EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use

CVMP assessment report for Cytopoint (EMEA/V/C/003939/II/0009)

Vaccine common name: lokivetmab

to add a new therapeutic indication for the treatment of pruritus associated with allergic dermatitis in dogs. As a consequence, section 4.2 of the SPC and section 4 of the PL are updated accordingly. The MAH also took the opportunity to add a dog pictogram in point 7 of the package leaflet.

Assessment report as adopted by the CVMP with all information of a commercially confidential nature deleted.

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1. Introduction

1.1. Submission of the variation application

In accordance with Article 16 of Commission Regulation (EC) No 1234/2008, the marketing authorisation holder, Zoetis Belgium SA (the applicant), submitted to the European Medicines Agency (the Agency) on 7 February 2020 an application for a type II variation for Cytopoint.

On 9 September 2020, the CVMP adopted an opinion and CVMP assessment report.

1.2. Scope of the variation

Variation requested		**Type**
C.I.6.a	Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	II

To add a new therapeutic indication for the treatment of pruritus associated with allergic dermatitis in dogs. As a consequence, section 4.2 of the SPC and section 4 of the PL are updated accordingly. The MAH also took the opportunity to add a dog pictogram in point 7 of the package leaflet.

1.3. Changes to the dossier held by the European Medicines Agency

This application relates to the following sections of the current dossier held by the Agency:

Part 1 and Part 4.

1.4. Scientific advice

The applicant received scientific advice from the CVMP on 10-12 September 2013 (EMEA/V/SA/156/13/I/EMA/CVMP/SAWP/331254/2013). The scientific advice pertained to clinical aspects of the dossier. Comments are raised in the relevant section of the CVMP Assessment Report Part 3 concerning compliance with the scientific advice given.

1.5. MUMS/limited market status

Not applicable.

2. Assessment

Cytopoint, a caninised monoclonal antibody (mAb) specifically targeting canine interleukin-31 (IL-31), is currently authorised for the treatment of clinical manifestations of atopic dermatitis in dogs. By binding canine IL-31, Cytopoint prevents IL-31 from binding to its co-receptor and thereby inhibits IL-31 mediated signalling, relieving atopic dermatitis-associated pruritus and anti-inflammatory activity. The current variation seeks to add a therapeutic indication; to treat pruritus associated with allergic dermatitis in dogs.

One clinical EU field trial has been conducted to investigate efficacy under field conditions in client-owned dogs with allergic dermatitis in support of the proposed change, in addition to a clinical expert report and provision of two studies submitted in the original dossier in support of the omission of longer-term clinical data in the proposed new sub-category of target species. The recommended dose and treatment interval are the same as that currently authorised for treatment of atopic dermatitis (AD).

It was proposed that the currently authorised dose regimen for the atopic dermatitis indication is appropriate also for the allergic dermatitis indication and this was the dose used in the pivotal clinical study submitted in support of this application. The proposed dose and treatment interval were accepted based on the clinical data submitted in support of the original new product application.

A new study was provided to evaluate the efficacy and safety of Cytopoint for the treatment of pruritus associated with allergic dermatitis in client-owned dogs in Europe. The objective was to demonstrate efficacy and safety of Cytopoint compared to placebo for the treatment of pruritus associated with allergic dermatitis in client-owned dogs.
This was a multi-site study involving 14 different veterinary practices in Portugal, Hungary, France and Germany. In the test group, Cytopoint was administered in accordance with recommendations, at a dose of 1 mg/kg by the subcutaneous route (actual doses administered ranged from 1.0 to 2.86 mg/kg). The study evaluated the efficacy of a single dose for the treatment of pruritus associated with allergic dermatitis, the primary efficacy parameter (reduction in pruritus) was evaluated at 28 days post-treatment.

The approach to randomisation and blinding is considered appropriate. For blinding, the product (placebo or Cytopoint) was provided by an independent Dispenser to the examining veterinarian so that the owner and examining veterinarian had no knowledge of the treatment administered. This blinding was maintained throughout the entire duration of the study

Although the active substance in the batches used in this trial was manufactured in accordance with the approved process at the time of initiation of the study, comparability of drug substance manufactured through this and the current method was demonstrated and therefore, the data from this field study can be accepted.
Saline sterile solution for injection (NaCl 0.9%) was used a control.

