Guideline no. 9259 of 11 March 2022

Danish Ministry of Health

Guideline on variations to marketing authorisations for medicinal products for animal use

Contents

1. INTRODUCTION

This guideline covers variations to marketing authorisations for medicinal products for veterinary use (hereinafter “veterinary medicinal products”).

Variation means any amendment to the terms of an authorisation to market a veterinary medicinal product as well as any change to the summary of product characteristics and the documents forming the basis for a marketing authorisation.

Pursuant to articles 61 and 62 of Regulation (EU) No 2019/6 on veterinary medicinal products (hereinafter the “Veterinary Regulation”), the marketing authorisation holder (hereinafter the “MAH”) must register or apply for authorisation of a variation.

This guideline provides general information on the rules for amending a marketing authorisation and offers practical instructions in special situations.

In the context of variations, “the same MAH” means applicants belonging to the same parent company or group of companies and applicants having entered into agreements on or exercising concerted practices in relation to the placing on the market of the veterinary medicinal product concerned. The term “same marketing authorisation” includes all pharmaceutical forms and strengths of a given veterinary medicinal product, i.e. one D.Sp.No. (Danish speciality number).

1.1. The rules on variations in brief

The Veterinary Regulation lays down rules for the marketing, manufacture, import, export, supply, distribution, pharmacovigilance, control and use of veterinary medicinal products. As of 28 January 2022, the Veterinary Regulation must be applied in all EU countries.

The Veterinary Regulation replaces previous regulation in the area. The regulation thus replaces the Veterinary Directive that has been implemented in the Danish Medicines Act and related executive orders.

Articles 60-68 of the Veterinary Regulation introduce a body of rules applicable to the assessment of variations. The rules replace the Commission Regulation (EC) No 1234/2008 as amended concerning medicinal products for human use and veterinary medicinal products (hereinafter the “Variation Regulation”). However, a few veterinary medicinal products are exempt from the Veterinary Regulation, cf. article 2(7) of the Regulation. Variations of these veterinary medicinal products will remain subject to the rules of the Variation Regulation.

The rules applicable to variations described in articles 60-68 of the Veterinary Regulation are supplemented by a so-called implementing regulation and guidance on the details of classification of variations from the Coordination group for mutual recognition and decentralised procedures for veterinary medicinal products (CMDv).

The implementing regulation contains an annex which is a list of variations not requiring assessment by the Danish Medicines Agency prior to their implementation by the MAH (hereinafter “VNRA” = variations not requiring assessment). MAHs are responsible for registering these variations in the Union Product Database (“UPD”), the European database of medicinal products.

The CMDv guidance is a list of variations requiring assessment by the Danish Medicines Agency prior to their implementation by the MAH (hereinafter “VRA” = variations requiring assessment). The MAH must apply to the Danish Medicines Agency for approval of these variations.

In the case of both VNRA and VRA, the Danish Medicines Agency decides whether to grant of refuse the variation.

The implementing regulation and the CMDv guidance also apply from 28 January 2022.

1.2. Additional information on the website of the Danish Medicines Agency

Supplementary information about variations can be found on the website of the Danish Medicines Agency in the form of links to regulations, guidelines and the like as well as questions and answers about variations, if available. The information is updated regularly, and MAHs are advised to acquaint themselves with any relevant details.

2. THE SCOPE OF THIS GUIDELINE

This guideline applies to variations of marketing authorisations for veterinary medicinal products granted by the Danish Medicines Agency before 28 January 2022 pursuant to the rules in force up until then (i.e. the Danish Medicines Act and related executive orders), or on or after 28 January 2022 pursuant to the rules of the Veterinary Regulation.

The guideline covers marketing authorisations granted by the Danish Medicines Agency under the purely national procedure, the decentralised procedure (*DCP*), the mutual recognition procedure (*MRP*) or the subsequent recognition procedure (*SRP, previously RUP*).

The guideline does not, however, cover marketing authorisations granted by the European Commission pursuant to the centralised procedure.

