

Roche Position on Pre-Approval Access to Investigational Medicinal Products

Background

Roche discovers, develops, manufactures and markets medicines to treat people living with serious or life-threatening medical conditions. We seek to do this as safely and rapidly as possible. To achieve this, we conduct clinical trials to evaluate the safety and efficacy of Investigational Medicinal Products (hereinafter referred to as “unauthorized¹ medicines”) in order to obtain clinical data that enable regulatory and reimbursement authorities to review and decide on whether these unauthorized medicines should be marketed and reimbursed thus allowing broad access for use under the supervision of a qualified healthcare professional or doctor. It may not be possible, however, for all patients who might receive benefit from the unauthorized medicine to enroll in the ongoing clinical trials, and nor is it possible to have clinical trials for all potential disease settings available.

During the research process, new data may be generated indicating a substantial clinical benefit for some people living with serious or life-threatening medical conditions. The greater the degree of benefit for these people the greater the urgency to make the unauthorized medicine more widely available. Under specific circumstances, Roche may provide pre-approval access (PAA) to these medicines. This document summarizes Roche’s underlying principles regarding the ability of patients to receive unauthorized medicines before they have been approved by regulatory authorities. It does not pertain to continuing access of investigational medicines for those patients who received these products while clinical trial participants (refer to [Roche Global Policy on Continued Access to Investigational Medicinal Product](#)).

Unauthorized medicines may be made available to patients through the following pre-approval access pathways. Further details of the criteria for these programs appear below, but in general, there are three approaches:

- Pre-Approval Access programs are company run clinical programs which provide a framework where the unauthorized medicine is made available to a group of people outside of a clinical trial. Patients have the same specific disease or condition that is being studied and which would fall within the marketing indication that is actively being pursued with regulatory authorities.
- Individual Patient Compassionate Use (CU) is a mechanism to provide an

¹ Throughout the document, use of the term “unauthorized medicines” refers either for any indication or for a further indication(s) after initial approval.

unauthorized medicine to an individual patient or set of individual patients who have a serious or life threatening disease or condition for which no satisfactory alternative therapy exists or who cannot enter a clinical trial.

- Individual Named Patient Supply enables physicians, on behalf of their patients, to access medicines approved in other countries before marketing authorisation has been granted in their home country. There is a fee to obtain the medicine as it is commercially available.

Stakeholders' Expectations and Concerns

For some people living with serious or life-threatening medical conditions the potential benefit of an unauthorized medicine justifies the potential risks of taking a medicine which has not yet received regulatory approval. In recent years, patient groups and individual patients have publicly asked for access to certain unauthorized medicines and have called on pharmaceutical companies to meet this need.

Roche Position

Roche understands the concerns that people living with serious or life-threatening conditions have about accessing unauthorized medicines as soon as possible. Roche is therefore committed to putting in place arrangements so that people with serious or immediately life threatening diseases or conditions, for which no satisfactory alternate treatments are available may have access to unauthorized medicines outside of on-going clinical trial programs and before such unauthorized medicines receive regulatory approval and are commercially available.

Various regulatory mechanisms exist in different countries to provide pre-approval access to unauthorized medicines and as a result, regional variations in pre-approval access will occur. Any pre- approval access to unauthorized medicines must always comply with the applicable country-specific laws and regulations, including medicine importation requirements.

In general, we believe that patients receive the best access and care when they participate in clinical studies, and this is the best way to access our unauthorized medicines. When this is not possible, and when supported by strong clinical data, we may put in place a specific program to meet these needs – Pre-Approval Access programs or Compassionate Use.

We also believe that the involvement of the patient's own doctor is a very important part

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of this process and all of our programs are conducted and supported by doctors well qualified in their respective areas. We will not discontinue any patient who is participating in this program based on their ability to pay for the medicine after marketing approval.

All inquiries will be evaluated in an unbiased fashion and decisions will be based entirely on the patient's clinical condition in the context of the clinical data available. Roche clinical teams will work closely with the patient's qualified doctor and this will be the primary communication channel.

Pre-approval access may be limited in scope due to limited resources (e.g., whether there is sufficient unauthorized medicine supply available to support pre-approval access). Mechanisms to fairly allocate limited supply of unauthorized medicine may be used as needed.

Additional criteria are outlined below, and all of these must be met before we will consider granting pre-approval access to an unauthorized medicine.

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Roche will consider granting pre-approval access to an unauthorized medicine prior to approval only when all of the following criteria are met:

- The patients for whom PAA is sought have a serious or life threatening disease or condition.
- The potential patient benefit justifies the potential risks of the unauthorized medicine use and there is a clear biological rationale to anticipate that the patient will benefit from treatment.
- The medicine requested must be part of an active and ongoing development program within the Roche group.
- The PAA must not interfere with, or in any way compromise, the conduct of any ongoing or planned clinical trials that could support health authority approval of the medicine or future commercial access to the molecule:
 - Patients for whom PAA is requested must not be eligible for ongoing clinical studies or studies that will be about to start.
 - Geographic limitations to participation in a clinical trial of the unauthorized medicine would generally not meet this criterion.
- Considerations to special safety risks must also be present:
 - Patients with exceptional safety risks that have not been sufficiently studied (e.g., patients with renal failure, heart failure or other similar co-existing conditions) should be excluded.
 - There is sufficient clinical data to identify a recommended dose that might be effective and is reasonably safe.
 - Similarly, there is sufficient clinical data to identify an appropriate dose for use in children, if the request is for a child.
- PAA programs:
 - The PAA is limited to groups which have been shown to derive benefit based on sufficient clinical data and who have the specific disease or condition that would fall within the marketing indication that is actively being pursued with regulatory authorities.
 - Whether or not other therapies to treat the disease or condition may be available, the benefit of the test medicine in the main clinical study being submitted to the regulatory authorities must be robust and persuasive.

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Pre-Approval Access to Gene Therapies

At this time, Roche is unable to offer free pre-approval access programs and Compassionate Use for gene therapies due to a constellation of unique features of gene therapy, as well as the ethical requirement to maintain fair, equitable, and sustainable future access. Prior to regulatory approval, we believe that patients receive the best care and access to potential unauthorized medicines when they participate in clinical studies, and this is the best way to access our unauthorized gene therapies. We are committed to enabling rapid and broad access through obtaining clinical data that meets regulatory requirements for potential health authority approval of our gene therapies and sustainable assessment of their value as efficiently and as fast as possible.

Gene therapies are still considered novel treatments with limited data to support that the potential patient benefit justifies the potential long term risks. Most gene therapies are treatments for rare diseases with low patient numbers in clinical trials. This further limits data on risk profiles including potential limitations to receive other future gene therapies. Also, due to complex manufacturing and supply chain processes, there are potential implications on clinical development programs.

For further information about how this policy is being implemented in your local area please contact the medical information team in your country or submit your question using [Roche's Medical Information portal](#).

This position paper was proposed by the Corporate Sustainability Committee and adopted by the Corporate Executive Committee on May 13, 2013 and entered into force the same day.

It was revised in May 2022 and November 2023.

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