Pharmaceuticals	TITLE Expanded Access Programs		
GMA-POL-22, v1.0	PROCESS OWNER Global Medical Affairs Global Clinical Development	EFFECTIVE DATE APR 0 1 2015	SUPERSEDES Global Policy – 270, V 1.0

1 PURPOSE

To describe the requirements for planning, approving and implementing Expanded Access Programs (EAPs) globally.

2 SCOPE

This policy applies to Teva personnel or service providers working on behalf of Teva involved in planning, approving and implementing EAPs.

This policy does not apply to investigator-sponsored studies (refer to SOP-GBP-RD-801).

3 POLICY DETAILS

3.1 TYPES OF EAPS

There are several types of EAPs. This policy is intended to help ensure that access to an investigational drug/biologic is made in the best interest of the patient and consistent with Teva's research and pharmacovigilance strategy. The most commonly used are as described below.

3.1.1 **Individual patients** – Individual patient EAPs involve the use of an investigational drug/biologic by a licensed physician for the treatment of an individual patient with a serious or life-threatening disease or condition where conventional therapies/treatments have failed and no comparable or satisfactory alternative drug or treatment is available. These programs are typically implemented in response to unsolicited requests from licensed physicians. This category includes but is not limited to the following types of EAPs:

- Named patient supply programs (European Union [EU])
- Compassionate use programmes (EU, EMIA, APAC)
- Special access programs (Canada)
- Individual Patients (US)

3.1.2 **Group of patients** – This type of EAP involves the use of an investigational drug/biologic for the treatment of a group of patients. The applicable regulatory agency may request a sponsor to establish such an EAP when a significant number of requests are received for individual patient expanded access to an investigational drug for the same use. Examples of this type of program may be for a drug that is not being developed because the disease or condition is so rare that the sponsor is unable to recruit patients for a clinical trial, the drug is being developed but the requesting patients are not able to qualify to participate in ongoing trials, and/or approved product is no longer available or marketed. This category includes but is not limited to the following:

- Compassionate use programmes (EU)
- Intermediate-size patient populations (US)
- Treatment IND or treatment protocol (US) (Note: This type of EAP is typically for larger-sized patient populations and widespread treatment use.)

Note: Not all of the types of EAPs identified above are available in all countries.

3.2 EAP PRINCIPLES

3.2.1 EAPs are designed such that patients diagnosed with the condition under study, or as otherwise identified within the defined scope of the program, have an opportunity for access to the investigational drug/biologic which may benefit such patient.

3.2.2 Access to an investigational drug/biologic under an EAP may be considered only when all of the following (6) conditions are met:

- The investigational drug/biologic is intended to treat a serious or immediately life-threatening disease or condition.
- No comparable or satisfactory alternative drug or other therapy is available to treat that stage of the disease or condition.
- Where the investigational drug/biologic is under investigation, in one or more clinical trials conducted by Teva, supply under the EAP will not interfere with the implementation, continuation or completion of clinical investigations that could support marketing approval, or otherwise compromise the potential development of the product.
- Unless the drug or biologic is indicated for a rare disease or condition, EITHER it has been approved in at least one country by the governing regulatory agency, OR where it has not been approved anywhere in the world, Teva is actively pursuing marketing approval with due diligence in at least one country.

  NOTE: For rare diseases or conditions, and under special circumstances, the drug or biologic may be supplied to individual patients or intermediate size patient populations even when the conditions in the above bullet are not met. An exception would be documented and approved at a Teva VP level or above. Regulatory requirements stipulate that an exception from the requirement of pursuing marketing approval of the drug with diligence may not be granted for widespread treatment use, such as a treatment protocol or treatment IND.
- The available clinical evidence provides a reasonable basis for concluding that: (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.
- Clinical trials are completed, OR, if clinical trials are ongoing with the investigational drug/biologic, the patient either does not meet the enrollment criteria for any of those studies or their access to a trial center is not possible.

3.2.3 An investigational drug/biologic made available under an EAP must not be promoted or represented as being a treatment for the condition, or safe or effective for the purposes for which it is under investigation.

3.2.4 If a request is made for an EAP, the project team including Clinical, Medical Affairs, Pharmacovigilance, Legal, Clinical Supplies, Project Champion, and Regulatory Affairs will analyze the request and provide a recommendation to the Chief Medical Officer (CMO) and Head of GMA regarding approving or rejecting the request. A rationale to support that decision must be provided and documented. In making such decision, the following must be taken into consideration:

- Existing and available data for the investigational agent, including its risk-benefit profile.
- The details of the request and an assessment of the potential risk-benefit to that patient or group of patients.
- Access to the investigational compound regardless of the patient's financial or social status.

3.2.5 The EAP decision is documented and retained in the appropriate document repository. The decision may be updated when new data and information become available to substantiate a revision. Any revisions require the same level of approval as the initial plan.