2.1. Delimitation of veterinary medicinal products

Article 2 of the Veterinary Regulation establishes the veterinary medicinal products the regulation applies to. A few veterinary medicinal products are exempt from the regulation, cf. article 2(7) of the regulation.

Variations related to veterinary medicinal products not comprised by the Veterinary Regulation are instead regulated by the Variation Regulation and its related guidelines, see section 1.1.

2.2. Homeopathic veterinary medicinal products

Homeopathic veterinary medicinal products that are registered in compliance with article 86 of the Veterinary Regulation are not comprised by the Veterinary Regulation's rules on for example variations. Variations related to registered homeopathic veterinary medicinal products are subject to the rules of the Variation Regulation, cf. the Executive Order on Homeopathic Medicinal Products, etc.

2.3. Veterinary medicinal products imported in parallel

A parallel importer of a veterinary medicinal product is not required to hold a marketing authorisation for parallel import under the Veterinary Regulation. A parallel importer must hold a parallel trade authorisation, cf. article 102 of the Veterinary Regulation.

The obligation to register or apply for approval of a variation under the rules of the Veterinary Regulation is imposed on the MAH in the export country (termed the “source Member State” in the regulation). In other words, the parallel trader of a veterinary medicinal product is thus not required to register or apply to the Danish Medicines Agency for approval of variations of the parallel traded veterinary medicinal product. The parallel trader must instead notify the Danish Medicines Agency of any variations of the parallel traded veterinary medicinal product in the export country having been approved by the authorities in the export country, cf. the Executive Order on Authorisation of Parallel Trade in Medicinal Products for Animal Use. Please also see the guideline on parallel trade in medicinal products for animal use (in Danish only).

3. TYPES OF VARIATIONS

There are two types of variations under the Veterinary Regulation, namely:

1) Variations not requiring assessment (VNRA) (cf. article 61)

These types of variations are listed in the annex of the implementing regulation.

The annex lays down the requirements that each variation must meet to be classified as VNRA.

2) Variations requiring assessment (VRA) (cf. article 62)

These types of variations are listed in the CMDv guidance.

Furthermore, a variation is classified as VRA when a variation otherwise covered by the annex of the implementing regulation does not meet the established requirements.

It applies to both VNRA and VRA that if a variation leads to consequential changes to the summary of product characteristics, labelling and/or package leaflet (the “product information”) any such changes are considered part of the variation concerned.

3.1. Variations not requiring assessment (VNRA)

To be classified as VNRA, the variation must appear from the annex of the implementing regulation, and the requirements therein must be met. Requirements mean that the conditions specified must be met and that the required documentation must be provided. It is emphasised that the applicable requirements indicated for a main change (main section) must be met in addition to the requirements applicable to the specific change (sub-section).

Example of a quality change:

Classification “B. 3” is the main change (main section), the applicable requirements being documentation to be provided.

Classification “B. 3.a” is the specific change (sub-section), the applicable requirements being both conditions to be met and documentation to be provided.

If just one of the applicable requirements are not met, the variation in question is to be classified as VRA.

Editorial changes cannot be included in a registration of a VNRA. See the definition of editorial changes in section 3.2.

The annex of the implementing regulation is divided in these sections:

A) Administrative changes
B) Quality changes
C) Safety, efficacy and pharmacovigilance changes
D) Vaccine antigen master file (VAMF) changes

3.1.1. VNRA registration procedure

If a variation meets the requirements referred to in section 3.1, the MAH must register the variation in UPD within 30 days of having implemented the change.

Guidance on how the MAH is to register the change in UPD can be found on the website of the European Medicines Agency (EMA).

When the MAH registers the variation in UPD, a clear explanation of the scope/background for the change must be provided in the “submission comments” field. The MAH must also indicate what is authorised at present as well as the proposed changes being applied for. The purpose is to provide an overview of the variation applied for. The text must be unambiguous and as concise and precise as possible. The MAH must include a reference to the related updated sections of the dossier.

