APPLICATION OF MEASURES RELATING TO THE SUNSET CLAUSE IN BELGIUM FOR MEDICINAL PRODUCTS AUTHORISED AT THE NATIONAL LEVEL

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The purpose of this document is to explain in greater detail the application of the provisions of the Sunset Clause in Belgium for all human or veterinary medicinal products for which a marketing authorisation or registration has been approved at the national level.

More information may be added to this document as a result of further questions or cases that may arise. The most up-to-date version will always be available on our website www.famhp.be *– in the Human medicines/Distribution & delivery/Sunset clause and Veterinary medicines/Distribution & delivery/Sunset clause sections.*

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LEGAL BASIS

A marketing authorisation or registration of a medicinal products expires if:

- the medicinal product is not available on the market within three years of this authorisation being approved,
- the medicinal product has previously been available on the market, but has not or has no longer been effectively marketed for three consecutive years.

In exceptional circumstances, and for reasons of public health or for the protection of animal or human health, a derogation may be granted.

All this falls under Article 6, section 1ter of the law of 25 March 1964 on medicinal products, as amended by the law of 1 May 2006 revising pharmaceutical legislation.

This article is transposed from Article 24 (4, 5 and 6) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended by Directive 2004/27/EC of 31 March 2004 and Article 28 (4, 5 and 6) of Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products, as amended by Directive 2004/28/EC of 31 March 2004.

SCOPE OF APPLICATION

Which medicinal products fall under the scope of application of the sunset clause?

The instructions as described in this document apply to all human and veterinary medicinal products for which a marketing authorisation or registration has been approved at the national level, independent of the type of procedure followed to obtain this approval (national procedure, MRP or DCP).

Medicinal products for which a parallel import authorisation or temporary use authorisation [1] (for veterinary medicinal products only) has been approved are not covered by the provisions of the sunset clause.

The application of the provisions of the sunset clause to medicinal products for which a marketing authorisation has been approved by the European Commission (centralised procedure) falls under the competency of the European Commission and is described in Article 14 (4, 5 and 6) of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

What do we mean by MA or registration in the "global" sense?

The MA or registration in the "global" sense includes all doses, pharmaceutical forms, methods of administration and different presentations of the same medicinal product.

To determine which medicinal products are part of the MA or registration in the global sense, the following selection criteria are used: the same name, the same qualitative composition of active ingredients and the same marketing authorisation or registration holder.

As far as the sunset clause is concerned, this means that as soon as one of the presentations of the medicinal product is available on the market (e.g. *5 mg tablets in a blister pack*), the three year period no longer counts for other presentations of this same medicinal product (e.g. *5 mg tablets in a bottle, 10 mg tablets, 1 mg/ml syrup,* etc.) and the MA or registration remains valid for all presentations.
The sunset clause shall be applied to the different presentations of a medicinal product covered by an MA or registration in the global sense 3 years after the end of availability on the market of the most recent of one of these presentations, or 3 years after the latest MA or latest registration has been approved if none of these presentations has been marketed since this date.

Duplicates of an MA or registration (originating from the same dossier, with the same legal basis, a different name, the same or another authorisation holder) are not considered as falling under the MA or registration in the global sense.
The availability on the market of a medicinal product covered by an original MA or original registration is therefore not sufficient to keep a duplicate of this MA or of this registration, and vice-versa.

1 Article 229 of the royal decree of 14 December 2006 on human and veterinary medicinal products.

How should the term "marketing" be understood?

The term "marketing" includes being freely available to other commercial operators than the marketing authorisation or registration holder, such as wholesalers, wholesaler-distributors and pharmacists (retail pharmacies and hospital pharmacies) and veterinary depot managers.

Medicinal products that are made available in the form of samples or under compassionate use or a medical emergency programme do not meet this definition and are therefore not subject to the provisions of the sunset clause.

What happens if there is a change in MA or registration holder (transfer of MA or registration)?

Usually, a change of MA or registration holder makes no difference whatsoever to the application of the sunset clause provisions. If, for example, after 2 years, the MA or registration holder sells a medicinal product not available on the market, the new authorisation holder still has 1 year remaining to market the medicinal product.

There are, however, 2 exceptions to this rule:

1) In the case of an MA where the Sunset Clause is already in application but which is protected thanks to the "global MA" notion.

