Annex I

List of the names, pharmaceutical form, strength of the veterinary medicinal products, animal species, route of administration, marketing authorisation holders in the Member States

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Austria	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Separon 40 mg/ml Injektionslösung für Schweine	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Austria	Serumwerk Bernburg AG Hallesche Landstrasse 105 b 06406 Bernburg/Saale Germany	Azaporc 40 mg/ml Injektionslösung für Schweine	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Austria	Elanco GmbH Heinz-Lohmann-Straße 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml Injektionslösung für Schweine	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Belgium	Elanco GmbH Heinz-Lohmann-Straβe 4 27472 Cuxhaven Duitsland	Stresnil 40 mg/ml	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Bulgaria	Elanco GmbH Heinz-Lohmann-Straβe 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml injectable solution	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Bulgaria	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Croatia	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Cyprus	Elanco GmbH Heinz-Lohmann-Str. 4 27472 Cuxhaven Germany	Stresnil, 40mg/mL ενέσιμο διάλυμα για χοίρους	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Czech Republic	Elanco GmbH Heinz Lohmann Str. 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml injekční roztok pro prasata	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Czech Republic	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml injekční roztok pro prasata	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Denmark	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Separon vet.	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Estonia	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Finland	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Separon vet.	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
France	Elanco GmbH Heinz-Lohmann-Strasse 4 27472 Cuxhaven Germany	Stresnil	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Germany	Serumwerk Bernburg AG Hallesche Landstr. 105b 06406 Bernburg Germany	Azaporc 40 mg/ml Injektionslösung für Schweine	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Germany	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Germany	Elanco GmbH Heinz-Lohmann-Straße 4 27472 Cuxhaven Germany	Stresnil	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Greece	Elanco GmbH Heinz-Lohmann-Str.4 27472 Cuxhaven Germany	Stresnil ενέσιμο διάλυμα 40 mg/ml	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Greece	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Separon 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Hungary	Elanco GmbH Heinz-Lohmann-Straße 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml oldatos injekció sertéseknek A.U.V.	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Hungary	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Iceland	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Separon vet.	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Ireland	Elanco GmbH Heinz-Lohmann-Straße 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Ireland	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Italy	Eli Lilly Italia S.P.A. Via Gramsci, 731-733 50019 Sesto Fiorentino (FI) Italy	Stresnil 40 mg/ml soluzione iniettabile per suini	Azaperone	40 mg/ml	Solution for injections	Pigs	Intramuscular use
Italy	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Latvia	Elanco GmbH Heinz-Lohmann Str. 4 27472 Cuxhaven Germany	Stresnil	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Latvia	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Lithuania	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Lithuania	Elanco GmbH Heinz-Lohmann Str. 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml injekcinis tirpalas kiaulėms	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
The Netherlands	Elanco GmbH Heinz-Lohmann-Strasse 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml oplossing voor injectie voor varkens	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
The Netherlands	Kernfarm B.V. De Corridor 14D 3621 ZB Breukelen The Netherlands	Stresnil 40 mg/ml oplossing voor injectie voor varkens	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Norway	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Separon vet. 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Poland	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Poland	Elanco GmbH Heinz-Lohmann-Strasse 4 27472 Cuxhaven Germany	Stresnil	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Portugal	Ecuphar Veterinaria S.L.U Avenida Río de Janeiro, 60-66, planta 13 08016 Barcelona Spain	Stresnil 40mg/ml solução injetável para suínos	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Portugal	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solução injetável para suínos	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Romania	Elanco GmbH Heinz-Lohmann-Strasse 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Romania	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Slovakia	Elanco GmbH Heinz-Lohmann-Str. 4 27472 Cuxhaven Germany	Stresnil 40 mg/ml injekčný roztok pre ošípané	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Slovakia	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml injekčný roztok pre ošípané	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Slovenia	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Member State EU/EEA	Marketing authorisation holders	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Spain	Ecuphar Veterinaria S.L.U. Avda. Rio de Janeiro, 60-66 planta 13 08016 Barcelona Spain	Stresnil 40 mg/ml solución inyectable para porcino	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
Sweden	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Separon vet.	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
United Kingdom	Eli Lilly and Company Limited Elanco Animal Health Lilly House Priestley Road Basingstoke RG24 9NL United Kingdom	Stresnil 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use
United Kingdom	Richter Pharma AG Feldgasse 19 4600 Wels Austria	Sedanol 40 mg/ml solution for injection for pigs	Azaperone	40 mg/ml	Solution for injection	Pigs	Intramuscular use

