Safety and efficacy of ECONASE® XT (endo-1,4-β-xylanase) as a feed additive for laying hens

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Guido Rychen, Gabriele Aquilina, Giovanna Azimonti, Vasilios Bampidis, Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli, Gerhard Flachowsky, Jurgen Gropp, Boris Kolar, Maryline Kouba, Marta Lopez-Alonso, Secundino Lopez Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace, Pieter Wester, Paul Brantom, Noël Albert Dierick and Montserrat Anguita

Abstract

ECONASE® XT is an enzyme preparation with endo-1,4-β-xylanase which is authorised as a feed additive for chickens for fattening or reared for laying, turkeys for fattening or reared for breeding, laying hens, weaned piglets, pigs for fattening and minor poultry species. The authorisation of the additive for laying hens is at 24,000 BXU/kg feed. The applicant asked for a modification on the conditions of use in laying hens, which consists in the reduction of the minimum recommended level from 24,000 BXU/kg feed to 12,000 BXU/kg feed. In previous opinions, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) assessed the safety of the product when used as a feed additive and concluded that the use of the product as a feed additive raises no concerns for consumer safety and no risks for the environment are expected. The Panel also concluded that the additive is non-irritant to the skin, and the liquid form is non-irritant to the eyes and is not a dermal sensitiser; however, it is considered a respiratory sensitiser. Regarding the use of the additive in laying hens, the Panel concluded that under the conditions of use the additive is safe for laying hens and that it can be efficacious at 24,000 BXU/kg. The results of the studies previously assessed showed in two cases improvements on the efficacy at the dose of 12,000 BXU/kg or below. The applicant provided two new studies which showed improvements at the new recommended dose on the performance of the laying hens in one trial and on the energy content in another trial. Therefore, the Panel concluded that the additive has a potential to be efficacious as a zootechnical additive in laying hens at the dose of 12,000 BXU/kg feed.

© 2018 European Food Safety Authority. EFSA Journal published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

Keywords: efficacy, zootechnical additive, digestibility enhancer, xylanase, laying hens

Requestor: European Commission

Question number: EFSA-Q-2017-00254

Correspondence: feedap@efsanews.eu
Panel members: Gabriele Aquilina, Giovanna Azimonti, Vasileios Bampidis, Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli, Gerhard Flachowsky, Jürgen Gropp, Boris Kolar, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Guido Rychen, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace and Pieter Wester.

Acknowledgements: The EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed) wishes to thank the following for the support provided to this scientific output: Jaume Galobart, Lucilla Gregoretti and Jordi Tarrés-Call.

Suggested citation: EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, López Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Brantom P, Dierick NA and Anguita M, 2018. Scientific Opinion on the safety and efficacy of ECONASE® XT (endo-1,4-β-xylanase) as a feed additive for laying hens. EFSA Journal 2018;16(3):5216, 7 pp. https://doi.org/10.2903/j.efsa.2018.5216

ISSN: 1831-4732

© 2018 European Food Safety Authority. EFSA Journal published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

This is an open access article under the terms of the Creative Commons Attribution-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.

The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.
Table of contents

Abstract ..................................................................................................................................................... 1
1. Introduction ........................................................................................................................................ 4
   1.1. Background and Terms of Reference .......................................................................................... 4
   1.2. Additional information .................................................................................................................. 4
2. Data and methodologies ...................................................................................................................... 4
   2.1. Data ................................................................................................................................................ 4
   2.2. Methodologies ................................................................................................................................. 4
3. Assessment ......................................................................................................................................... 5
   3.1. Characterisation ............................................................................................................................... 5
   3.2. Safety ............................................................................................................................................... 5
   3.3. Efficacy for laying hens .................................................................................................................... 5
   3.4. Post-market monitoring .................................................................................................................... 7
4. Conclusions ......................................................................................................................................... 7

Documentation provided to EFSA ................................................................................................................ 7
References ................................................................................................................................................. 7
Abbreviations ............................................................................................................................................. 7
1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003\(^1\) establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 13(3) of that Regulation lays down that if the holder of an authorisation proposes changing the terms of the authorisation by submitting an application to the Commission, accompanied by the relevant data supporting the request for the change, the Authority shall transmit its opinion on the proposal to the Commission and the Member States.

The European Commission received a request from Roal Oy\(^2\) for a modification of the terms of the authorisation of the product ECONASE® XT (endo-1,4-β-xylanase), when used as a feed additive for laying hens (category: zootechnical additives; functional group: digestibility enhancers).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 13(3) (modification of the authorisation of a feed additive). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 18 May 2017.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product ECONASE® XT (endo-1,4-β-xylanase), when used under the proposed conditions of use (see Section 3).