When registering a variation in UPD, the MAH must also enclose all necessary documentation and, where relevant, the summary of product characteristics, labelling and package leaflet. In the case of variations to veterinary medicinal products marketed in Denmark, the relevant material must be in Danish.

Variations linked to a VRA can be submitted via UPD with a future implementation date.

The Danish Medicines Agency will decide whether to accept or reject the variation. The Danish Medicines Agency notifies the MAH of its decision by registering it in UPD. The Danish Medicines Agency aims to make this registration within 30 days of the date when the MAH registered the variation in UPD.

If the variation is rejected, the Danish Medicines Agency will at the time of registering its decision in UPD also inform the MAH of the outcome by letter.

If an approved variation concerns the summary of product characteristics, labelling and/or package leaflet, the Danish Medicines Agency will at the time of registering its approval also send a letter to the MAH. This letter will detail the date by which the approved variation must be made in the labelling and/or package leaflet and whether the MAH must notify the variation to Medicine Prices via DKMAnet, see sections 5.2 and 5.3. In the case of a variation for a marketing authorisation granted by the Danish Medicines Agency via DCP, MRP or SRP with Denmark as Reference Member State, the Danish Medicines Agency will inform the MAH and the competent authorities of the relevant Member States as to whether the variation is accepted or rejected.

If the Danish Medicines Agency decides to reject a registration, the MAH must ensure to revert matters to the situation existing before the implementation of the change.

3.2. Variations requiring assessment (VRA)

Variations requiring assessment are classified in the CMDv guidance. Furthermore, a variation is classified as VRA when a variation otherwise covered by the annex of the implementing regulation does not meet the established requirements.

In the case of VRA types listed in the CMDv guidance and where requirements for documentation apply, the required documentation must be provided. Note, however, that the list is not exhaustive and does not mention all documentation requirements of relevance, the reason being that the documentation requirements depend on the specific nature of the variation. In case the variation will affect the content of the dossier of the veterinary medicinal product, all updated sections of the dossier must be provided with the variation application.

Editorial changes of the dossier of veterinary medicinal products are generally considered part of the VRA concerning the relevant part of the dossier. In such cases, there is no need to process the editorial changes as a separate VRA. These must instead be highlighted clearly in the variation application as editorial changes. In addition, the MAH must submit with the application a statement indicating that the content of the relevant part of the dossier has not been changed by the editorial change beyond the variation applied for. For example, an editorial change comprises the removal of outdated or superfluous text, but not the removal of specification parameters or manufacturing descriptions.

The CMDv guidance is divided as follows, thus supplementing the annex of the implementing regulation:

E) Administrative changes
F) Quality changes
G) Safety, efficacy and pharmacovigilance changes
H) Vaccine antigen master file (VAMF) or platform technology master file (PTMF) changes

I) Changes of active substance(s), strength, pharmaceutical form, route of administration or food producing target species.

3.2.1. VRA application procedure

A variation application must be submitted to the Danish Medicines Agency via CESP (Common European Submission Platform).

The application must consist of a cover letter, a completed electronic application form and any required documentation, including an updated quality overall summary, expert report or expert opinion and CV of expert and where applicable the summary of product characteristics, labelling and package leaflet in the relevant language. If the MAH has obtained a classification recommendation on a variation from the CMDv or from the EMA (see section 4), a copy of that recommendation must be attached.

The variation application form must be downloaded from the website of the European Commission (esubmission.ema.europa.eu).

In case of medicinal products authorised under the purely national procedure, the summary of product characteristics, labelling and package leaflet are required in Danish only. This product information must be presented with the submitted variation application. Mock-ups or specimens must be made available as necessary.

In case of variations resulting in changes to the summary of product characteristics, the submission of a draft version of the updated summary of product characteristics in an electronic and editable format (Word) is required. The same applies to the draft versions of the package leaflet and labelling if the variation results in changes to these documents. The documents must be enclosed in an annotated version and a clean version.