Annex II

Scientific conclusions and grounds for amendment of the summary of product characteristics

Overall summary of the scientific evaluation of Stresnil 40 mg/ml solution for injection for pigs and associated names, and generic products thereof (see Annex I)

1. Introduction

The veterinary medicinal products Stresnil 40 mg/ml solution for injection for pigs and associated names, and generic products thereof are solutions for injection containing 40 mg azaperone per ml. Azaperone is a neuroleptic sedative, used for the treatment of aggressive behaviour, control of aggression in sows, prevention of stress, obstetric conditions, as pre-medication in local or general anaesthesia and for palliative treatment of enzootic muscular dystrophy in pigs.

Azaperone as injectable solution is given to pigs by a single intramuscular injection at recommended doses ranging from 0.4 to 2 mg azaperone per kg body weight (bw).

An application was submitted under Article 13(1) of Directive 2001/82/EC, i.e. a generic application for a marketing authorisation under the decentralised procedure for the veterinary medicinal product Sedanol 40 mg/ml solution for injection for pigs, with Germany as reference Member State (DE/V/0300/001/DC). The reference product is Stresnil lnjektionslösung für Schweine (hereafter named 'Stresnil'), marketed by Lilly Deutschland GmbH and authorised in Germany since 1979.

Having reviewed the available residue data for the reference product 'Stresnil' and because there were residues at the injection site tissue above the established MRL at the last slaughter time point (7 days after administration), Germany and some other Member States were unable to confirm that the authorised withdrawal period of 9 days is safe for the consumer. No other residue depletion data were made available to Germany to establish a scientifically justified safe withdrawal period.

In addition, Germany noted that, for Stresnil and associated names, and generic products thereof, the Member States across the EU/EEA have established different withdrawal periods for pig meat and offal, i.e. between seven and eighteen days.

Germany considered that it is in the interest of protecting consumer safety in the Union to review the adequacy of the withdrawal periods for pigs meat and offal and referred the matter to the Committee for Medicinal Products for Veterinary Use (CVMP).

Therefore, on 17 September 2019, Germany initiated a procedure under Article 35 of Directive 2001/82/EC, for Stresnil 40 mg/ml solution for injection for pigs and associated names, and generic products thereof. The CVMP was requested to review all available residue depletion data and recommend withdrawal periods for meat and offal derived from treated pigs.

2. Discussion of data available

Qualitative and quantitative composition

Information regarding the composition of the affected products was provided and the qualitative and quantitative composition of the active substance of the concerned products are similar. Also, the composition of the excipients can be regarded as essentially similar.

Overall, the formulations being very similar and the fact that they are to be administered at the same dosage, the CVMP considered that all products show a similar absorption from the injection site and concluded that a common withdrawal period could be applied to the veterinary medicinal products concerned by this referral procedure.

Residue depletion in pigs

Four residue depletion studies in pigs were made available to the Committee. Three studies were conducted with Stresnil 40 mg/ml, all being Good Laboratory Practice (GLP)-compliant. One study was conducted with a solution containing radiolabelled azaperone.

In addition, some literature data including MRL reports were provided.