1.2. Additional information

The EFSA Panel on Additives and Products or Substances used in Animal feed (FEEDAP) released two opinions on the safety and efficacy of ECONASE® XT P/L as a feed additive for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding and piglets (weaned) (EFSA, 2008, 2009), which included the assessment of the safety for the consumer, the user and the environment as well as the safety aspects of the genetic modification of the production strain. The FEEDAP Panel adopted a further opinion on the safety and efficacy of ECONASE® XT when used as a feed additive for laying hens, minor poultry species and pigs for fattening (EFSA FEEDAP Panel, 2011a). The additive is currently authorised for use in chickens for fattening or reared for laying, turkeys for fattening or reared for breeding, laying hens, weaned piglets, pigs for fattening and minor poultry species.\(^3,4\) The additive is authorised in laying hens at the dose of 24,000 BXU/kg feed. The applicant has now requested a modification of the conditions of use in laying hens which consists in lowering the recommended dose from 24,000 BXU/kg feed to 12,000 BXU/kg feed.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier\(^5\) in support of the authorisation request for the use of ECONASE® XT as a feed additive. The technical dossier was prepared following the provisions of Article 13 of Regulation (EC) No 1831/2003, Regulation (EC) No 429/2008\(^6\) and the applicable EFSA guidance documents.

---

\(^1\) Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

\(^2\) Roal Oy, Tykkimäentie 15, 05200 Rjämakki, Finland.

\(^3\) Commission Regulation (EC) No 902/2009 of 28 September 2009 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (CBS 114044) as a feed additive for weaned piglets, chickens for fattening, chickens reared for laying, turkeys for fattening and turkeys reared for breeding (holder of authorisation Roal Oy. OJ L 256, 29.9.2009. p. 23.

\(^4\) Commission Implementing Regulation (EU) No 1110/2011 of 3 November 2011 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (CBS 114044) as a feed additive for laying hens, minor poultry species and pigs for fattening (holder of authorisation Roal Oy). OJ L 287, 4.11.2011, p.27.

\(^5\) FEED dossier reference: FAD-2017-0011.

\(^6\) Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.
The European Union Reference Laboratory considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.\(^7\)

### 2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of ECONASE\(^®\) XT is in line with the principles laid down in Regulation (EC) No 429/2008 and the relevant guidance documents: Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012) and Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011b).

### 3. Assessment

The current assessment deals with the request from the applicant to reduce the authorised minimum recommended dose in laying hens. The additive is intended to be used in diets of laying hens at a minimum dose of 12,000 BXU/kg feed.

#### 3.1. Characterisation

ECONASE\(^®\) XT is an enzyme preparation with endo-1,4-\(\beta\)-xylanase (xylanase) as the main activity. It is available in powder (P) and liquid (L) forms ensuring activities of 4,000,000 and 400,000 BXU/g,\(^8\) respectively. The production organism is a genetically modified strain of *Trichoderma reesei* (CBS 114044). The production strain and the final formulations have been described and characterised in previous opinions (EFSA, 2008, 2009).

The applicant submitted new data on the shelf-life of the two formulations at different temperatures and longer periods of storage than the ones previously reported. The shelf-life was measured in three batches of each formulation.\(^9\) Samples of the solid formulation were stored at 20–23°C in closed containers for 24 months and the enzyme activity recovery after storage was 93%. Other samples were stored at 25 or 30°C in closed or open containers for 12 months. Recovery values were 73 and 63% for closed containers stored at 25 or 30°C, the corresponding values for the open containers were 79 and 68%.

Samples of the liquid formulation were stored at 6, 25 or 30°C for 24 months in closed containers. The mean recovery values in these conditions were 96%, 95% and 80%, respectively.

#### 3.2. Safety

Safety aspects regarding the use of this additive in feed including the safety of the genetic modification of the production strain, the safety for the consumers, for the users and for the environment have been previously assessed (EFSA, 2008, 2009). The Panel concluded that the use of the product as a feed additive raises no concerns for consumer safety or for the environment. Considering the safety for the user, ECONASE\(^®\) XT P/L is non-irritant to the skin, and the liquid form is non-irritant to the eyes and is not a dermal sensitiser; the additive ECONASE\(^®\) XT is considered a respiratory sensitiser. The FEEDAP Panel is not aware of any new information that would lead it to reconsider the conclusions drawn previously.

