Federal agency for medicines and health products
Eurostation II - Place Victor Horta 40/40
1060 Brussels
www.afmps.be

DG Pre/R&D/UMN

FAQ's – Unmet Medical Need

I.   General

1.   When is a product considered as "commercially available"?

Commercially available means that the product is available on the Belgian market (independently of its reimbursement status).

2.   Can a product that is commercially available be provided in the frame of an unmet medical need program for the authorized indication?

General: Once a product is commercially available for a given indication, the product cannot be provided any longer in the frame of an unmet medical need program for the same indication, even if reimbursement criteria are not fixed yet. There is one derogation: if a product that was already on the market for indication X, has been authorized for indication Y and reimbursement procedure is ongoing for indication Y, an MNP can be requested for indication Y. The MNP can run in indication Y until the reimbursement procedure has ended for indication Y, regardless of its outcome.

3.   Could we apply for an UMN program in place of an extension trial/open label study?

The main goal of an UMN program is to provide an early access to a new innovative medicinal product which addresses an unmet medical need or a major therapeutic advantage. Hence no other data except pharmacovigilance data can be gathered which will only be used for the evaluation of the UMN program. Therefore and as stated in the European regulation, UMN programs should not be opened in place of clinical trials even open label studies.

4.   Could we request for Scientific-Technical advice regarding Unmet Medical Need?

Yes. Scientific-Technical advice can be requested regarding all Unmet Medical Need questions. For the STA procedure please refer to http://www.fagg-afmps.be/en/human_use/medicines/medicines/scientific_technical_advice/generalites/.

5.   How to proceed if the applicant wants to request for a cohort (Early Temporary Reimbursement)?

At the moment of submission for a CUP/MNP (Early Temporary Authorization or ETA), the applicant needs to notify his intention to request a cohort. Once the CUP/MNP is approved the request for cohort (Early Temporary Reimbursement or ETR) can be done at the RIZIV/INAMI. The starting date of the CUP/MNP cannot be later than the date of cohort request. For further information on cohort request please refer to http://www.inami.fgov.be/nl/themas/kost-terugbetaling/door-ziekenfonds/geneesmiddel-gezondheidsproduct/terugbetalen/Paginas/unmet-medical-need.aspx. Having the intention to request or not for a cohort (ETR) does not influence CUP/MNP approval/refusal (ETA).

6.   Is a MNP with a biosimilar possible?

A MNP with a biosimilar (for instance in a new indication) is not excluded but should fulfill all conditions for the set-up of a MNP.

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7. Can a CUP/MNP be requested for a medicinal product for prophylactic vaccination?

The prophylactic vaccination in healthy persons falls outside the scope of the compassionate use definition. Please be aware that Art. 110 of the RD of 14/12/2006 might be applicable for these cases.

II. Application

8. Do we have to submit the complete EMA dossier?

If an application for Marketing Authorization has been introduced at EMA it is not necessary to provide the whole dossier. Please mention in the cover letter that an MA application has been introduced and the reference of the dossier. In this way we can consult the dossier.

9. Do we have to use the protocol and other templates available on the [website](#)?

It is highly recommended to use the template documents in order to capture all necessary information.

10. What is the purpose of the 'Summarized information for publication'?

The idea of the document 'Summarized information for publication' is to have a proposal made by the applicant so that there is clarity from the start of what will be made public at the end of the procedure regarding the conditions of the program. Therefore it should be written with the patient in mind, i.e. in a user friendly way, suitable for a layman to understand. The [template](#) of the Summarized information for publication is available on our website.

11. What should be done if the shelf life of the medicinal product used in the UMN program is different for the commercial product?

The IMPD for the compassionate use product containing the stability-extension protocol should be provided to support its shelf life.

III. Labeling, distribution and delivery

12. What should be the labeling for the medicinal product used in the MNP if there is not yet a Belgian packaging available?

In case the product is not yet commercially available in Belgium (no Belgian packs available) the label of the medication has to be conform with the Annex 13 of GMP Volume 4. In this last case, the requirement "for clinical trial use only" should be replaced by "MNP – cannot be sold". A labeling derogation (English labeling) is possible if patient does not take the medication at home and if the hospital staff that is in contact with the product understands the English language. If the patients takes the medicinal products home, the (hospital) pharmacist can stick labels in the 3 national languages. These derogations should be notified in the cover letter of the application.

13. Do medicinal products used in a compassionate Use program, need to be released by a Qualified Person prior to be used?

Yes, a release by a Qualified Person is always needed, regardless of the status of the medicinal product. The company that performs the release has to possess a European manufacturing authorization.

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14. On what basis can a (hospital) pharmacist deliver a medicinal product for unmet medical need?