Study 1

A GLP-compliant residue depletion study in pigs was submitted, conducted in 2004 using thirty animals (15 castrated males and 15 females), with a body weight at study initiation between 26.7–40.4 kg that were assigned to one of five test groups, each consisting of 6 animals. Animals were administered a single intramuscular injection of Stresnil at the maximum recommended dose of 2 mg azaperone per kg bw. The animals used were smaller than recommended in VICH GL48 (EMA/CVMP/VICH/463199/2009)[1], which does not cover the total target animal population, resulting in small injection volumes ranging from 1.3-2.0 ml.

Tissue samples (liver, kidney, muscle, skin/fat in natural proportions and injection site) were obtained for analysis at 1, 3, 5, 7 and 14 days after dosing (n = 6 animals at each timepoint, equal numbers of males and females). The weights of the samples were in accordance with the recommendations in the VICH GL 48[1]. However, only core samples from the injection site and no surrounding samples were collected.

The residues were quantified using a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method with a limit of quantification (LOQ) of 0.025 mg/kg for all tissues and both substances, i.e. azaperone and azaperol. Residue concentrations above the MRL (100 µg/kg) were only measured in skin/fat (in natural proportions) on day 1 after administration and in the injection site at day 1, 3 and 7 after administration.

Therefore, keeping in mind that only a core sample for the injection site and no surrounding sample was taken, and because the animals used were smaller than recommended in VICH GL48[1] (which does not cover the total target animal population, resulting in small injection volumes (1.3-2.0 ml)), the Committee considered that the results of this study are associated with some not further defined uncertainties with potential impact on the determination of the withdrawal period.

Study 2

Another GLP-compliant residue depletion study was provided, conducted in 1992 with the concerned veterinary medicinal product Stresnil.

In total, twelve neutered males and twelve females Belgian Landrace pigs were included in this study. Twenty pigs were divided into 5 groups (with two males and two females each) and received an intramuscular injection in the neck of the test substance (commercial Stresnil formulation containing 40 mg azaperone per ml) at the maximum recommended dose of 2 mg azaperone per kg bw (injection volumes ranged from 4–4.8 ml). The remaining four animals did not receive any test substance and served as control (one of these animals was slaughtered at the first study day). The weight of the animals was between 86–96 kg for males and between 79–86 kg for females.

Tissue samples (250 g of ham muscle, 100 g of subcutaneous fat, 100 g of skin, 100 g of lard, whole liver, both kidneys and the injection site [10 cm in diameter and 6 cm in depth, 317–510 g] were collected at 1, 2, 3, 5 and 7 days after dosing. The samples were stored below -20 °C until analysis.

[1] VICH topic GL48: Studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing animals: marker residue depletion studies to establish product withdrawal periods (EMA/CVMP/VICH/463199/2009) – link

A validated HPLC-UV (243 nm) method was used and the validated LOQ was reported to be 25 µg/kg for azaperone and azaperol for all tissues.

The marker residue was below the MRL (100 µg/kg) two days after administration in all tissues, with the exception of the injection site. In injection site samples, there is still one value above the MRL at the latest sampling time point (7 days after administration).

The Committee considered that based on the results of this study, it can be concluded that the injection site tissue represents the withdrawal period determining tissue and that a restriction of the maximum injection volume is needed. However, since in the injection site tissue there is still one value above the MRL at the latest sampling time point (7 days after administration), a reliable withdrawal period for meat and offal cannot be determined from this study.

Study 3

In the third GLP-compliant residue depletion study provided, the authorised formulation Stresnil was tested together with an experimental formulation. Only the residue depletion of Stresnil as marketed is considered relevant for this referral procedure, and therefore only those results are described below. The study was reported in 1999 using thirty animals.

For the study of the commercial 'Stresnil' formulation, only 12 pigs were selected out of 30 animals (weighing between 20–30 kg at arrival). Twelve neutered male Belgian landrace pigs received an intramuscular injection in the neck, at the maximum recommended dose of 2 mg azaperone per kg bw (corresponding to 1 ml of Stresnil per 20 kg bw).