For example, **authorisation holder X** holds the two following MAs for similar medicinal products:

1. WONDERPIL 5 mg tablets: **not available on the market for over 3 years.**

2. WONDERPIL 10 mg tablets: **available on the market**

In this case, thanks to the "global MA" (linked to the same holder) notion, WONDERPIL 5 mg's MA is protected from the application of the sunset clause as long as WONDERPIL 10 mg is still available on the market.

Now, let's imagine that **authorisation holder X** decides to transfer only the MA for WONDERPIL 5 mg to a new holder, **authorisation holder Y**.

According to current legislation, since WONDERPIL 5 mg therefore becomes an MA linked to **new authorisation holder Y**, its MA would be simultaneously cancelled on the day of transfer because its period of unavailability on the market is greater than 3 years.

In this case, an extension of the duration of validity of the MA is granted for a period of 12 months from the date of transfer of the authorisation holder.

Conditions for granting the derogation:

1. This procedure is only valid in the case of the **first change** of MA holder (**non-cumulative** with other previous transfers).

2. This extension would be granted based on a "commitment" from **new authorisation holder Y** that they will do everything in their power to effectively market this newly transferred medicinal product.

2) In the case of an MA for which the Sunset Clause is not yet

in application, but will be in a period of less than 12 months.

For example, **authorisation holder X** has an MA:

1. SUPRAPIL 1 mg tablets: **not available on the market and with an MA that will fall under scope of application of the Sunset Clause in less than 12 months.**

Authorisation holder X transfers the aforementioned MA to authorisation holder Y after the second year of unavailability on the market.

In this case, an extension of the duration of validity of the MA is granted for a period of 12 months from the date of transfer of the authorisation holder.

Conditions for granting the derogation:

1. This extension will be granted based on a "commitment" from **new authorisation holder Y** that they will do everything in their power to effectively market this newly transferred medicinal product within 12 months.
2. It is still possible to transfer this MA to a third party, but the final deadline of the derogation to market the product would remain unchanged.

What date is considered as the starting point of the "period of 3 years of unavailability on the market"?

Here, we differentiate between two cases:

1. MA or registration not followed by effective marketing or registration

MA or registration approved for the first time before April 1 2007

Date of commencement of the "period of 3 years of unavailability on the market"
= 1 April 2007

Article 269 of the royal decree of 14 December 2006 states that authorisation holders, from 1 January 2007 (= entry into effect of this decree) must report, within the first three months, if their medicinal product is effectively being

marketed. The three-year period therefore only begins from the 1 April 2007.

MA or registration approved for the first time after 1 April 2007

Date of commencement of the "period of 3 years of unavailability on the market"
= first date of approval of the MA or registration

2. The medicinal product has previously been marketed but has not been available on the market for three consecutive years

Medicinal product unavailable on the market on 1 April 2007

Date of commencement of the “period of 3 years of unavailability on the market”
= 1 April 2007

Article 269 of the royal decree of 14 December 2006 states that authorisation holders, from 1 January 2007 (= entry into effect of this decree) must report, within the first three months, if their medicinal product is effectively being marketed. The three-year period therefore only begins from the 1 April 2007.

Medicinal product no longer available on the market after 1 April 2007

Date of commencement of the “period of 3 years of unavailability on the market”
= date of notification of the discontinuation of marketing.

DEROGATIONS

The Minister or their delegate may grant exemption from the application of the sunset clause provisions.
Derogations shall only be granted on an exceptional basis.
Please ensure you provide sufficient details to justify your request.

Below, there are several cases for which it may or may not be possible to request a derogation. This section will also provide details on how to submit a request.

To whom can I send a derogation request?

Requests for a derogation from the provisions of the sunset clause should preferably be sent by email to the following address: derog.sunsetclause@fagg-afmps.be.

with the following subject line in the email:

- HUM derogation → if the derogation is in reference to a human medicinal product,
- VET derogation → if the derogation is in reference to a veterinary medicinal product,
- the name of the medicinal product.

For example: Subject: HUM derogation – medicinal product's name.

including the following in the body of the email:

- the authorisation number(s) of the medicinal product(s) in question
- the authorisation holder of the medicinal product(s) in question

You may also send your request by post to the following address:

Federal agency for medicines and health products
DG Post
Place Victor Horta 40/40
1060 Brussels

When can I submit a derogation request?

You can submit a derogation request at the earliest 12 months before the provisions of the sunset clause become applicable.