Although a common prescription is not necessary, it is highly recommended to use a form for obtaining the medicinal product, completed by the treating physician with the coordinates of the patient.

IV. <u>Ongoing programs</u>

15. What are the responsibilities of the actors in a CUP/MNP?

Actors - modalities	Responsibilities
Treating physician - any Belgian physician	- Explain the ICF and the benefit/risk to the patient - Send his motivated request to the responsible physician with a signed ICF and a copy of the identity card of the patient*
Responsible physician - A physician understood as stipulated in the Royal Decree nr. 78. The task of the responsible physician falls within the practice of medicine (art. 2) and so art. 7 (license to practice) is applicable. This assures (because of the ethical oversight) the independency of the responsible physician with respect to the responsible of the program - The responsible physician does not need to be an employee of the applicant company - The responsible physician cannot act as treating physician in a program given that in this case this responsible physician would have to include his/her own patients to the program	- Check the inclusion/exclusion criteria - Check ongoing clinical trials suitable for the patient - Give his authorization to enroll the patient in the program to the responsible of the program - Codify adverse events and send these data to the responsible of the program*
Responsible of the program - The responsible of the program stated in art.106 §3 can be a sponsor in the comprehension of the law of 7 May 2004 regarding experiments on humans, meaning that the responsible can be a person, an enterprise, an institution or an organism responsible for the launch, management and/or financing of an experiment with the concerned medicinal product	- Implement the CUP/MNP - Assign the responsible physician for the program - Manage a central register of patients included - Manage the record of coded suspected serious adverse events - Report the SUSARs to the FAHMP

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*A waiver can be requested to keep the key for the codification on the treating physician's side.

16. Do we have to include every patient that fulfils the inclusion/exclusion criteria?

Once the CUP/MNP has been set up, all patients that fulfill the inclusion/exclusion criteria should have access to the CUP/MNP unless objective and motivated limitations are stipulated in the program.

17. Do we need to submit the central registry to the FAMHP?

It does not need to be submitted but should be available in view of control by FAMHP, so it is necessary that it is accessible in Belgium. In view of a control by the FAMHP, traceability and pharmacovigilance.

18. What is published on the FAMHP website?

All programs that have been submitted after 01/06/2014 and have been approved are published on the [website](#) in the appropriate section: 'authorized programs', 'closed programs' or 'on hold programs'. For each of these programs, the 'Summarized information for publication' and the 'Informed Consent Form' that have been approved are published annexed to the official approval of the FAMHP.

19. How should we notify when the program will end?

If the program ends, a notification e-mail should be send to umn@afmps-fagg.be. Please indicate in this e-mail the motivation for ending the program, the number of patients that have been included in the program, the number of patients that are still treated and will be further provided with the medicinal product after the end of the program. Once the program is ended, pharmacovigilance data should no longer be sent in the frame of the re-evaluation of the program however the applicant stays responsible for the implementation of the program for the patients included before the date of termination of the program unless the medicinal product is available on the market.

20. Does a CUP has to switch to a MNP when Marketing Authorization is received?

A CUP approved according to the legislation of 25 April 2014 can continue to run at the moment a Marketing Authorization is obtained. The CUP can run until the product comes effectively on the market. If a Marketing Authorization is granted after the application for a CUP but before the CUP is authorized, it will be categorized as a CUP.

V. Pharmacovigilance

21. If a program ends before the deadline for notification of the pharmacovigilance data, should this notification still be done?

Periodical pharmacovigilance data should only be notified if the program is ongoing (open for new patients). The applicant should notify the FAMHP regarding the end of the program (see question 19).

22. Will the pharmacovigilance timelines change, if during a program, MA is requested at EMA (for the same medicinal product in the same indication)?

Yes, however the upcoming deadline for pharmacovigilance reporting (6 months after approval or re-evaluation) is kept. From then on, yearly reporting is planned.

VI. <u>Urgent situations</u>

23. Can the Urgent Procedure be used if the medicinal product can be imported?

No, if the medicinal product can be imported in time, the Urgent Procedure cannot be used but the product needs to be imported. The application of Art. 105 of the RD of 14/12/2006 for importation is applicable for import from any country in which the medicinal product is authorized.

24. Can the Urgent Procedure be used if the medicinal product is commercially available in Belgium?

No, one of the conditions of Art. 107/1 is that the patient cannot be treated with a medicinal product that is commercially available or under hospital exemption, or with a magisterial preparation.

25. Is Pharmacovigilance Reporting necessary for medicinal product used in an Urgent Situation?

For medicinal products used according to art. 107/1 (urgent situations), there is no need for pharmacovigilance reporting to the UMN division of the FAMHP as for UMN Programs. However regular pharmacovigilance should be applied for urgent cases conform the EU pharmacovigilance legislation.