Tissue samples (≈ 250 g of ham muscle, 100 g of skin/fat, the whole liver, both kidneys and the injection site [cylinder 10 cm in diameter and 6 cm in depth]) were collected at 7, 14 and 21 days after dosing (n = 4 pigs per timepoint), and stored at or below -18 °C until analysis.

Samples were analysed for azaperone and its metabolite azaperol using a validated HPLC-UV method and the LOQ for both analytes across all matrices was 25 µg/kg.

Values above the MRLs (100 µg/kg) were found only in one injection site sample at 7 days after administration.

The animals included in this study had a very low body weight (i.e. pigs therefore received only a low injection volume), which does not cover the target animal population. Weights of pigs at time of administration of the product are not clearly described in the study (weights are mentioned at arrival only, i.e. 20–30 kg) and therefore it is not clear what actual volumes of the product were administered to the injection site. The exact timetable of works, especially in animal phase, is not described in the study and no samples surrounding the injection site were collected.

In conclusion, the CVMP considered that the uncertainties mentioned above should be considered for the determination of the withdrawal period.

Study 4

In a radiolabelled study conducted in 1976, eight pigs (body weight 15–25 kg) were injected with 4 mg/kg ^{3}H azaperone.

Tissue samples (liver, kidney, muscle, skin, fat and injection site) were collected at 2, 24, 48 and 72 hours after administration, and subjected to a 'nature of residue' analysis as well as 'total radioactive residue' analysis.

Injection site samples were approximately 2 x 2 x 10 cm. Samples were subjected to combustion and total radioactivity was determined as µg/g (ppm) as well as percentage of the administered dose. The tissues with the highest concentrations of azaperone and azaperol were injection site and liver.

This rather old study is not in compliance with current guidelines. It was conducted with a radioactive formulation of azaperone and only two animals were slaughtered per timepoint. Moreover, the test item was administered at a higher dose than recommended, but the injection volume was relatively low due to the low body weight of the animals. Therefore, the CVMP is of the opinion that this study is not relevant for withdrawal period determination.

Withdrawal period determination

Overall, from all the residue depletion data provided, it can be concluded that the injection site is the tissue determining the withdrawal period calculation. The CVMP concluded that the statistical approach cannot be used to estimate a withdrawal period from the studies provided. In accordance with the CVMP guideline on determination of withdrawal periods for edible tissues (EMA/CVMP/SWP/735325/2012)[2], slaughter timepoints with more than half of the values below the LOQ should be deleted from the statistical evaluation. By doing so, the provided data sets cannot be evaluated using the statistical approach.

The Committee agreed to use the alternative approach, in line with the CVMP guideline on determination of withdrawal periods for edible tissues[2], together with a ~30% safety span to account for all uncertainties in the provided studies (e.g. only core samples collected, small body weight animals). The safety span is also considered necessary since the acceptable daily intake (ADI) for azaperone is based on a pharmacological (e.g. acute) endpoint. This approach would result in a withdrawal period of 18 days (first timepoint with all values below the MRL (day 14 + ~30% safety span)).

Additionally, a limitation of the maximum injection volume per injection site is considered necessary by the CVMP. The MAH proposed a restriction to 5 ml, although the study with the highest injection volumes (conducted in 1992) covers only volumes of 4–4.8 ml. The CVMP considered that this slight derivation is acceptable, because the timespan between the last timepoint with values above the MRL (7 days after administration) and the next slaughter timepoint (14 days after administration) provides an additional safety span.

3. Benefit-risk assessment

Introduction

The CVMP was requested to review all available residue data for the veterinary medicinal product Stresnil 40 mg/ml solution for injection for pigs and associated names, and generic products thereof and to recommend appropriate withdrawal periods for meat and offal derived from treated pigs.

Benefit assessment

While the efficacy of the concerned products in pigs has not been specifically assessed as part of this referral, the products under assessment are considered to be effective in pigs for their sedative effects. The recommended doses for the different indications range from 0.4 to 2 mg azaperone per kg bw.

