

Implementation of the regulations on compliance with time limits for national MA variation applications

Field: MAs registered via the national procedure

Scope: MA variation applications

Date of application: Applications submitted from 6 November 2017 onwards

INTRODUCTION

The ANSM is introducing a new approach to managing MA variation applications, designed to ensure compliance with regulatory deadlines, in accordance with Commission Regulation (EC) 1234/2008 of 24 November 2008.

For MA variation applications submitted from 6 November 2017 onwards, the ANSM will send an acknowledgement of receipt of a valid application to the holder. The time limit for notification of an express decision begins as of the date of this acknowledgement.

However, applications that do not receive an express decision from the ANSM within the regulatory time limit will result in an implicit decision, in accordance with the regulations:

- Implicit decision to accept the variation, for variations of type IA and IB
- Implicit decision to reject the variation, for variations of type II.

PRACTICALITIES

MA variation applications will be processed in accordance with the procedure detailed below.

1. **Receipt of application:** For all applications submitted via the CESP, an acknowledgement of receipt is automatically sent to the applicant.
2. **Application validation :** For all variations of type IB and II, an acknowledgement of receipt of a valid or an invalid application will be automatically sent to the applicant via email within 14 days of receipt of the variation application.

If the dossier is complete and deemed compliant, the acknowledgement of receipt of a valid application marks the start of the evaluation phase (procedure launch date or D0) and the regulatory time limit applies as of this date.

3. **Evaluation of application:** Compliance with time limits and impact on decision

- **For type IA variations:**

If no express decision is issued within 30 days of receipt of the application, the application is to be considered accepted.

NB: There is no validation phase for type IA variations and no D0 is therefore issued for these applications.

- **For type IB variations:**

If no express decision is issued within 30 days of the procedure launch date (D0), or the re-launch date where the procedure has been paused, the variation is to be considered accepted.

- **For standard type II variations:**

If no express decision is issued within 60 days of the procedure launch date (D0), or the re-launch date where the procedure has been paused, the variation is to be considered rejected.

- **For type II variations regarding a modification to or addition of a therapeutic indication, and variations listed in part 2 of Annex V of the regulation:**

If no express decision is issued within 90 days of the procedure launch date (D0), or within 60 days of the re-launch date where the procedure has been paused, the variation is to be considered rejected.

- **For a grouping:** The regulatory time limits for the highest category of MA variation (listed above) apply to the whole of the application.

4. **Requests for supplementary information/clock-stop:**

MA holders are reminded that supplementary information requested by the ANSM must be provided within the specified time limit. If the information is not provided within this time limit, the MA variation application is to be considered rejected.

Moreover, when requests for supplements are sent by mail, 7 days are granted to the holders to receive these requests and to mitigate possible postal delays.

- **During the validation phase:**

- ✓ If the MA holder has not submitted the requested information within 15 days of receiving an acknowledgement of receipt of an invalid application from the ANSM, the MA variation application is to be considered rejected.
- ✓ If the requested information is submitted and deemed to be valid, a D0 will be issued within 7 days of receipt of the supplementary information.

- **In the event of a clock-stop (during the evaluation phase):**

- ✓ For type IB variations: the MA holder has 30 days to provide the requested supplementary information. If the information is not submitted within this time limit, the MA variation application is to be considered rejected.
- ✓ For type II variations: the MA holder has 60 or 90 days (indication extension) to provide the requested supplementary information. If the information is not submitted within this time limit, the MA variation application is to be considered rejected.

5. **Confirmation of decisions:** Express notification or publication

The procedure for express notification remains unchanged. Express notifications are sent out by post within the regulatory time limit and, where applicable, the MA annexes are sent

by email at the same time. The electronic file containing the MA annexes must be used for all subsequent variation applications.

If no express decision is issued, the decision is implicit and no notification is therefore given.

Implicit decisions will only be published where they accept a variation that has an impact on the MA annexes. In this case, the updated MA annexes will be published in the Public Medicines Database (BDPM) and Drug Directory (RSP) in the two months following the end of the regulatory time limit.

The following will not be published in any way:

- Implicit decisions to accept a variation that has no impact on the MA annexes
- Implicit decisions to reject a variation, whether or not it has an impact on the MA annexes.

Implicit decisions are made without prejudice to any subsequent measures that the agency may need to take in the interests of public health.

To ensure that MAs are always updated fully, all subsequent variation applications can only be submitted once the regulatory time limits have expired and/or, where applicable, the updated annexes have been published, to ensure that the variations are based on the last approved annex.

If a holder needs to submit a variation urgently, the relevant division should be contacted in advance, copying in the Standard and Flow Management Department (DMFR) (maxime.collet@ansm.sante.fr).