Only one authorised summary of product characteristics with associated package leaflet and labelling can exist. If, for a veterinary medicinal product, several variation applications are submitted and reviewed simultaneously and which result in changes to the product information, each variation must be based on the authorised summary of product characteristics and the associated package leaflet and labelling. Immediately after the approval of one of the variations, the applicant is responsible for submitting a consolidated summary of product characteristics, package leaflet and labelling for the variations that are still in the review procedure. The purpose is to ensure that the product information is harmonised in line with all variations.

Generally, only one variation per application form can be applied for to the Danish Medicines Agency. It is possible, however, to derogate from this rule in connection with grouping of variations and worksharing procedures, where the MAH can submit all variations on the same application form.

3.2.2. Grouping

Grouping of variations is only possible for VRA, cf. article 64 of the Veterinary Regulation. This means grouping is not possible for VNRA. This also rules out grouping VRA and VNRA together.

It is recommended not to group variations that are not related, e.g. grouping of quality changes and safety/efficacy changes

If several variations related to the same marketing authorisation granted by the Danish Medicines Agency are submitted at the same time, all variations can be submitted on the same application form.

If for several purely national marketing authorisations held by the same MAH and granted by the Danish Medicines Agency one or more identical changes are applied for, all changes can be submitted on the same application form.

3.2.3. Worksharing

Worksharing is only possible for VRA, cf. article 65 of the Veterinary Regulation. This means worksharing is not possible for VNRA.

If for several marketing authorisations held by the same MAH and granted by different competent authorities one or more identical changes are applied for, all changes can be submitted on the same application form.

3.2.4. Review of the application

Articles 66 and 67 lay down the procedures for the assessment of variation applications, including the review time allowed. The CMDv website provides access to additional information, including CMDv guidelines, which, for example, provide information on the procedures, review times and timetables.

Upon receipt of an application, the Danish Medicines Agency acknowledges receipt of a valid application within 15 days.

If information and/or documentation is lacking in an application, the Danish Medicines Agency will set a reasonable deadline for the MAH to submit the missing information and/or documentation.

Once the Danish Medicines Agency has received a valid application, it will review the application.

The annex of the CMDv guidance on the classification of variations provides general estimates of the review times for assessment of the variations listed therein.

In general, the Danish Medicines Agency must prepare its assessment within 60 days of receipt of a valid application (standard timetable). This time limit may, however, be extended to 90 days if the Danish Medicines Agency finds the variation application to be of a more complex nature (extended timetable). If so, the MAH will be notified of the extended timetable. The review time of certain less complicated VRA types is reduced to 30 days (reduced timetable). For variations requiring urgent assessment, there is a possibility to apply for a shorter review time of 22 days.

If after reviewing the application, the Danish Medicines Agency requires further information, it may within the review time allowed request the MAH to provide supplementary information within a set time limit. The review times of 30, 60 or 90 days will in this case be suspended. This means the indicated review times do not include the time it takes the MAH to answer requests made by the Danish Medicines Agency.

Grouped variations including more than one variation will be processed according to the longest review time of the variations in the group. As mentioned in section 3.2.2, it is recommended not to group variations that are not related, e.g. quality changes and safety/efficacy changes. If any such variations are grouped, the review time of 90 days will apply (extended timetable).

The Danish Medicines Agency will decide whether to accept or reject the application. The review of an application covering several variations is closed with a decision in which the Danish Medicines Agency has considered each submitted variation. The decision may therefore include both accepted and rejected variations.

In the case of a variation for a marketing authorisation granted by the Danish Medicines Agency via DCP, MRP or SRP with Denmark as Reference Member State, the Danish

Medicines Agency will inform the MAH and the competent authorities of the relevant Member States as to whether the variation is accepted or rejected.

The MAH may not implement the variation before the Danish Medicines Agency has approved the variation and has amended the marketing authorisation in accordance with that variation and has set a time limit for the implementation, cf. article 68(1) of the regulation.