Risk assessment

Quality, target animal safety, user safety and the environmental risk for the concerned veterinary medicinal products have not been assessed in this referral procedure. Furthermore, for generic products, bioequivalence was not evaluated, since this was already done within the respective marketing authorisation procedures.

[2] CVMP guideline on determination of withdrawal periods for edible tissues (EMA/CVMP/SWP/735325/2012-Rev. 1) – link

Azaperone was previously evaluated by the CVMP[3] in order to establish MRLs. The ADI was derived from an acute pharmacological no effect level (NOEL) of 0.08 mg/kg bw and a safety factor of 100, corresponding to an ADI of 0.8 µg/kg bw (equivalent to 48 µg for a 60 kg person). As this ADI is set on the basis of pharmacological activity, it applies for pharmacologically active components only (i.e. azaperone and the metabolite azaperol).

The marker residue is the sum of azaperone and azaperol. MRLs for the sum of azaperone and azaperol are 100 µg/kg in all tissues (muscle, skin/fat, liver and kidney). These MRLs will theoretically result in a daily intake of 50 µg. As this intake is largely overestimated (based on the worst-case scenario that the pharmacological activity of azaperol is equal to that of azaperone), it is compatible with the ADI of 48 µg for a 60 kg person.

A risk has been identified regarding the length of the authorised withdrawal periods for pig meat and offal. For some veterinary medicinal products, the authorised withdrawal period may be insufficient to allow residues of the sum of azaperone and azaperol to fall below the respective MRL in edible tissues, thereby posing a risk to consumers after oral intake of injection site tissue from pigs treated with these products.

Risk management or mitigation measures

To ensure the safety of consumers of food and food products derived from animals treated with these veterinary medicinal products, the CVMP considered that the withdrawal period for meat and offal of pigs treated with Stresnil 40 mg/ml solution for injection for pigs and associated names, and generic products thereof should be amended.

On the basis of residue depletion data in pigs, a withdrawal period for pig meat and offal of 18 days and a limitation of the maximum injection volume to 5 ml per injection site have been derived for all products. This withdrawal period and the restriction of the maximum injection volume per injection site are considered adequate to ensure consumer safety.

Evaluation and conclusions on the benefit-risk balance

Having considered the grounds for this referral procedure and the data available, the CVMP concluded that the withdrawal periods for meat and offal derived from pigs treated with the concerned products should be amended as recommended and a limitation of the maximum injection volume per injection site is also needed to provide assurance for consumer safety.

The overall benefit-risk balance for the veterinary medicinal products Stresnil 40 mg/ml solution for injection for pigs and associated names, and generic products thereof remains positive, subject to the recommended changes in the product information.

Grounds for amendment of the summary of product characteristics, labelling and package leaflet

Whereas

- on the basis of the available residue depletion data, the CVMP considered that the withdrawal periods for meat and offal derived from treated pigs should be amended and a limitation of the maximum injection volume per injection site is also required to provide assurance for consumer safety;
- the CVMP considered that the overall benefit-risk balance for the veterinary medicinal products under this procedure remains positive subject to amendments in the product information;

[3] EMA MRL Summary report for azaperone (EMEA/MRL/300/97-FINAL) – link

the CVMP has recommended the amendment of the marketing authorisations for Stresnil 40 mg/ml solution for injection for pigs and associated names, and generic products thereof as referred to in Annex I for which the summary of product characteristics, labelling and package leaflet are set out in Annex III.

Annex III

Amendments in the relevant sections of the summary of product characteristics, labelling and package leaflet

Summary of product characteristics

4.9 Amounts to be administered and administration route

Do not administer more than 5 ml per injection site.

4.11 Withdrawal period(s)

Meat and offal: 18 days.

Labelling

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Do not administer more than 5 ml per injection site.

8. WITHDRAWAL PERIOD(S)

Meat and offal: 18 days.

Package leaflet

8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

Do not administer more than 5 ml per injection site.

10. WITHDRAWAL PERIOD(S)

Meat and offal: 18 days.