

Orphan Drug Development Guidebook

Building Block E122

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	EU Compassionate Use Programs (EU CUP)
References	https://www.ema.europa.eu/documents/regulatory-procedural-guideline/guideline-compassionate-use-medicinal-products-pursuant-article-83-regulation-ec-no-726/2004_en.pdf
Description	<p>Compassionate use is a treatment option that allows the use of an unauthorised medicine. Under strict conditions, products in development can be made available to groups of patients who have a disease with no satisfactory authorised therapies and who cannot enter clinical trials.</p> <p>This procedure will enable patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening to receive an unauthorized drug while waiting for registration and market access.</p>
Category	Early Access Building Block
Geographical scope	European Union
Availability	Applicants developing medicines for rare and non-rare diseases.

Scope of use	<p>Article 6 of Directive 2001/83/EC1 requires that medicinal products are authorised before they are marketed in the Community. Unauthorised medicinal products may be available through an approved clinical trial protocol.</p> <p>The EU regulatory framework makes it possible for non-authorized medicines to be made available under certain circumstances. This is achieved through a compassionate use program. According to article 83 of Regulation (EC) No 726/2004, medicinal products without a Marketing Authorisation ‘may be made available for compassionate reasons to a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorized medicinal product.’</p> <p>Compassionate use programs fall under national jurisdiction and, in most Member States under the remit of National Competent Authorities (NCA). Article 83 of Regulation (EC) No 726/2004, states that the Committee for Medicinal Products for Human Use (CHMP) has an advisory role at the request of a Member State. The individual NCA decide whether or not to approve the use of medicinal products without a market authorization.</p> <p>The NCA in the Member State decides if such a program fulfils an unmet medical need according to their clinical practices and available alternatives. Some Member States have a long tradition on early access programs, including compassionate use, and others have different provisions in their national legislation.</p> <p>Most of the compassionate use program notifications are submitted directly to the NCA within the different Member States.</p> <p>Established by Article 83 of Regulation (EC) No 726/2004, this tool is designed to:</p> <ul style="list-style-type: none"> – facilitate and improve access to compassionate use programs by patients in the EU; – favor a common approach regarding the conditions of use, the conditions for distribution and the patients targeted for the compassionate use of unauthorised new medicines; – increase transparency between Member States in terms of treatment availability.
Stakeholders	<ul style="list-style-type: none"> • National Competent Authorities (CHMP opinion on compassionate use cannot be requested by applicants, they should liaise with national competent authorities) • CHMP
Enablers /	<p>These programs are only put in place if the medicine is expected to help patients with life-threatening, long-lasting or seriously debilitating illnesses, which cannot be treated satisfactorily with any currently authorised medicine.</p>

Require ments	The medicine must be undergoing clinical trials or have entered the marketing-authorisation application process and while early studies will generally have been completed, its safety profile and dosage guidelines may not be fully established.
Output	EMA provides recommendations through the Committee for Medicinal Products for Human Use (CHMP), after consulting the manufacturer or the applicant, on the conditions for use on how to administer, distribute and use certain medicines for compassionate use.
Best time to apply and time window	Planning for Compassionate Use has to be planned as early as possible. Application for Compassionate Use is usually enabled when clinical trials are completed, while waiting for registration and market access (i.e., patient availability).
Expert tips	<ul style="list-style-type: none"> – National competent authorities can ask EMA for an opinion on how to administer, distribute and use certain medicines for compassionate use. The CHMP also identifies which patients would benefit, and Member States should take note of these recommendations when making decisions. – Manufacturers and marketing-authorisation applicants should not contact EMA to request an opinion, but they may wish to inform the Agency of applications underway at national level. National competent authorities will inform the Agency if they are making a product available to a group of patients for compassionate use. – Compassionate use should not be confused with 'named-patient basis' treatments, which may see in some Countries doctors obtain medicines directly from manufacturers before authorisation. This is done on an individual basis under the direct responsibility of the doctor, and the Agency does not need to be informed (in some Countries has to be at least informed). – Compassionate Use Programs are of high importance for the patients: EURORDIS has developed a position paper on the matter (https://www.eurordis.org/compassionate-use) <p>PROs:</p> <ul style="list-style-type: none"> – CHMP advice on the compassionate use program should help the final decision at the National level by the single Member State – The Agency's recommendations aim to standardise compassionate use programmes across the European Union <p>CONs:</p> <ul style="list-style-type: none"> – EMA provides recommendations through the Committee for Medicinal Products for Human Use (CHMP), but these do not create a legal framework. Compassionate

	<p>use programs are coordinated and implemented by Member States, which set their own rules and procedures.</p> <ul style="list-style-type: none"> – Only the single Member States are responsible for the final approval of the treatment under expanded access
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