VETERINARY MEDICINAL PRODUCTS – legal requirements for use, production, import, trade and control

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I. Definition of Veterinary Medicinal Product (VMP)

“Veterinary Medicinal Product" is a substance or a combination of substances, intended for the following purposes:

a) use for prevention or treatment of animal diseases;

b) use for the restoration, correction or alteration of physiological functions in animals by pharmacological, immunological or metabolic action or for the diagnosis of diseases.

II. Procedures for authorisation of the use of VMP

1. National Procedure - registered only in Bulgaria.

2. Procedure for Mutual Recognition – the product has already been registered in another EU state but the applicant wants to receive authorisation for use in other member states.

3. Decentralized Procedure – the product has not been previously authorised for use in EU and the applicant wants to register it in several member states.


http://eudrapharm.eu/eudrapharm/eudrapharm_help.do

Communication information system: EudraPharm
III. Use of Veterinary Medicinal Products

1. Authorisation of Marketing License for the use of VMP

   For the issuance of a marketing authorisation for the VMP, the applicants submit a standard application to the BFSA Executive Director, accompanied by:
   - certificate of current status;
   - the registration dossier of the VMP, consisted of:
     a) Part One - administrative data, a brief product specification, and expert reports on the documentation in the following sections;
     b) Part Two - physico-chemical, pharmaceutical, microbiological and biological documentation;
     c) Part Three - safety data and residues;
     d) Part Four - preclinical and clinical documentation;
   - samples, standard drug substances, reference strains, toxins and serums for immunological VMP that are sufficient to carry out three tests;
   - a copy of a manufacturing license or a contract with a licensed VMP manufacturer in cases where the applicant is not a manufacturer;
   - Qualified Person details - name, address and professional qualification;
   - a copy of the Good Manufacturing Practice Certificate (GMP);
   - document for paid fee.

   up to 210 days (7 months)

Therapeutic VMP Commission

Immunological VMP Commission

The License for use of VMP is issued for 5 years period
2. Refusal and termination of a marketing authorisation of VMP.

The BFSA Executive Director:

- **Refuse the marketing authorisation** - The risk/benefit ratio is unfavourable under the terms of use of the VMP.

- **Termination of the marketing authorisation** - when the active substance is excluded from Table 1 “Allowed substances” or is included in Table 2 “Prohibited substances” of Regulation (EC) 37/2010.

### Table 1
Pharmacologically active substances and their classification regarding maximum residue limits (MRL)

<table>
<thead>
<tr>
<th>Pharmacologically active Substance</th>
<th>Marker residue</th>
<th>Animal Species</th>
<th>MRL</th>
<th>Target Tissues</th>
<th>Other Provisions (according to Article 14(7) of Regulation (EC) No 470/2009)</th>
<th>Therapeutic Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac</td>
<td>Diclofenac</td>
<td>Bovine</td>
<td>5 μg/kg</td>
<td>Muscle</td>
<td>For porcine species the fat MRL relates to 'skin and fat in natural proportions'.</td>
<td>Anti-inflammatory agents/Nonsteroidal anti-inflammatory agents</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 μg/kg</td>
<td>Fat</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>5 μg/kg</td>
<td>Liver</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>10 μg/kg</td>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.1 μg/kg</td>
<td>Milk</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Porcine</td>
<td>5 μg/kg</td>
<td>Muscle</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1 μg/kg</td>
<td>Skin and fat</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>5 μg/kg</td>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 μg/kg</td>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2
Prohibited substances

<table>
<thead>
<tr>
<th>Pharmacologically active substance</th>
<th>MRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aristolochia spp. and preparations thereof</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Chloroform</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Colchicine</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Dapsone</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Dimetridazole</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Nitrofurans (including furazolidone)</td>
<td>MRL cannot be established</td>
</tr>
<tr>
<td>Ronidazole</td>
<td>MRL cannot be established</td>
</tr>
</tbody>
</table>
3. Use of unauthorised VMP

- In case of a complicated epizootic situation/outbreak;
- When the product is needed for the execution of measures, part of the strategy programmes for prevention, control and eradication of animal diseases and zoonoses;
- When an animal is exported/imported to a third country and preventive measures have to be taken;

When there is no licensed appropriate VMP in the country to alleviate the suffering of non-productive animals and equidae not intended for human consumption, the veterinarian may:
- use a veterinary medicinal product licensed in the country for another species or for the same species, but with other therapeutic indications;
- medicinal product authorised for human use.