Primary efficacy variable (evaluated at day 28):

- Percentage reduction from baseline for Owner-assessed pruritus (10.0 cm long enhanced Visual Analogue Scale [VAS], combining behavioural features and severity-based information with the VAS scale. The enhanced VAS is a continuous 10 cm long scale which combines behavioural features and severity-based information with a visual analogue scale (Hill *et al*, 2007). The owner draws a mark on the vertical line at the point at which they consider their dog's level of itching lies; six behavioural descriptors placed alongside the vertical line from the lowest point to the top of the scale comprise the following: 'normal dog –itching is not a problem', 'very mild itching/only occasional episodes', 'moderate itching/regular episodes', 'severe itching/prolonged episodes', 'extremely severe itching/almost continuous'. Each behavioural descriptor is accompanied by an example. After the mark is placed on the VAS, a transparent sheet containing graduated markings is overlaid on the VAS to measure the score (from 0 to 100 mm). The Investigator VAS is the same continuous 10 cm long scale with the same six descriptors using non-layman terminology ('Extreme severe dermatitis - extensive evidence of chronic lesion and/or active infections/excoriations', 'severe dermatitis', 'moderate dermatitis', 'mild dermatitis', 'very mild dermatitis', or 'normal dog -dermatitis is not a problem'.

Secondary efficacy variables:

- Mean Owner-assessed pruritus VAS score at each Owner-assessment of pruritus.

- Percentage reduction from baseline for Owner-assessed pruritus VAS score at individual time-points post treatment – at 4 hours on Day 0 and on Days 1, 2, 3, 4, 5, 6, 7, 14 and 21.
- Proportion of dogs achieving 50% and 75% decrease in Owner-assessed pruritus VAS score compared to Day 0, at each Owner-assessment of pruritus.
- Mean Investigator assessment of skin condition VAS score (Investigator VAS) at each study visit.
- Percentage reduction from baseline for Mean Investigator assessment of skin condition VAS score (Investigator VAS) at each study visit.
- Mean of the Response To Treatment (RTT) VAS scores from the Owner and the Investigator.

Safety data was also collected: physical examination and body weight on Day 0, 7, 14 and 28. Blood and urine samples obtained prior to treatment for baseline CBC, serum chemistry and urinalysis on Day 0 and on Day 28. Animals were observed for hypersensitivity reactions for at least 30 minutes post-treatment. Bacteriology, including antibiogram (skin and/or outer ear swabs were taken in cases of suspected bacterial infections occurring after Day 0), adverse events, concomitant medications, body weight. Adverse events, serious adverse events and concurrent disease and mediation were monitored throughout the study.

The individual dog was the experimental unit. Continuous variables measured repeatedly (owner pruritus VAS, % change from baseline for owner pruritus VAS, investigator dermatitis VAS, % change from baseline for investigator VAS) were analysed using a general linear mixed models for repeated measures with the fixed effects of treatment, time point and treatment by time point interaction and, where appropriate, baseline data was used as a covariate. The random effects included clinic, clinic by treatment interaction, block within clinic, the interaction of treatment and block within clinic (animal term), the interaction of clinic, treatment and time, and the residual. Least squares means, 95% confidence intervals, minimums and maximums were reported by treatment and time point. If the treatment effect or treatment by time interaction was significant at the 0.05 level of significance, then treatment contrasts at each time point were performed and reported.

The results for the primary efficacy variable show that there was a statistically significant difference in the primary efficacy parameter between the test and control group; on Day 28, the LS mean percentage reduction from baseline for owner-assessed pruritus was significantly higher in the Cytopoint-treated group (57.71%) compared to the placebo group (21.78%), $p<0.0001$ (owner-assessed pruritus).

The results for the secondary efficacy variables were as follows:

Owner assessments

- For all timepoints from Day 1 post-treatment, the percentage reduction from baseline for owner-assessed pruritus VAS LS mean was significantly higher in the Cytopoint-treated group compared to the placebo group.
- *50% reduction from baseline of Owner assessment of pruritus*: At every study time point from Day 2 onwards, the proportion of animals achieving at least 50% reduction from baseline of Owner assessment of pruritus VAS was significantly higher ($p \leq 0.0213$) in the group of animals treated with Cytopoint (T02) versus the control group (T01).

  In T01, treatment success defined as at least 50% reduction in pruritus, reached a maximum of 26% six days after treatment and decreased as from then. In T02, the treatment success reached a maximum of 73% on Day 14 and averaged between 66 and 70% during the last two weeks of the in-life phase. Twenty-eight days after dosing, 70% of the animals achieved at least 50% reduction in itch in the Cytopoint treated group (T02), compared to 12% in the control group (T01).