4. UNCLASSIFIED VARIATIONS

Variations that are not classified in the annex of the implementing regulation (applicable to VNRA) or in the CMDv guidance (applicable to VRA) must automatically be classified as VRA, in general using a review time corresponding to the reduced timetable. This time limit may, however, be extended if the Danish Medicines Agency finds the variation application to be of a more complex nature (standard timetable or extended timetable). The CMDv guidance already includes these VRA types, indicated with a “z” in the guidance e.g. quality change F. I.a. 1.z.

However, the MAH may request the Danish Medicines Agency to provide a recommendation on the classification of a variation. The procedure for such request is described in the CMDv guidance on requests for classification. The recommendations given through this procedure are, as standard, published on the respective websites of the CMDv and the EMA.

5. IMPLEMENTATION OF VARIATIONS, IMPACT ON LABELLING AND/OR PACKAGE LEAFLET AS WELL AS NOTIFICATION OF VARIATIONS TO MEDICINE PRICES

For variations affecting the veterinary medicinal product’s labelling and/or package leaflet, the implementation of the variation means the time when the Qualified Person (QP) releases the new packages. These variations are subject to a special process for implementation on the market of new packages with the changed labelling and/or package leaflet and in certain cases also a process for notification to Medicine Prices via DKMAnet. The process is described in general in sections 5.2 and 5.3, whereas special situations are described in section 5.4.

For other variations not affecting the veterinary medicinal product’s labelling and/or package leaflet, the implementation of the variation means the time when the MAH implements the change. For instance, in respect of changes related to quality, the implementation of the variation is the time when the MAH implements the change in the MAH’s quality system.

5.1 Implementation of variations not affecting the veterinary medicinal product’s labelling and/or package leaflet

If a variation affects only the content of the summary of product characteristics, but not the labelling and/or package leaflet, the Danish Medicines Agency will generally update the summary of product characteristics at the time of approving the variation.

5.2 Implementation of variations affecting the veterinary medicinal product’s labelling and/or package leaflet

A variation affecting the labelling and/or package leaflet must be implemented for the labelling and package leaflet simultaneously. Changes to the labelling and/or package leaflet must generally be implemented within one year of the Danish Medicines Agency’s approval of the variation.

The implementation must comprise all medicinal products and associated pack sizes covered by the authorisation, including medicinal products that are currently not on the market.

However, the 1-year deadline requires that the following conditions are met:

1) It appears from the current package leaflet (in the packages) that the newest package leaflet is available at www.indlaegsseddel.dk, and

2) The updated package leaflet is uploaded to www.indlaegsseddel.dk no later than three months after the Danish Medicines Agency approved the variation.

In the case of condition 1, we recommend inserting this information between the package leaflet heading and the section with the name and address of the MAH. The standard sentence defined by the Danish Medicines Agency is: ”Se den nyeste indlægsseddel på www.indlaegsseddel.dk” (“See the newest package leaflet at www.indlaegsseddel.dk”).

If these two conditions are not met, the Danish Medicines Agency requires that the changes to the labelling and/or package leaflet be implemented within six months of the Danish Medicines Agency’s approval of the variation.

However, the Danish Medicines Agency may in each specific case always set a shorter or longer deadline for implementation of changes to the labelling and/or package leaflet. Any such special implementation terms will be established in connection with the approval of the variation.

Up until the deadline for implementation, both new packages reflecting the approved variation and old packages with the old labelling may be released. Upon expiry of the implementation deadline, only new packages with the updated labelling, etc. may be released.

If a change to the summary of product characteristics of a veterinary medicinal product involves matters related to the safety of using the veterinary medicinal product, the Danish Medicines Agency’s approval will detail if the package leaflet must be changed immediately and if a withdrawal of the veterinary medicinal product is required.

5.3 Notification to Medicine Prices of variations affecting the veterinary medicinal product’s labelling and/or package leaflet

After their approval certain variations affecting medicinal products on the market or previously on the market must also be notified to the Danish Medicines Agency to be changed in Medicine Prices via DKMAnet – Prices & Packages. When the Danish Medicines Agency approves these variations, the approval is made subject to this notification requirement.

