Teva's Policy on Compassionate Use Programs

Teva Pharmaceutical Industries Ltd (hereinafter "Teva"), including all its directors, executives, employees and subsidiary and affiliated companies, is committed to applying our expertise and resources to advance access to quality medicine for people around the world. Being a leader in global healthcare means consistently providing innovative and quality medicines to those in need. In line with our mission to improve patient lives, we strive to make medicines widely accessible, while continuing to deliver innovative solutions for unmet needs across our core therapeutic areas. These commitments are consistent with our Mission, Values and Code of Conduct and form the foundation for Teva's Policy on Compassionate Use Programs (hereinafter "the Policy").

Overview

This Policy is intended to help ensure the provision of Teva medicines for compassionate use is conducted in the best interests of the patients and is consistent with Teva's policies and requirements.

Teva Compassionate Use Programs (CUPs) offer a mechanism to provide access to Teva medicines, when deemed appropriate, to eligible patients outside, or after conclusion, of clinical trials or normal marketing access channels.

CUP regulations and terminology vary by country. In some instances, countries use identical terms to describe different approaches. Although not all-encompassing or fully available in every country, for the purposes of this Policy, types of CUPs are described below.

1. **Individual patients:** An unsolicited request for a Teva medicine, submitted by a licensed physician for the treatment of an individual patient. Examples include, but are not limited to, Named Patient Programs (NPP) (EU), Special Access Programme (Canada), Compassionate Use (EU) and Individual (or Single) Patients Expanded Access IND Program (EAP) (US).

2. **Group of patients:** A request for use of a Teva medicine for the treatment of a group of patients. Under this category, Teva may also consider initiating a CUP for multiple patients (e.g., patients who have completed a Teva sponsored study according to the protocol). In such a cohort program, Teva still requires that unsolicited request(s) from a licensed physician are submitted for approval and demonstration of approval from the local regulatory authority. Examples include, but are not limited to, After Care (Israel), Compassionate Use (EU), EAP (US) and Treatment IND or Treatment Protocol (US).

Teva-sponsored CUPs are also posted on ClinicalTrials.gov, when required.

The table below illustrates some of the differences in regional approaches and terminology between US and EU CUPs.[1]

Criteria	EAP (US)	CUP (EU)	NPP (EU)
Legislation in place	Expanded Access Programs (FDA, 1997)	Article 83 (1) of Regulation (EC) NO 726/2004	Article 5 of Directive 2001/83/EC
Who can benefit from program?	Group of patients; individual patients	Group of patients	Individual patients
Who initiates the program?	Sponsor; treating physician	Sponsor; group of physicians	Treating physician
Criteria to define/select target population is set by:	Sponsor/FDA	Sponsor/The Committee for Medicinal Products for Human Use (CHMP)	Sponsor; treating physician
Liability	Sponsor	Sponsor	Treating physician
Should the medicinal product be undergoing clinical trials or awaiting market authorization?	✔	✔	✘
Is off-label use permitted?	✘	✘	✔
Can physicians be paid for taking part in the program?	✔	✘	✘
Can the supplier charge for the medicines in the program?	✘	✘	✔

[1] Adapted from "Initiating Early Access Programs: 5 Things to Consider" by Morteza Yazdani & Francesca Boggio, Executive Insight https://www.executiveinsight.ch/en/insights/initiating-early-access-programs-5-things-consider

Eligibility Criteria

Teva considers granting access to a Teva medicine only when all of the following criteria are met:

1. The Teva medicine is intended to treat a serious or immediately life-threatening disease or condition.
2. No comparable or satisfactory alternative drug or other therapy is available to treat the particular stage of the disease or condition.
3. If relevant, CUP supply will not interfere with the implementation, continuation or completion of clinical trials conducted by Teva that could support marketing approval, or otherwise compromise the potential development of the medicine.
4. When the Teva medicine is no longer under investigation for that indication, it has **either** been approved by the governing regulatory agency in at least one country **or** Teva is actively pursuing marketing approval with due diligence in at least one country for that indication.
5. Available clinical evidence provides a reasonable basis for concluding (a) the potential benefit justifies the potential risks **and** (b) the potential risks are not unreasonable in the context of the disease or condition to be treated and the medical history of the recipient patient.

Request Process

Information on submitting a CUP request can be found at:
https://www.tevaclinicaltrials.com/en/for-researchers/#compassionate-use-programs

Treating Physician Criteria and Responsibilities

The physician(s) attending to the patient receiving Teva's medicine thorough a CUP must be properly licensed and fully qualified to treat the patient. As applicable per local regulations, before Teva's medicine is shipped under a CUP, the requesting physicians must agree to the following in writing:

- Notify, or, where required, obtain approval from, the country's regulatory agency for use of the Teva medicine.
- Inform the patient of risks associated with the Teva medicine, including whether it has been approved for marketing in any country.
- Obtain informed consent from the patient (or the patient's representative) before administering the Teva medicine, in accordance with local laws and regulations, and provide any written patient information (e.g., patient leaflet).
- Report safety information according to Teva's policies and requirements or as dictated by local regulatory authorities. All serious and non-serious adverse events, irrespective of treatment relatedness, pregnancy, special situation reports and protocol defined adverse events (PDAEs), must be reported to Teva, or per country-specific laws and regulations.

- Maintain the confidentiality of information about the Teva medicine (e.g., IB and dosing information) and only disclose or disseminate such information as necessary.
- Store and handle the Teva medicine according to instructions.
- Use the Teva medicine only for the CUP and return/destroy any unused amounts as applicable, in compliance with local laws and regulatory requirements.

Governance Structure for Compassionate Use Programs

Compassionate Use Programs are approved and implemented by Teva R&D.