- *75% reduction from baseline of Owner assessment of pruritus*: At Days 1, 3, 4, 5, 6, 7, 14, 21 and 28, the proportion of animals achieving 75% reduction from baseline of Owner assessment of pruritus VAS was significantly ($p \leq 0.0451$) higher in the group of animals treated with Cytopoint (T02) versus the control group (T01).

  Twenty-eight days after dosing, 31% of the animals achieved 75% reduction in itch in the Cytopoint treated group (T02), compared to none in the control group (T01).

Investigator-Assessed Dermatitis:

- For all timepoints, the percentage reduction from baseline of Investigator-assessed skin condition VAS LS means was significantly higher ($P < 0.0001$) in the Cytopoint group (T02) compared to the control group (T01). On Day 28, the LS mean percent reduction in the control group was 20.49%, compared to 57.05% in the Cytopoint group.

Owner and Investigator RTT

- Both the Owner and Investigator RTT were significantly higher in the Cytopoint treated group (T02) compared to the control group (T01), with a 34.70% treatment difference for Owner RTT and a 40.18% treatment difference for Investigator RTT.
- The LS Means treatment difference for T01 vs T02 for RTT was statistically significantly different for both Owner (-34.70, $p<0.0001$) and Investigator (-40.18, $p<0.0001$) assessed RTT.

The safety data collected were as follows:

- For various serum chemistry and haematology parameters, increasing and/or decreasing shifts were observed, but these were not clinically relevant and generally occurred in both treatment groups. Urinalysis did not reveal any treatment-related abnormalities.
- The number of animals sampled for bacteriology due to a suspected skin or outer ear infection after Day 0 was identical between both treatment groups (2 animals/treatment group).
- The rate of adverse events were comparable between both treatment groups: 14.5% in the control group (n=9; T01) versus 11.5% in the Cytopoint group (n=7; T02). (Due to the pre-existing conditions of animals, Investigators were to report only a worsening of clinical signs as an AE).
- Overall, use of concomitant medication was comparable between both treatment groups. That is, there were no differences in frequency of any concomitant medications which may be expected to have a more favourable effect on clinical signs of allergic dermatitis between T01 and T02.
- However, as from Day 0, in the control group (T01) 24.2% (n=15) of the animals were treated at early withdrawal with oclacitinib due to lack of efficacy (rescue treatment). This is compared to only 6.6% (n=4) in the Cytopoint group (T02) (three animals were treated at early withdrawal, with one animal receiving oclacitinib treatment after study completion).
- There was no clinically relevant change in body weight in either group during the 28-day treatment period.

The CVMP concluded that this was a good quality, GCP-compliant, randomised, double-blinded, placebo-controlled field safety and efficacy study conducted in client-owned dogs with a presumptive diagnosis of allergic dermatitis.

It was overall considered that the animals enrolled in the study can generally be considered sufficiently representative of the target population as seen in veterinary clinical practice and the spectrum of underlying conditions in dogs with a diagnosis of "allergic dermatitis".

To be enrolled, dogs suffering from pruritus had to exhibit at least "moderate" itch (approximately 50 mm on a 100 mm long VAS scale, based on the descriptions in Appendix 9). It is noted that mean baseline pruritus scores were 69 and 70 out of 100 in the two groups, and thus most enrolled animals could be categorised as suffering from "moderate" to "severe" itch (again, based on the descriptions in Appendix 9). Other treatments, which could have decreased pruritus and lesions of atopic dermatitis (such as corticosteroids, antihistamines, ciclosporin or other anti-inflammatory and immunosuppressive agents), were not permitted for some time before and during the study.

It was accepted that the inclusion and exclusion criteria were generally appropriate. However, while accepting that the test population included animals with 'allergic dermatitis' and that those animals were pruritic at study initiation, it has to be acknowledged that for the majority of animals included in the study the primary measure to alleviate clinical signs is 'avoidance', be it to fleas, contact allergen or offending food. Indeed, based on information in the clinical expert report, it is clear that 'avoidance' when complete will lead to complete resolution of clinical signs within a period of weeks to months after elimination of the allergen. Therefore, the focus of any treatment strategy for dogs with allergic dermatitis should be on 'avoidance'. This would suggest, therefore, that the use of Cytopoint in animals with allergic dermatitis would be limited to alleviation of clinical signs in the weeks to months immediately after elimination of the allergen or when there has been a 'flare-up' associated with inadvertent exposure to the allergen (rather than as an ongoing repeated monthly treatment). The applicant was requested to comment further on the intended use of this product and propose appropriate text describing the intended use for inclusion in sections 4.4 and/or 4.9 of the SPC. This was resolved and appropriate SPC wording was added as requested.