The following variations must be notified to Medicine Prices:

- Change in the name or address of the MAH or representative
- New representative or removal of representative
- New MAH
- New medicinal product name.

If a variation is subject to notification to Medicine Prices, notification must take place by the implementation deadline for changing the labelling and/or package leaflet in line with the approved variation. When the MAH or the representative notifies the variation to Medicine Prices, they also indicate being ready to place on the market the first packages with the change. Notification for the entire D.Sp.No. (Danish speciality number) must be made at the same time. At the time of releasing the new packages, an updated package leaflet must be uploaded to www.indlaegsseddel.dk.

5.4. Special situations

5.4.1 Change in the name or address of the MAH or representative

A change in the name or address of the MAH is a VNRA and can thus be implemented through registration in UPD, see section 3.1.

A change in the name or address of a representative is a VRA with classification E.z. The change must thus be approved by the Danish Medicines Agency upon application.

For both types of variation, the variation must be notified to Medicine Prices via DKMAnet, unless the affected medicinal products are not or have not previously been marketed. The change must be notified for the entire D.Sp.No. at the same time. When making the notification, the MAH indicates being ready to place on the market the new packages with the approved variation.

From the time when the notification to Medicine Prices takes effect, there is an implementation period of two years. Within this period the new packages with the changed labelling and/or package leaflet must be implemented on the Danish market. During this period, both new and old packages within the relevant D.Sp.No. can be released on the market. For each implementation of a new package, the MAH indicates that going forward, only new packages of the specific package of medicine are released.

When new packages have been implemented for all the marketed medicine packages with the concerned D.Sp.No. or by the expiry of the implementation period, only new packages with the updated labelling etc. can be released. There is no requirement for withdrawing packages with the old labelling, unless the MAH is part of the medicinal product name, see section 5.4.4.

If the MAH changes its name, the marketed packages are not required to have a new product number pursuant to the rules of the Executive Order on Product Numbers for Human and Veterinary Medicinal Products, unless the MAH's name change affects the medicinal product name, see section 5.4.4.

5.4.2 New representative or removal of representative

A change to a new representative or removal of a representative is a VRA with classification E.z. The change must thus be approved by the Danish Medicines Agency upon application.

After approval, the variation must be notified to Medicine Prices via DKMAnet, unless the affected medicinal products are not or have not previously been marketed. Notification for the entire D.Sp.No. must be made at the same time. When making the notification, the MAH indicates being ready to place on the market the new packages with the approved variation.

From the time when the notification to Medicine Prices takes effect, there is an implementation period of two years. During this period, both new and old packages within the relevant D.Sp.No. can be released on the market. For each implementation of a new package, the MAH indicates that going forward, only new packages of the specific package of medicine are released.

When new packages have been implemented for all the marketed medicine packages with the concerned D.Sp.No. or by the expiry of the implementation period, only packages with the new labelling can be released. Withdrawal of packages with the old labelling is not required.

Implementation of a change of representatives for parts of a D.Sp.No. must be notified for all the affected marketing authorisation numbers (MA numbers). The same implementation process and the same deadlines will continue to apply.

5.4.3 New MAH and any consequential changes to the medicinal product name

A change to a new MAH is a VRA with classification E.z. The change must thus be approved by the Danish Medicines Agency upon application.

If the name of the MAH is part of the name of the veterinary medicinal product (the common name), an application for approval of the variation to change the MAH must include an application to change the name of the medicinal product. When changes are made to both the

MAH and the medicinal product name, the implementation process for changing the name of a medicinal product must be followed, see section 5.4.4 below.

After the approval of a new MAH, the variation must be notified to Medicine Prices via DKMAnet, unless the affected medicinal products are not or have not previously been marketed. Notification for the entire D.Sp.No. must be made at the same time. When making the notification, the MAH indicates being ready to place on the market the new packages with the approved variation.

From the time when the notification to Medicine Prices takes effect, there is an implementation period of two years. During this period, both new and old packages within the relevant D.Sp.No. can be released on the market. For each implementation of a new package, the MAH indicates that going forward, only new packages of the specific package of medicine are released.