If the derogation is granted for a certain duration, the time granted begins starting from 3 years after the date considered as the starting point for the "period of 3 years of unavailability on the market" (*see pages 5 and 6*).

Under what circumstances can a derogation be requested/granted?
And for how long?
How to submit a request? What documents/information do I have to attach to my request?

A. Medicinal product intended exclusively for export

Law of 25 March 1964 on medicinal products,
Article 12bis, section 2, sub-paragraph 2

> "If a medicinal product has obtained an MA or a registration and this medicinal product is exclusively intended for export to third party countries, it is exempted from the provisions of article 6, section 1ter, sub-paragraphs 4 and 5, on request from the authorisation or registration holder."

This concerns medicinal products that are effectively exported.

Please provide the following documents:

- *a declaration, signed by the authorisation or registration holder, accompanied by the list of countries to which the medicinal product is exported, specifying for each country the quantity (number of packagings) exported (through invoicing, for example).*
- *a declaration confirming that the exported medicinal product was manufactured in accordance with the registration dossier as approved in Belgium.*
- *if possible, proof of import of this medicinal product into at least one other country, issued by the authorities of the importing country.*

After examination of the documents, in the case of a favourable decision, a derogation shall be granted for a period of 3 years.

Once this deadline is reached, another request for derogation may be submitted. Please ensure that an updated version of the aforementioned documents is provided for the new submission. After examination of the documents, in the case of a favourable decision, a derogation shall be granted each time for a period of 3 years.

B. Reasons of public health

Law of 25 March 1964 on medicinal products,
Article 6, section 1ter, sub-paragraph 7

> "The minister or their delegate may, in exceptional circumstances and for reasons of public health or the protection of human or animal health, make exceptions to sub-paragraphs 4 and 5. "

In this case, two conditions must always be met, namely "in exceptional circumstances" and "for reasons of public health or the protection of human or animal health".

B.1. Vaccinations, immunological medicinal products, essential medicinal products, etc.

Please justify your request.
Requests will be examined on a case by case basis by the competent division of the FAMHP.

After evaluation, in the case of a favourable decision, a derogation shall be granted for an unlimited time period.

B.2. Certificate of pharmaceutical product (CPP) [2]

This concerns medicinal products that are not marketed in Belgium (and often not in Europe) and which are also not exported, but for which the MA or registration approved in Belgium is used as a reference for the approval of the medicinal product in another country. These CPP are required to be able to market the medicinal product in this country.

Please provide a document in which it clearly appears that, for the approval of the MA in the country in question, reference is made to the MA or registration approved in Belgium.
This document should be issued by the authority in the country in which the medicinal product is marketed.
If this is not possible, a signed declaration by the authorisation or registration holder shall suffice.

After examination of the documents, in the case of a favourable decision, a derogation shall be granted for a period of 3 years.

Once this deadline is reached, another request for derogation may be submitted. Please ensure that an updated version of the aforementioned documents is provided for the new submission. After examination of the documents, in the case of a favourable decision, a derogation shall be granted each time for a period of 3 years.

B.3. Belgium = RMS

Medicinal products for which Belgium acts as the RMS as part of the MRP or DCP.

Please justify your request.
Requests will be examined on a case by case basis by the competent division of the FAMHP.

After evaluation, in the case of a favourable decision, a derogation shall be granted for a period of 3 years.

Once this deadline is reached, another request for derogation may be submitted. Please justify your request. After evaluation, in the case of a favourable decision, a derogation shall be granted each time for a period of 3 years.

[2] According to the format recommended by the World Health Organisation

C. Patent right[3]

The authorisation holder intends to market the medicinal product, but due to the existence of a patent or a dispute over the patent (ongoing legal proceedings), the medicinal product in question cannot be marketed.

In the case of a patent, please provide information about the existing patent, clearly indicating the date on which this patent expires.

After examination of the documents, in the case of a favourable decision, a derogation shall be granted up to the expiry date of the patent. The "period of 3 years of unavailability on the market" shall only begin starting from this date.

In the event of a dispute, please provide the supporting documents proving the existence of an ongoing dispute (e.g. summons).

After examination of the documents, if it is justified, a derogation shall be granted for a period of 1 year.

Once this deadline is reached, another request for derogation may be submitted. Please ensure that an updated version of the aforementioned documents is provided for the new submission. After examination of the documents, in the case of a favourable decision, a derogation shall be granted for a period of 1 year.