Overall, it was accepted that the choice of the primary efficacy variable, in combination with the Investigator-based assessment of the same parameter as a secondary efficacy variable, was suitable, considering the indication which is proposed (reduction of pruritus) in the current variation.

Regarding the safety evaluation, it was noted that the number and nature of adverse events recorded during the study was similar in both groups. Of these events, six were considered severe (four in the Cytopoint group and two in the placebo group). However, these events were linked to disorders related to the underlying allergic dermatitis, such as otitis and dermatitis, including bacterial skin and ear infection. Blood and urine samples were collected at enrolment as well as study completion. For various blood and urine parameters increasing or decreasing shifts were equally observed in both groups, they remained within the reference range and were thus considered clinically not relevant. Based on these data, there are no safety concerns arising from this study and the information currently included in sections 4.6 and 4.10 of the SPC remains appropriate.

Based on the mode of action, the rapporteur considers it reasonable to assume that repeat treatments, if needed, in these animals will be as effective as it was in the atopic dermatitis animals.

In conclusion, the data provided in this study were considered adequate to support the proposed claim 'treatment of pruritus associated with allergic dermatitis in dogs'.

3. Scientific Overview

Cytopoint, a caninised monoclonal antibody (mAb) specifically targeting canine interleukin-31 (IL-31), is currently authorised for the treatment of clinical manifestations of atopic dermatitis in dogs. By binding canine IL-31, Cytopoint prevents IL-31 from binding to its co-receptor and thereby inhibits IL-31

mediated signalling, relieving atopic dermatitis-associated pruritus. The current variation seeks to add a new therapeutic indication - to treat pruritus associated with allergic dermatitis in dogs.

One clinical EU field trial has been conducted to investigate efficacy under field conditions in client-owned dogs with allergic dermatitis in support of the proposed change, in addition to a clinical expert report and provision of two studies submitted in the original dossier in support of the omission of longer-term clinical data in the proposed new sub-category of target species. The recommended dose and treatment interval are the same as that currently authorised for treatment of atopic dermatitis (AD). The CVMP can accept that the proposed dose and proposed treatment interval are justified based on the clinical data submitted in support of the original new product application and that the evaluation of this dose regimen in the pivotal clinical study presented in support of the present application is justified.

The clinical EU field trial (Study C866C-XC-19-255) has been conducted to investigate the efficacy and safety of Cytopoint compared to placebo, for the treatment of pruritus associated with allergic dermatitis in client-owned dogs. This was a GCP-compliant study that utilized a randomised, double-blinded, placebo-controlled design.

A total of 123 dogs that had previously been diagnosed with allergic dermatitis (food hypersensitivity, flea allergy, contact dermatitis, unspecified allergic dermatitis, or atopic dermatitis - only if in combination with one of the above) and were pruritic at the time of enrolment were recruited from 14 different veterinary practices in Portugal, Hungary, France and Germany. Animals were randomly allocated to one of two treatment groups in a 1:1 ratio of saline control (T01, n=62) or Cytopoint (T02, n=61).

Dogs received one injection of saline (T01) or Cytopoint (1.0 – 3.3 mg/kg bw, T02) on Day 0 and were followed for 28 days after treatment. Pruritus was assessed by the owner on a 10.0 cm long enhanced visual analog scale (VAS) and skin condition (dermatitis) by the investigator on a similar VAS scale.

To be enrolled in the study, dogs had to have history of allergic dermatitis, the owners had to assess their dogs as having at least "moderate" pruritus, and the dog had to be otherwise healthy. Dogs with documented food allergy could be enrolled if they remained on their diet throughout the study. All dogs had to be on appropriate flea control for a minimum of 4 weeks prior to enrolment with no presence of fleas on Day 0 (no more than a mild infestation, i.e. flea faeces or debris present at most, no actual fleas visible).

The mean age for dogs enrolled in the study was approximately six years and the mean weight of the dogs was 20.5 kg. Both sexes were represented equally.