When new packages have been implemented for all the marketed medicine packages with the concerned D.Sp.No. or by the expiry of the implementation period, only packages with the new labelling can be released. Withdrawal of packages with the old labelling is not required.

5.4.4 New medicinal product name

A change in the name of a veterinary medicinal product is a VNRA with classification A. 2 and can thus be implemented through registration in UPD, see section 3.1. However, this presupposes that the Danish Medicines Agency has approved the new name. Guidance on how the MAH can apply for a new medicinal product name can be found on the website of the Danish Medicines Agency.

The variation must be registered in UPD within 30 days of the name being accepted. It is possible to have a future implementation date approved.

The change of the medicinal product name must be notified to Medicine Prices via DKMAnet after approval of the variation, unless the affected medicinal products are not or have not previously been marketed. Notification for the entire D.Sp.No. must be made at the same time. When making the notification, the MAH indicates being ready to place on the market the new packages with the approved change in name.

If the name of the MAH is part of the name of the veterinary medicinal product (common name + MAH), a transfer to a new MAH or change in name of the MAH implies that the name of the medicinal product must be changed. If so, the change in the name of the medicinal product and the MAH must be notified to Medicine Prices simultaneously.

Changing the name of a medicinal product implies that the medicine packages concerned must receive a new product number.

Product numbers are administered by Danish Drug Information (Dansk Lægemiddel Information A/S) and can be ordered directly from the Pharmaceutical Information Center in Finland.

A new product number is not required for medicine packages which have a product number but have never been placed on the market, regardless if the name of the medicinal product is changed.

Upon notification of the change in the medicinal product’s name, the old medicine packages must be removed (withdrawn) from the market. When making this notification, the companies can therefore also notify the product numbers of the new medicine packages being introduced. After that, only medicine packages with the new labelling are marketed.

5.4.5 Deregistration of a pharmaceutical form or strength

Deregistration of one or more veterinary pharmaceutical forms and/or strengths (partial deregistration) can take place without the submission of a variation but must be notified to the Danish Medicines Agency.

For veterinary medicinal products placed on the market, the notification must always be made to Medicine Prices via DKMAnet – Prices & Packages.

For veterinary medicinal products not placed on the market, the notification can be made either to Medicine Prices via DKMAnet – Prices & Packages, or alternatively by email to godkendelse@dkma.dk or by ordinary post to the Danish Medicines Agency, Quality Assessment & Clinical Trials, Workflow, Axel Heides Gade 1, 2300 Copenhagen S.

If the deregistration of a pharmaceutical form or a strength implies changes to the summary of product characteristics, the MAH must also send a revised summary of product characteristics to the Danish Medicines Agency by e-mail to godkendelse@dkma.dk.

If the deregistration is expected to influence animal welfare, e.g. because no substitutable alternatives exist, the MAH must send a report about this no later than two months before the planned deregistration, to the Danish Medicines Agency, by email to shortage@dkma.dk. The report must contain information about the reason why the veterinary medicinal product is no longer to be marketed.

It may be relevant to send direct information to veterinarians, etc. with advice on how to deal with the supply shortage. Likewise, the Danish Medicines Agency may also provide information about the situation on the website of the Danish Medicines Agency.

5.4.6 Changed composition

If the composition of the veterinary medicinal product is changed, the MAH is obliged to ensure that the relevant stakeholders, e.g. veterinarians and pharmacies, have been duly informed of the changes prior to the placing of the altered version on the market. Likewise, the MAH is obliged to ensure that all relevant information about the changed composition has been provided on the packaging material.

If the product's appearance or active substances are changed, the Danish Medicines Agency requires that the change of the labelling and package leaflet takes place at the same time as the placing on the market of the packages with the implemented changes. The updated package leaflet must be uploaded to www.indlaegsseddel.dk by the time when the packages are placed on the marketed.