3.2.6 A plan must be put in place to address the timing and conditions under which the program will be terminated (e.g., upon regulatory approval and commercial availability of the product in that region, availability of an alternative therapeutic in the same or similar class).

3.2.7 Requests for an investigational drug/biologic under an EAP must originate from a qualified physician licensed in the country where the investigational drug/biologic is to be distributed or from a regulatory agency. Documentation of the requester's qualifications (e.g., curriculum vitae and/or medical license/medical license number) is verified and obtained, as appropriate, before shipment of the requested investigational drug/biologic.

3.2.8 Before an investigational drug/biologic is approved for shipment under an EAP, all required regulatory notifications and/or approvals are completed, and it is confirmed that the planned distribution within the jurisdiction complies with applicable local laws and regulations.

3.2.9 Upon approval of an EAP, Pharmacovigilance is notified that the program will be implemented.

3.2.10 Import licenses are secured as necessary and required before the shipment of the investigational drug/biologic.

3.2.11 As applicable per local regulations, requesting physicians agree in writing to the following before an investigational drug/biologic is shipped under an EAP:

- Notify or, where required, obtain approval from the country's regulatory agency for its use.
- Inform patients of the risks associated with the investigational drug/biologic, including whether or not it has been approved for marketing in any country. Obtain the patient's (or the patient's representative) informed consent before administration of the investigational drug/biologic 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 (refer to Pharmacovigilance Policy 06-001 Handling Safety information on Company Products or consult with Pharmacovigilance regarding the requirements for reporting for the drug/biologic). All serious adverse events irrespective of treatment relatedness, non-serious adverse reactions and pregnancy reports must be reported to Teva.
- Maintain the confidentiality of information provided about the investigational drug/ biologic (e.g., IB and dosing information) and disclose or disseminate such information only as necessary.
- Use the investigational drug/biologic only for the EAP and return/destroy (in compliance with local laws and regulatory requirements) any unused amounts as applicable and as instructed by Teva.
- Activities for which Teva is financially responsible (e.g., administrative, monitoring by healthcare providers, institutional review board/ethics committee fees, pharmacy fees, importation licenses).

3.2.12 Teva maintains records of the shipment, receipt, disposition, return, or destruction of the investigational drug/biologic.

4 DEFINITONS & ACRONYMS

Term	Definition
Expanded Access Program	Program that provides access to an investigational drug/biologic outside of a clinical trial in a country where that agent has not received marketing approval; the agent may have received marketing approval in another country. The agent must be intended to treat a serious or immediately life-threatening disease or condition for which no comparable or satisfactory alternative drug or other therapy is available to diagnose, monitor or treat that stage of the disease/condition in the intended patient population. EAPs can be structured to cover the supply of an investigational drug/biologic to (i) individual subjects (e.g., individual patients, including for emergency use, named patient supply) or (ii) groups of patients (e.g., treatment protocols). For the purposes of this policy, expanded access programs may include but are not limited to the following: • Aftercare (continued supply of study drug at study completion) • Individual patient expanded access (US) • Named patient supply programs (EU) • Special access programs (Canada) • Compassionate use programmes (EU, EMIA, APAC) • Intermediate-size patient population (US) • Treatment IND or treatment protocol (US) • Special access scheme (Australia) • Compassionate care (Israel) • Expanded access, compassionate use (Brazil)
Immediately life-threatening disease or condition	A stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment
Serious disease or condition	A disease or condition associated with morbidity that has a substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent.

List of Acronyms

CFR = Code of Federal Regulations

CUP = Compassionate use programme

EAP= Expanded access program

FDA = US Food and Drug Administration

IB= Investigator's brochure

IND= Investigational new drug

NPS = Named Patient Supply

SAP = Special access program

5 REFERENCES

SOP-GBP-RD-801 Investigator-Sponsored Studies

TEVACORP-POLICY-06-001 Handling Safety Information on Company Products

21 CFR Part 312 Subpart I Expanded Access to Investigational Drugs for Treatment Use

21 CFR Part 312.8 Charging for investigational drugs under an IND

Guideline on Compassionate Use of Medicinal Products, Pursuant to Article 83 of Regulation (EC) NO 726/2004, July 2007

Guidance for Industry, Expanded Access to Investigational Drugs for Treatment Use – Q & As (May 2013)

6 REVISION HISTORY

Policy # Version#	Description of revision	Author(s)	Effective Date
GMA-POL-22, V1.0	Supersedes Global Policy 270, V1.0, Expanded Access Programs	Jennifer Fiorenza, Director, Global Medical Affairs, Training and Procedures	APR 0 1 2015

TEVA Pharmaceuticals	TITLE Expanded Access Programs	
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POLICY APPROVAL PAGE

The following individuals have reviewed and approved this document. Signatures are on file with the original version of this Policy.

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