The primary efficacy variable for pruritus was defined as the percentage reduction from baseline for owner-assessed pruritus on Visit 4 (Day 28 ± 3). At Day 28 the mean percentage reduction from baseline was significantly higher in the Cytopoint-treated animals (57.71%) compared to the placebo group (21.78%; $P < 0.0001$); therefore, the primary efficacy objective of the study was met. It is noted that the onset of effect is rapid, with a mean 35.69% decrease of pruritus after just one day of administration, compared to 21.22% of the placebo group (significant difference). This is in keeping with data submitted in the original dossier, which supported an onset of effect of 8 hours in a laboratory model of canine pruritus. While some degree of placebo effect was observed in the control group, it is noted, based on comments of the clinical expert, that a placebo effect of about 20-30% is usual for studies investigating treatment options for canine allergic dermatitis.

In cases where repeat administration is required, a between treatment interval of one month is proposed; therefore, the choice of the evaluation time point (Day 28) is appropriate. This reflects the expected duration of efficacy based on the laboratory data presented in support of the original new product application.

All secondary parameters regarding pruritus or pruritus reduction were significantly better for Cytopoint compared to placebo from Day 0+4h or Day 2, depending on the parameter, until Day 28. This included mean pruritus owner-assessed VAS score achieved at each time point and percentage of pruritus decrease greater than 50% or 75%. Regarding mean pruritus score achieved at each time point, it is noted that for the placebo group this remained above 40 out of 100 (this may be considered the threshold for a "moderate pruritus") while, for the Cytopoint treated group, this reduced and remained below this threshold (achieving "mild pruritus") from Day 2 onwards and throughout the remainder of the study. Based on other analyses, it is noted that 66-73% of animals treated with Cytopoint showed a greater than 50% decrease of pruritus on Days 14 to 28, compared to 10-14% of the placebo dogs. Further, 31-32% of animals treated with Cytopoint showed a greater than 75% decrease of pruritus on Days 14 to 28, compared to 0% of the placebo dogs.

The only real clinical parameter evaluated in this study, i.e the investigator assessment of skin condition by means of a visual analogue scale (Investigator VAS), was designed by the applicant and is not considered a validated evaluation tool. Further, as recognised by the clinical expert, this tool aims at measuring skin condition (lesions), which is a parameter not directly pertinent to the label extension requested ("for the treatment of pruritus associated with allergic dermatitis in dogs"). Nonetheless, it is argued that this parameter can be considered useful for the evaluation of treatment results, as a deteriorated skin condition can be consequence of scratching and rubbing due to pruritus. Using this tool, the percentage reduction in skin condition score was significantly greater for the Cytopoint treated dogs compared to the placebo group (LS mean difference between groups of 21.1% at Day 28, $p<0.0001$). These results, although not directly pertinent to the proposed new indication, provide some additional support for a treatment effect.

Overall, it was accepted that the choice of the primary efficacy variable, in combination with the investigator-based assessment of the same parameter as a secondary efficacy variable, was suitable, considering the indication which is proposed (reduction of pruritus) in the current variation.

Finally, it is of note that 19 dogs were withdrawn from the study prior to Day 28 due to worsening clinical signs, of which only 3 were in the Cytopoint group compared to 16 in the placebo control group, further supporting a clinically relevant effect of treatment.

The applicant was requested to address if the inclusion of dogs diagnosed with allergic dermatitis with an atopic dermatitis component may have favourably biased the efficacy outcome of the study (considering that Cytopoint has already been demonstrated to be efficacious for the reduction of pruritus in dogs with atopic dermatitis). The applicant provided supplementary analyses, in which cases with a presumptive atopic component were excluded from the original dataset. These data demonstrated that the primary efficacy objective of the study was met and that the results of secondary efficacy parameters were similar following exclusion of this subset of dogs from the dataset. Thus, it was accepted that inclusion of dogs with an atopic component in the diagnosis of allergic dermatitis did not bias the study outcome of the overall study population.

Regarding the safety evaluation, it is noted that the number and nature of adverse events recorded during the study was similar in both groups. Of these events, six were considered severe (four in the Cytopoint group and two in the placebo group). However, these events were linked to disorders related to the underlying allergic dermatitis, such as otitis and dermatitis, including bacterial skin and ear infection. Blood and urine samples were collected at enrolment as well as study completion. For various blood and urine parameters increasing or decreasing shifts were equally observed in both groups, but they remained within the reference range and were thus considered clinically not relevant. Based on these data, there are no safety concerns arising from this study and the information currently included in sections 4.6 and 4.10 of the SPC remains appropriate.