D. Procedural reasons/unforeseen circumstances

The effective marketing is planned sufficiently far in advance before the sunset clause provisions become applicable, but cannot yet be carried on as a result of procedures that are not yet complete or of circumstance that may or may not have been foreseen.

Example: Price or reimbursement request pending
MA transfer in the specific cases set out above in the *"What happens if there is a change in MA or registration holder (transfer of MA or registration)?"* section.
Variation dossier not yet finalised by the FAMHP
Unexpected problems with production, logistics, delivery, etc.

The marketing authorisation or registration holder must be able to demonstrate that they have done everything in their power to market the medicinal product within **a reasonable time frame** following the approval of the MA or of the registration. Persistent problems or the submission of a variation or price and/or reimbursement request are not in themselves valid reasons for a derogation to be granted.

What factors are taken into account when evaluating the request?

- A price request must have be submitted at least 90 days prior to the application of the provisions of the sunset clause

[3] The assessment and evaluation of patents does not fall within the FAMHP's remit. Their decision is based solely on the information submitted by the authorisation holders in question. Consequently, the FAMHP cannot be held responsible for the correction or the accuracy of the information provided. This responsibility falls solely to the authorisation holder.

A reimbursement request must have be submitted at least 180 days prior to the application of the provisions of the sunset clause.
However, with regards to medicinal products for which the provisions of the sunset clause are applicable before 1 November 2010, it is sufficient to demonstrate that the price or reimbursement request has been submitted.

- Problems with production that have been ongoing for over a year and for which no solution has yet been found are not considered to be an acceptable reason.

Please provide the following documents:

- *in the case of a pending variation dossier with the FAMHP – indicate the dossier number,*
- *in the case of an ongoing dossier regarding price or reimbursement – provide a document in which the dossier is shown to be pending,*
- *in all other cases: clear arguments and proof of existing problems. Please also provide any available information relating to the date of the end of the procedure and/or the problems and the anticipated marketing date.*

After evaluation, in the case of a favourable decision, a derogation shall be granted for a limited time period. The duration shall depend on the information provided in the document, up to a maximum duration of 1 year.

Once this deadline is reached, another request for derogation may be submitted. Please ensure that an updated version of the aforementioned documents is provided for the new submission. After examination of the documents, in the case of a favourable decision, a derogation shall be granted for a maximum period of 1 year.

Under what circumstances will a derogation not be granted?

E. Belgium = CMS

Medicinal products for which Belgium acts as CMS as part of the MRP or DCP and which are not marketed in Belgium, but which are marketed in another Member State.

In the case of an MRP or DCP, the marketing authorisation is approved on the national level. The potential cancellation of the MA in Belgium does not have any effect on the continuance or discontinuance of an MA in another Member State.

F. Medicinal product = reference medicinal product

The medicinal product for which the dossier is used as a reference for the MA of another medicinal product.

The withdrawal of the MA of a medicinal product for which the dossier is used as a reference for another medicinal product in no way constitutes a hindrance to the application of the sunset clause. This is because the information on which the approval of the MA for the first medicinal product was based remains available to the FAMHP. The withdrawal of the MA for the first medicinal product can therefore not constitute a hindrance to the approval or continuation of the MA for the medicinal product referring to the first medicinal product.

How long does it take to get an answer from the FAMHP?

Except in the case of exceptional circumstances, the FAMHP shall respond to a request for a derogation from the application of the provisions of the sunset clause within 2 months of receipt of the request.

If any documentation or additional information must be provided by the authorisation or registration holder, this deadline may be extended.
The marketing authorisation or registration holder has 1 month after the dispatch of the letter to submit the requested documentation or information. Should they fail to react within this time frame or if their response is incomplete, the procedure to cancel the MA applicable under Article 6, section 1ter, sub-section 6 of the law of 25 March 1964 on medicinal products shall be carried out.

CANCELLATION OF THE MARKETING AUTHORISATION OR OF THE THE REGISTRATION

Before cancelling a marketing authorisation or registration, the FAMHP shall inform the authorisation or registration holder of their intention to do so.

If the authorisation or registration holder is not in agreement, they may request a derogation from the application of the provisions of the sunset clause.

If there has been no reaction from the authorisation or registration holder within 2 months of the sending of the FAMHP's first letter, the effective cancellation of the MA or registration is carried out.

CONTACT

If you have any more questions concerning the application of the provisions of the sunset clause in Belgium, please send an email to fagg-afmps.sunsetclause@fagg-afmps.be.