guidelines for treatment of individual patients with an Investigational New Drug (IND).

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Eligibility Criteria

An Early Access program for a specific investigational medicine may be opened if AstraZeneca determines that all the following criteria are met:

Investigational Medicine Eligibility:

1. The investigational medicine is the subject of an active clinical development program.
2. An adequate supply of the investigational medicine exists to perform necessary clinical studies as well as to provide Early Access to patients who do not have alternative treatment options.
3. Early Access does not impede or compromise the clinical development or regulatory approval of the medicine under investigation.
4. There are sufficient clinical data available with respect to both the investigational medicine and the disease condition for which the application is being sought, to anticipate that any potential benefits from treatment are likely to outweigh any associated risks to the patient.
5. AstraZeneca has a reasonable likelihood of regulatory submission and approval for the investigational medicine in the country from which the Early Access request originates.

Patient eligibility:

1. The patient is suffering from a serious or life-threatening disease, has exhausted other comparable or satisfactory alternative therapeutic options and is not eligible to enroll in a clinical study for medically valid reasons or is otherwise unable to participate in one of our clinical trials.
2. The patient will be receiving treatment in a country or jurisdiction where AstraZeneca plans to seek marketing approval for the investigational medicine.
3. The patient must be able to routinely travel to the treating site for monitoring and follow up as required.
4. The patient's medical status is deemed appropriate to receive the investigational medicine.

Treating Physician eligibility:

1. The treating physician(s) meets all **Treating Physician Criteria and Responsibilities** on the following page.

Request Process

Requests for Early Access to an AstraZeneca investigational medicine outside of a clinical study must be made by a patient's treating physician. Requests must not include the patient's name or specific identifying information.

Physicians seeking information about how to apply for Early Access, or who wish to submit a request are advised to firstly contact the AstraZeneca Medical Affairs team in the local country as follows:

- US: Medical Information Call Center: 1800-236-9933
- Outside the US: an overview of websites of the individual countries where AstraZeneca has subsidiaries can be found at "Local AstraZeneca Affiliates".

Alternatively, physicians may submit a request via our online Early Access Request Platform Early Access Request Platform (registration is required).

General e-mail enquiries may be submitted to: EarlyAccess@AstraZeneca.com.

For the US, expanded access programs can be found at US programs on ClinicalTrial.gov.

Early Access requests submitted via the online Early Access request platform and e-mails submitted to EarlyAccess@AstraZeneca.com will be acknowledged immediately upon receipt via an automated email reply.

Access programs to drugs under **Alexion's label** are not included through this portal. For more information about Alexion's access programs, please visit Alexion's Global Access to Medicines page

https://alexion.com/our-commitment/global-access-to-medicines-program

General enquiries or access requests may be submitted to (registration is required):

https://myaccessprograms.parexel.com/prd/f?p=177:150

How We Use the Information Submitted

The information submitted is only used to evaluate requests for Early Access to our investigational medicines

How We Protect Information Submitted to Our Early Access Program

We have in place appropriate privacy and security policies which are intended to ensure, as far as reasonably possible, the security and integrity of all our information, including information submitted by you, whether the information is your personal information or pertains to another individual (e.g., the patient), however, as previously noted, requests for early access should not include patient identifiable information.

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Evaluation of Requests

In considering and administering requests for Early Access, our patient-focused principles are based on a commitment to be fair, impartial and transparent. Our decisions are guided by the best clinical and scientific evidence currently available for any given IMP.

To ensure a fair and prompt evaluation of early access requests, AstraZeneca will base its decisions on the patient information submitted by the requesting physician to support the request, and meeting all Eligibility Criteria listed on the proceeding page. *Requests will be considered on a first come first served basis for all patients dependent on drug availability.*

Please note:Not all AstraZeneca investigational medicines are available for Early Access and submission of a request does not guarantee access to those investigational medicines that are available will be provided. Eligibility will be determined by AstraZeneca based on the established Early Access policy and Eligibility Criteria for the investigational medicine *concerned.* We may not be able to provide IMP in response to all requests received.

Treating Physician Criteria and Responsibilities

The physician(s) treating the patient receiving an investigational medicine through Early Access must be properly licensed and fully qualified to administer the product.

The physician will be responsible for collecting and submitting clinical data as specified by AstraZeneca during the treatment process and any required post-treatment follow-up period. In addition, the physician will be responsible for ensuring all local legal, regulatory and Health Authority requirements are met, including Investigational Review Board or Ethics Committee approval and reporting of Adverse Events.

The physician must agree in writing to comply with the following terms:

1. To use the product only for the patient specified.
2. Adhere to any applicable country-specific legal and regulatory requirements related to providing an investigational medicine under Early Access.
3. Adhere to any AstraZeneca requirements applicable to patient confidentiality and data privacy, medical criteria, adverse event/safety reporting, treatment monitoring, drug supply handling and use, and protection of intellectual property and confidential information.
4. Obtain written informed consent from the patient approved by an Institutional Review Board. This must include a statement that the investigational medicine will be provided free of charge, until regulatory approval has been secured. However, any associated costs of treatment, including but not limited to drug administration costs, costs associated with laboratory or radiological monitoring, travel, physician and hospital fees will be the responsibility of the insurer, health care system, and/or patient.

AstraZeneca will send to the treating physician:

- Letter of Acceptance (including a request for confirmation that the patient signed an IRB approved informed consent form)
- Instructions for Use for the investigational medicine
- Adverse Event Report Form.

By signing a Letter of Acceptance the treating physician agrees to fulfill all the responsibilities outlined in the letter.

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Early Access Program Closure

Early Access may be discontinued at any time at the discretion of the treating physician or the patient. Early Access may also be discontinued by the treating physician, the patient or AstraZeneca when:

1. The patient is no longer receiving any clinical benefit, typically documented by progression or deterioration of the underlying disease or adverse events that are deemed by the treating physician or patient to outweigh the potential benefit of the investigational medicine
2. An alternative effective medicine is available
3. The patient becomes eligible to enroll in a clinical trial for the investigational medicine
4. The product receives marketing approval
5. The benefit/risk profile of the investigational medicine has been determined by AstraZeneca to no longer support further use of the investigational medicine
6. The local Health Authority rejects the application for marketing approval
7. Unanticipated shortage of investigational medicine