4. Withdrawal periods

For meat of poultry and mammals, fats and by-products - 28 days
IV. Manufacturing and Import of VMPs

1. Manufacturing authorisation

A manufacturing authorisation is issued for full and partial production of active substances and various processes such as packaging, repackaging, re-labeling, labeling.

Manufacturing of VMPs in the country may be performed by individuals and legal persons registered under the Commerce Act and granted a manufacturing authorisation license issued by the BFSA Executive Director.

Up to 90 days after the application submission

The manufacturing authorisation license is indefinite.

2. Requirements towards the manufacturing holders

The manufacturing VMP license holder is obliged to employ at least one qualified person for the purpose of quality control of the manufacturing process.

The qualified person is responsible for signing an analytical report by which it is guaranteed each batch of VMP is manufactured and controlled under the terms of the license.
3. VMPs Import from third countries

Imports can only be performed by registered manufacturers of VMPs. By order of the Executive Director of BFSA, a committee is appointed for inspection of the documentation, storage, control and sales office of the manufacturer’s representative in Bulgaria. This committee visits the manufacturer in the third country to verify the compliance with the GMP (Good Manufacturing Practices).

4. EU Procedure for recognition of GMP in third countries – allowed the direct recognition of third countries GMP certificates without spot check visits. This is possible for countries covered by the MRA (Mutual Recognition Agreement) between the EEA (European Economic Area) and third countries. Such countries appear to be Canada, USA, Japan, Australia, New Zealand. This procedure also allows remote verification of the manufacturer.
V. Wholesale of VMPs

Wholesale of VMPs may be performed by individuals and legal persons registered under the Commerce Act and authorised by the BFSA Executive Director. The issuance or refusal to issue a license by the Director shall take place within three months of the submission of the application.

Requirements to wholesalers are determined by an ordinance of the Minister of Agriculture and Food.

In the wholesale trade with VMPs containing narcotic substances, the requirements of the Narcotic Substances and Precursors Control Act are applied.

BFSA keeps a record of the licenses issued for wholesale of VMPs.

As a manager of a wholesale setting could only be authorised a veterinarian.

The wholesale license holder is obliged to develop and maintain a system for blocking and withdrawing hazardous VMPs from the market.

The wholesale license holder develops and implements an emergency plan in order to guarantee the effectiveness of any withdrawal operation provided by the BFSA, by performing the withdrawal jointly with the manufacturer or the marketing holder.

Wholesalers complete once a year a complete revision of the received, sold and available quantities of VMP, and describe all identified discrepancies.
VI. Retail sale of veterinary medicinal products

1. Retailers and retail settings

Retail sales of VMPs are performed by individuals and legal persons registered under the Commerce Act after authorisation by the BFSA Executive Director. BFSA keeps a record of the retail licenses for VMPs. Retail of VMPs is only available at veterinary pharmacies.

The manager of the veterinary pharmacy and the persons selling the VMP should be veterinarians.

2. Sale of VMPs under prescription.

The prescription is issued only by a registered veterinary practitioner, in duplicate, one for the purchase of the VMP at the pharmacy and the other for the owner of the animals for which the treatment is intended.
BFSA implements and maintains a pharmacovigilance information system. The BFSA also participates in cooperation with the competent authorities of the European Union for the exchange of information from the pharmacovigilance system concerning VMPs licensed for use in the European Union.

The Pharmacovigilance System processes data, coming from different stakeholders as:
1. Marketing license holders;
2. Veterinary practitioners;
3. Animal owners.
VIII. State Veterinary Control of Veterinary Medicinal Products

- Competent Control Authorities

The BFSA controls the manufacturing, wholesale and retail trade, import, advertising and use of VMPs. The BFSA shall also carry out a check at the request of the competent authority of a Member State concerned, the European Commission and the European Medicines Agency.

Inspection is carried out by BFSA inspectors and experts.

Inspectors perform regular and unannounced inspections and laboratory tests on samples of VMPs.

- Control Measures
Ветеринарно законодательство и менеджмент