In 2011, the FEEDAP Panel evaluated a tolerance trial carried out with laying hens. Based on the results obtained in that tolerance study, the Panel concluded that ECONASE\(^®\) XT is safe for laying hens at the maximum recommended dose of 24,000 BXU/kg feed. The proposed reduction in the minimum recommended dose would not affect that conclusion.

#### 3.3. Efficacy for laying hens

In a previous assessment, the FEEDAP Panel concluded that the additive has the potential to be efficacious at 24,000 BXU/kg feed (EFSA FEEDAP Panel, 2011a). In that assessment, there were three efficacy studies which showed improvements in the performance of laying hens, one at 6,000 BXU/kg feed, another one at 12,000 and the third at 24,000 BXU/kg feed. The applicant has now provided two new trials to support the efficacy at the newly recommended dose (12,000 BXU/kg feed).

---

\(^7\) The full report is available on the EURL website: [https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2010-0006.pdf](https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2010-0006.pdf)

\(^8\) One BXU is the amount of enzyme that produces, under Standard conditions (pH 5.3 and 50°C), one nmol of reducing sugars from birch xylan as xylose in one-second.

\(^9\) Technical dossier/Section II/Annex II.20 and II.21.
The details of the design of the newly submitted trials are presented in Table 1 and the results in Table 2. In the two trials, hens were caged (enriched cages) at the onset of laying and were allocated to one of two treatments, a non-supplemented diet (control) or a diet supplemented with ECONASE XT to provide 12,000 BXU/kg feed. The enzyme activities were confirmed by analysis (Table 1). The diets were fed in mash form and on ad libitum basis for 24 weeks in trial 1 and for 28 weeks in trial 2. Mortality and general health were monitored throughout the study. Individual body weight was recorded at the beginning and at the end of the trial in trial 1 or on week 20 and 44 of life in trial 2. Feed consumption was recorded, eggs were collected and weighed throughout the experimental period. Egg production, daily egg mass and feed to egg mass ratio were calculated. In the second trial, a balance study was started from week 38 (titanium dioxide included as an external marker), after 6 weeks excreta were collected for 4 consecutive days from all replicates. Feed and excreta were analysed in order to study the metabolisable energy content of the diet (nitrogen corrected). An analysis of variance was performed on the data obtained, replicate basis. Differences were considered significant at a level of at least p < 0.05.

The results on the feed intake and laying performance (Table 2) showed no significant differences in trial 2 in any of the parameters measured. In trial 1, the hens receiving the xylanase at the recommended dose showed a significantly better daily egg mass per hen and a better feed to egg mass.

### Table 1: Trial design and dosages of the efficacy trials performed in laying hens

| Trial | Total N animals (hens/replicate) | Replicates/treatment | Breed (Age at start) | Diet composition | Enzyme activity (BXU/kg feed) |
|-------|----------------------------------|----------------------|----------------------|------------------|------------------------------|
|       | Total N (replicates/treatment)   |                      |                      |                  | Intended | Analysed |
| 1(a)  | 80                               | 4                    | 10                   | Bovan Brown      | Wheat, soya, barley          | 0        | 12,000   | 0        | 13,650   |
|       | (22 weeks)                       | 24 weeks             |                      |                  |                      | 0        |            | 0        |            |
| 2(b)  | 280                              | 10                   | 14                   | Isa Brown        | Wheat, barley, soybean meal, rye | 0        | 12,000   | 449      | 14,275   |
|       | (20 weeks)                       | 28 weeks             |                      |                  |                      | 0        |            |          |            |

(a): Technical dossier/Section IV/Annex IV.02 and IV.03 and Supplementary information October 2017/Annex 02. (b): Technical dossier/Section IV/Annex IV.04 to IV.09.

The results of the balance study conducted in trial 2 showed a significant increase in the metabolisable energy content (nitrogen corrected) in the group receiving the xylanase at 12,000 BXU/kg feed compared to the control group (10.66 vs 11.39 MJ/kg feed).

The results of the studies previously assessed showed in two cases improvements on the performance of the laying hens at the dose of 12,000 BXU/kg or below. The newly submitted studies showed improvements at the new recommended dose on the performance of the laying hens in one trial and on the energy content in another trial. Therefore, the Panel concludes that the additive has a potential to be efficacious in laying hens as a zootechnical additive at the dose of 12,000 BXU/kg feed.