As regards variations implying changes to the appearance or taste of the veterinary medicinal product, the altered version may for a transitional period be affixed with a supplementary label, specifying that the product's appearance or taste has changed but that the content is otherwise the same. For a transition period of six months, it is acceptable that both compositions are on the market at the same time. The transitional period starts when the first new package is introduced.

5.4.7 Change in shelf life or storage conditions

Where the shelf life of a veterinary medicinal product is changed, the Danish Medicines Agency requires that the veterinary medicinal product currently on the market be withdrawn if its shelf life is longer than that of the new one. However, this does not apply if the change is not made for reasons of durability, but for instance to harmonise the shelf life in different countries.

Where storage conditions change, the currently marketed veterinary medicinal product must, in principle, be withdrawn.

In connection with a change of the veterinary medicinal product's shelf life or storage conditions, any change to the labelling and package leaflet must be implemented at the time the packages concerned are placed on the market.

5.4.8 Temporary repackaging of veterinary medicinal products

If the MAH temporarily needs to repackage medicinal products at a new site, the submission of a VNRA with classification B. 21 is required and may thus be completed through registration in UPD, see section 3.1. This also applies to veterinary medicinal products authorised under MRP and DCP. Detailed information is available at the website of the Danish Medicines Agency.

6. FEES

The Danish Medicines Agency charges fees pursuant to the Danish Executive Order on Fees in force at any time. The website of the Danish Medicines Agency provides information on the charging of fees. The information is regularly updated, and familiarisation with the relevant aspects is recommended.

7. REPLACEMENT OF THE PREVIOUS GUIDELINE

This guideline replaces Guideline No 9846 of 24 November 2020 on variations to marketing authorisations for medicinal products with regard to veterinary medicinal products.

Danish Medicines Agency, 11 March 2022

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/Pernille Rahbek

Annex 1

References

Veterinary Regulation: Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC

Veterinary Directive: 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

Danish Medicines Act: Consolidation Act No 99 of 16 January 2018 as amended

Variation Regulation: Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products as amended

Implementing regulation: Commission Implementing Regulation (EU) 2021/17 of 8 January 2021 establishing a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council

Executive Order on Homeopathic Medicinal Products, etc.: Danish Executive Order No 1232 of 12 December 2005 on Homeopathic Medicinal Products, etc. (Danish title: *Bekendtgørelse*

nr. 1232 af 12. december 2005 om homøopatiske lægemidler m.v.) as last amended by Executive Order No 124 of 25 January 2022

Executive Order on Authorisation of Parallel Trade in Medicinal Products for Animal Use: Danish Executive Order No 112 of 25 January 2022 on Authorisation of Parallel Trade in Medicinal Products for Animal Use (Danish title: *Bekendtgørelse nr. 112 af 25. januar 2022 om tilladelse til parallelhandel med lægemidler til dyr*)

Executive Order on Product Numbers for Human and Veterinary Medicinal Products: Danish Executive Order No 767 of 22 June 2016 on Product Numbers for Human and Veterinary Medicinal Products (Danish title: *Bekendtgørelse nr. 767 af 22. juni 2016 om varenumre til lægemidler til mennesker og dyr*) as last amended by Executive Order No 2455 of 14 December 2021

Guideline on Parallel Trade in Medicinal Products for Animal use: The Danish Medicines Agency's Guideline No 9251 of 10 March 2022 on Parallel Trade of Medicinal Products for Animal Use (Danish title: *Lægemiddelstyrelsens vejledning nr. 9251 af 10. marts 2022 om parallelhandel med lægemidler til dyr*)

CMDv guidance on classification of VRA: Guidance on the details of the classification of variations requiring assessment according to Article 62 of Regulation (EU) 2019/6 for veterinary medicinal products and on the documentation to be submitted pursuant to those variations of 9 September 2021

CMDv guidance on requests for classification: Procedural advice for requests for the classification of variations not already listed in Commission Implementing Regulation (EU) 2021/17 or EMA/CMDv Guidance on the details of the classification of variations requiring assessment according to Article 62 of Regulation (EU) 2019/6