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

Your medicines and health products, our concern

DG Pre/R&D/UMN

FAQ's – Unmet Medical Need

I. General

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

A CUP approved according to the new legislation (after 1st July 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.

A CUP submitted before 1st July 2014 has to switch to a MNP as soon as the marketing authorization is granted. A MNP dossier should be submitted according to the new legislation.

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.

2. Can we request to change a running CUP into a MNP after Marketing Authorization is received?

Yes, but be aware that a MNP cannot be requested before Marketing Authorization is granted. If the CUP ends at the moment of Marketing Authorization there will be a gap (the period for the assessment of the MNP submission) in which the patients will not be able to enter an unmet medical need program.

3. Can a MNP be requested on the basis of « case reports » for the non-authorized indication?

No, if no Marketing Authorization for the non-authorized indication has been submitted, clinical trials should have been executed or running proving that the medicinal product is suitable for the treatment of the requested indication.

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

Commercially available means that the product is available on the market (independently of its reimbursement status). Once a product is available on the market for a given indication, the product cannot be provided any longer in the frame of an unmet medical need program for the same indication as the one for which the product is available on the market, 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.

5. What will be published on the FAMHP website?

The 'Summarized information for publication' and the 'Informed Consent Form' of the programs that have been approved will be published on the website annexed to the official approval of the FAMHP.

6. Can an approval letter of the designated Ethics Committee be obtained?

No, it is not foreseen in the legislation. According to art. 106 §11 and art. 108 §11 of Royal Decree relative to the human and veterinary medicines as modified on 25 April 2014 , FAMHP sends the dossier of a CUP/MNP to the designated Ethics Committee (EC). Within 14 opening days the EC provides its motivated opinion to the FAMHP. In case the motivated opinion has not been provided, it is considered as positive (tacit approval).

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The FAMHP's final decision is based on the EC's opinion and the opinion of the commission for human medicines. The approval letter of the FAMHP is available on the FAMHP's website.

7. **Do we have to include every patient that fulfills 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.

8. **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 CUM/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).

9. **Could we apply for an UMN program in place of an 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.

10. **Can 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/.

11. **How should we notify when the program has ended?**

    If the program ends, a notification e-mail should be send to umn@afmps-fagg.be. Once the program is ended, pharmacovigilance data should no longer be sent in the frame of the re-evaluation of the program.

II. Application

12. **Do we have to submit the complete EMA dossier?**

    If an application for Marketing Authorization has been introduced at EMA, this dossier should be part of the CUP/MNP request even if the Marketing Authorization has already been granted**.**

13. **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.

14. Do we have to include a Protocol as part of the application?

A protocol is not mandatory but it is highly recommended to provide such a document with at least the following information:

- Duration of the program
- Conditions of use and indication
- Conditions of distribution
- Conditions, delays and further rules for participation of patients
- Responsible person for the program
- Modalities for the disposal of non-used medicinal product
- The information for registration of suspected unexpected serious adverse events
- The informed consent form

Templates of protocols for CUP and MNP are available on our website.

15. Can we use available provisions for the payment of the initial request?

As the proof op payment is an essential part of the initial submission, package provisions cannot be used for the initial payment.

III. Responsibilities

16. Who can be the Responsible of 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.

17. Can the Responsible Person be a company?

As stated in question 16, the responsible of program could be an enterprise, nevertheless, a contact person within this company is requested.

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

Actors	Responsibilities
Treating physician	Explain the ICF and the benefit/risk to the patient. Send its motivated request to the responsible physician with a signed ICF and a copy of identity of the patient*.
Responsible physician	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

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	Codify adverse events and send these data to the responsible of the program*.
Responsible of the program	Implement the CUP/MNP, the assignment of a responsible physician for the program, keep a central register of patients included and the record coded suspected serious adverse events. Report the SUSARs to the FAHMP.

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

19. Should the responsible physician who approves each patient be based in Belgium?

Yes, a physician should be 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.

20. Does the Responsible physician need to be an employee of the applicant company?

No, the responsible physician does not need to be an employee of the applicant company.

21. Who is responsible for the central registry, is there a specific format for the registry and does it ever need to be submitted to the FAMHP?

The maintenance of the registry is the responsibility of the responsible person for the concerned program. 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, the central register contains:

- Administrative data (patient contact data, treating physician contact data)
- Copy of the informed consent form

A waiver can be requested to have a coded registry, with the key of the codes kept by the treating physicians.

22. What should be archived?

The responsible of the program should archive for at least 10 years:

- data registered in the central registry of patients included and
- suspected serious adverse events

The demands for patient inclusion with annexes should be archived by the responsible physician for at least 10 years.

IV. Labeling, distribution and delivery

23. 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

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case, the requirement "for clinical trial use only" should be replaced by "MNP – cannot be sold" (in line with the labeling requirements of Compassionate Use products).

24. 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 manufacturing authorization.

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

It is highly recommended to use a form for obtaining the medicinal product, completed by the treating physician with the coordinates of the patient.

V. Pharmacovigilance

26. Should the pharmacovigilance reporting for CUPs/MNPs be solicited or spontaneous?

The reporting should be solicited.

27. 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 11).

28. 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. Urgent situations

29. 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.

30. Can the Urgent Procedure be used if clinical trials in the indication are ongoing in another European country?

Yes, only if trials with the same medicinal product (in the same indication and for which the patient is eligible) are running in Belgium the Urgent Procedure cannot be used.

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

There is no need for pharmacovigilance reporting of a medicinal product used in an urgent situation to the FAMHP. However regular post marketing pharmacovigilance should be applied

for urgent cases safety reporting. That means that any adverse drug reaction has to be recorded in the post market eudravigilance database.