In this study on allergic (not atopic) dermatitis, dogs received a single injection of Cytopoint and were followed during the first month post injection, but no subsequent monthly doses were administered and therefore no data are available on the long-term efficacy in allergic dogs. The applicant justified the lack of longer term data in the target population on the basis that longer term data are available in dogs with atopic dermatitis (data supporting the original authorisation). On this point, it is accepted that safety of longer term use in dogs with atopic dermatitis can be extrapolated to the safety of dogs with allergic dermatitis, given that, in the rapporteur's opinion, there are no confounding effects which would predispose dogs with allergic dermatitis more adversely to longer term treatment compared to dogs with atopic dermatitis. Similarly, the rapporteur notes that the effectiveness of repeat treatments (once monthly) has been demonstrated for the control of pruritus in atopic dermatitis dogs but has not been tested for the control of pruritus in other allergic dermatitis conditions like contact dermatitis, flea allergic dermatitis and food allergy. However, based on the mode of action, the rapporteur considers it reasonable to assume that repeat treatments, if needed, in these animals will be as effective as it was in the atopic dermatitis animals.

However, the focus of any treatment strategy for dogs with allergic dermatitis should be on 'avoidance'. This would suggest, therefore, that the use of Cytopoint in animals with allergic dermatitis would be limited to alleviation of clinical signs in the weeks to months immediately after elimination of the allergen or when there has been a 'flare-up' associated with inadvertent exposure to the allergen (rather than being used as 'maintenance therapy' as may be required for atopic dogs). Therefore, extrapolation of the concept of monthly maintenance therapy to the allergic dermatitis indication was not considered appropriate/justified. The applicant was requested to comment further on the intended use of this product and in their response, the applicant acknowledged that whilst the preferred treatment strategy is avoidance, it was argued that there are often situations in which the allergic stimulus is difficult to identify and / or eliminate from the dog's environment, and that in these cases a longer treatment duration may be required. Additional precautions were proposed for inclusion in sections 4.5 and 4.9 of the SPC to specify that it is good medical practice to investigate and treat the underlying cause of allergic dermatitis. The CVMP considered that the precautions were acceptable, following further strengthening to provide a clearer instruction to investigate and treat the underlying cause of allergic dermatitis and to clearly state that the product is not intended to be used as a maintenance therapy for this indication.

In conclusion, the data provided in this study are considered adequate to support the proposed claim 'treatment of pruritus associated with allergic dermatitis in dogs'.

4. Benefit-risk assessment of the proposed change

This product is an immunological veterinary medicinal product containing lokivetmab as active substance, which is a caninised monoclonal antibody (mAb) specifically targeting canine interleukin-31, authorised for the treatment of clinical manifestations of atopic dermatitis in dogs.

The proposed variation is to add a new therapeutic indication for the treatment of pruritus associated with allergic dermatitis in dogs. The MAH also took the opportunity to add a dog pictogram in point 7 of the package leaflet.

4.1. Benefit assessment

The benefit of Cytopoint is its efficacy in the treatment of clinical manifestations of AD in dogs which was evaluated in a number of laboratory and field studies. Well conducted controlled laboratory and clinical trials demonstrated that the product is efficacious in treatment of canine AD. At the proposed

dose of 1 mg/kg bw, the efficacy data in the target species demonstrated a significant benefit of treatment for a reduction in pruritus, and a beneficial effect of treatment for the reduction of disease severity.
Based on the information presented in support of this variation application, Cytopoint is accepted as being effective for treatment of pruritus associated with allergic dermatitis in dogs.

4.2. Risk assessment

Quality:

Quality remains unaffected by this variation.

Safety:

Safety (risks for the target animal, user or the environment) remains unaffected by this variation. The risk mitigation measures included on the currently approved product information remain appropriate.

4.3. Evaluation of the benefit-risk balance

Based on the data presented, the overall benefit-risk is deemed positive. No change to the impact of the product is envisaged on the following aspects: quality, safety, user safety or environmental safety.

5. Conclusion

Based on the original data presented on efficacy, the Committee for Medicinal Products for Veterinary Use (CVMP) concluded that the application for variation to the terms of the marketing authorisation for Cytopoint can be approved, since the data satisfy the requirements as set out in the legislation (Commission Regulation (EC) No. 1234/2008).

The CVMP considers that the benefit-risk balance remains positive and, therefore, recommends the approval of the variation to the terms of the marketing authorisation for the above mentioned medicinal product.

Changes are required in the following Annexes to the Community marketing authorisation:

I and IIIB.

Please refer to the separate product information showing the tracked changes.