### Table 2: Effect of ECONASE® XT xylanase on the performance of laying hens

| Trial | Treatments | Body weight change (g/hen)(1) | Daily feed intake (g/hen) | Laying rate (%) | Egg weight (g) | Daily egg mass per hen (g/hen) | Feed to egg mass | Mortality (%) (2) |
|-------|------------|------------------------------|---------------------------|-----------------|---------------|------------------------------|------------------|-------------------|
| 1     | 0          | 292                          | 126                       | 86.3            | 62.8          | 54.5b                        | 2.32b            | 2.5               |
|       | 12,000     | 340                          | 126                       | 88.7            | 64.1          | 57.2a                        | 2.20b            |                   |
| 2     | 0          | 230                          | 117                       | 84.9            | 58.3          | 49.5                         | 2.36             | 6.6               |
|       | 12,000     | 235                          | 117                       | 87.5            | 57.8          | 50.6                         | 2.30             | 8.1               |

(1): Body weight change in trial 1 was measured from week 20 to week 44 of the study. (2): Trial 2 showed a slightly high mortality rate, the reason was that the study was conducted during the summer and at a certain point there was a power outage which resulted in some hens dying.

a,b: Values within one column for the same study with different superscripts are significantly different (p < 0.05).

The results of the balance study conducted in trial 2 showed a significant increase in the metabolisable energy content (nitrogen corrected) in the group receiving the xylanase at 12,000 BXU/kg feed compared to the control group (10.66 vs 11.39 MJ/kg feed).

The results of the studies previously assessed showed in two cases improvements on the performance of the laying hens at the dose of 12,000 BXU/kg or below. The newly submitted studies showed improvements at the new recommended dose on the performance of the laying hens in one trial and on the energy content in another trial. Therefore, the Panel concludes that the additive has a potential to be efficacious in laying hens as a zootechnical additive at the dose of 12,000 BXU/kg feed.

10 Technical dossier/Section IV/Supplementary information October 2017/Annex_03_Second study report re-edited.pdf
11 Technical dossier/Section IV/Supplementary information October 2017/Econase XT dossier Supplementary information_Oct 2017.pdf
3.4. Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation\(^{12}\) and Good Manufacturing Practice.

4. Conclusions

The use of the additive under the new proposed conditions of use is safe for laying hens and raises no concerns for consumer safety or for the environment. ECONASE® XT P/L is non-irritant to the skin, and the liquid form is non-irritant to the eyes and is not a dermal sensitiser, however it is considered a respiratory sensitiser.

The additive has a potential to be efficacious as a zootechnical additive in laying hens at a dose of 12,000 BXU/kg feed.

Documentation provided to EFSA

1) ECONASE® XT for laying hens. February 2017. Submitted by Roal Oy.
2) ECONASE® XT for laying hens. Supplementary information. October 2017. Roal Oy.
3) Comments from Member States.

References

EFSA (European Food Safety Authority), 2008. Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) and of the Panel on Genetically Modified Organisms (GMO) on the safety and efficacy of Econase XT P/L as feed additive for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding and piglets (weaned). The EFSA Journal 2008;6(6):712, 19 pp. https://doi.org/10.2903/j.efsa.2008.712

EFSA (European Food Safety Authority), 2009. Scientific Opinion of the Panel on Genetically Modified Organisms on a request from the European Commission related to the enzyme preparation of trade name ‘Econase XT P/L (endo-1,4 β-xylanase) as a feed additive for chickens and turkeys for fattening, chickens reared for laying, turkeys reared for breeding and piglets (weaned). The EFSA Journal 2009;7(4):1058, 6pp. https://doi.org/10.2903/j.efsa.2009.1058

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011a. Scientific Opinion on the safety and efficacy of Econase XT P/L (endo-1,4 β-xylanase) as a feed additive for laying hens, minor poultry species (including ducks, geese, quails, pheasants and pigeons) and pigs for fattening. EFSA Journal 2011;9(6):2277, 15 pp. https://doi.org/10.2903/j.efsa.2011.2277

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011b. Technical guidance: tolerance and efficacy studies in target animals. EFSA Journal 2011;9(5):2175, 15 pp. https://doi.org/10.2903/j.efsa.2011.2175

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012. Guidance for the preparation of dossiers for zootechnical additives. EFSA Journal 2012;10(1):2536, 19 pp. https://doi.org/10.2903/j.efsa.2012.2536

Abbreviations

FEEDAP  EFSA Panel on Additives and Products or Substances used in Animal Feed

\(^{12}\) Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.