SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as a feed additive for turkeys for fattening[1]

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The additive AveMix® XG 10 is an enzyme preparation of endo-1,4-beta-xylanase (xylanase) and endo-1,3(4)-beta-glucanase (glucanase), produced by two strains of *Trichoderma reesei*. This product is currently authorised for use in chickens for fattening, laying hens, minor poultry species and weaned piglets as a zootechnical additive, under the functional group of digestibility enhancers. The applicant is now seeking an extension of the authorisation to turkeys for fattening at a recommended dose of 4 000 XU (xylanase units) and 900 BGU (glucanase units) per kg complete feed. The results obtained in a tolerance study in turkeys for fattening showed that the birds tolerated well a 100-fold overdose of the recommended dose. Therefore, the additive is safe for turkeys for fattening when used at the recommended dose. Three efficacy studies carried out in turkeys for fattening showed that the additive has the potential to be efficacious at the dose of 4 000 XU and 900 BGU/kg complete feed.

KEY WORDS

Zootechnical additive, digestibility enhancers, endo-1,4-beta-xylanase, endo-1,3(4)-beta-glucanase, turkeys for fattening, safety, efficacy

[1] On request from the European Commission, Question No EFSA-Q-2012-00668, adopted on 12 March 2013.

[2] Panel members: Gabriele Aquilina, Alex Bach, Vasileios Bampidis, Maria De Lourdes Bastos, Gerhard Flachowsky, Mikolaj Antoni Gralak, Christer Hogstrand, Lubomir Leng, Secundino López-Puente, Giovanna Martelli, Baltasar Mayo, Derek Renshaw, Guido Rychen, Maria Saarela, Kristen Sejrsen, Patrick Van Beelen, Robert John Wallace and Johannes Westendorf. Correspondence: FEEDAP@efsa.europa.eu

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SUMMARY

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase, endo-1,3(4)-beta-glucanase) as a feed additive for turkeys for fattening.

The additive AveMix® XG 10 is an enzyme preparation of endo-1,4-beta-xylanase (xylanase) and endo-1,3(4)-beta-glucanase (glucanase), produced by two strains of *Trichoderma reesei*. This product is currently authorised for use in chickens for fattening, laying hens, minor poultry species and weaned piglets as a zootechnical additive, under the functional group of digestibility enhancers. The applicant is now seeking an extension of the authorisation to turkeys for fattening at a recommended dose of 4 000 XU (xylanase units) and 900 BGU (glucanase units)/kg complete feed.

A full description of the formulations, manufacturing processes, purity, stability and homogeneity of the product has already been provided in a previous assessment. The FEEDAP Panel considers that the safety aspects other than safety for the new target species have been covered in the previous assessment and would not be affected by the requested extension of use. Therefore, the present opinion focuses only on the safety and efficacy of this enzyme preparation for the new target species.

The applicant provided a tolerance study performed in turkeys for fattening. In this study the birds tolerated well a 100-fold overdose of the recommended dose (4 000 XU and 900 BGU/kg feed) and therefore the Panel concludes that the additive is safe for turkeys for fattening when used at the recommended dose.

Three efficacy studies performed in turkeys for fattening were provided. The supplementation of the diets with AveMix® XG 10 at the recommended dose (4 000 XU and 900 BGU/kg) resulted in a significantly higher body weight in two trials and in a significantly improved feed to gain ratio in two trials. Therefore, the FEEDAP Panel concludes that AveMix® XG 10 has the potential to be efficacious in turkeys for fattening at the dose of 4 000 XU and 900 BGU/kg feed.

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BACKGROUND

Regulation (EC) No 1831/2003[4] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7.

The European Commission received a request from the company AVEVE NV[5] for authorisation of the product AveMix® XG 10, endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase, when used as a feed additive for turkeys for fattening (category: zootechnical additives; functional group: digestibility enhancers) under the conditions mentioned in Table 1.

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 4(1) (authorisation of a feed additive or new use of a feed additive). EFSA received directly from the applicant the technical dossier in support of this application.[6] According to Article 8 of that Regulation, 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. The particulars and documents in support of the application were considered valid by EFSA as of 30 July 2012.

The additive AveMix® XG 10 is a preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754). This product is currently authorised for use as feed additive in feed for chickens for fattening[7,8] weaned piglets,[9] and laying hens and minor poultry species for fattening and laying.[10]

The European Food Safety Authority issued a scientific opinion on the safety and efficacy of AveMix® XG 10 as a feed additive for chickens for fattening (EFSA, 2009) and one on the modification of the terms of the authorisation of the product for this species (EFSA, 2010). Opinions on the safety and efficacy of the product as a feed additive for weaned piglets and laying hens and minor poultry species were published on 2011 and 2012, respectively (EFSA, 2011 and 2012).

TERMS OF REFERENCE

According to Article 8 of Regulation (EC) No 1831/2003, EFSA shall 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 the efficacy of the product

[4] 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.
[5] AVEVE NV, Minderbroedersstraat 8, 3000 Leuven, Belgium.
[6] EFSA Dossier reference: FAD-2012-0019.
[7] Commission Regulation (EC) No 1091/2009 of 13 November 2009 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754) as a feed additive for chickens for fattening (holder of authorisation Aveve NV) OJ L 299, 14.11.2009, p. 6.
[8] Commission Regulation (EU) No 335/2011 of 7 April 2011 amending Regulation (EC) No 1091/2009 as regards the minimum content of the enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754) as a feed additive in feed for chickens for fattening OJ L 94, 08.04.2011, p. 14.
[9] Commission Implementing Regulation (EU) No 1088/2011 of 27 October 2011 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MULC 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MULC 49754) as a feed additive for weaned piglets (holder of authorisation Aveve NV) OJL 281, 28.10.2011, p. 14.
[10] Commission Implementing Regulation (EU) No 989/2012 of 25 October 2012 concerning the authorisation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754) as a feed additive for laying hens and minor poultry species for fattening and laying (holder of authorisation Aveve NV). OJ L 297, 26.10.2012, p. 11.

AveMix® XG 10, endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase, when used under the conditions described in Table 1.

Table 1: Description and conditions of use of the additive as proposed by the applicant

Additive	endo-1,4-beta-xylanase EC 3.2.1.8 and endo-1,3(4)-beta-glucanase EC 3.2.1.6 (AveMix® XG 10)
Registration number/EC No/No (if appropriate)	4a9
Category(-ies) of additive	Zootechnical additive
Functional group(s) of additive	Digestibility enhancer

Description			
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)
Enzyme preparation containing endo-1,4-beta-xylanase (EC 3.2.1.8) produced by Trichoderma reesei and endo-1,3(4)-beta-glucanase (EC 3.2.1.6) produced by Trichoderma reesei. Solid or liquid having a minimum activity of endo-1,4-beta-xylanase: 40000 XU/g endo-1,3-(4)-beta-glucanase: 9000 BGU/g	Not applicable	Complies with JECFA guidelines on microbial quality, heavy metals, toxins and undesirable substances	Assay based on colometric reaction of dinitrosalicylic acid on reducing sugar yield produced by action of endo-1,4-beta-xylanase on a xylan containing substrate or endo-1,3(4)-beta-glucanase on a beta-glucan containing substrate

Trade name (if appropriate)	AveMix® XG 10
Name of the holder of authorisation (if appropriate)	AVEVE NV

Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		U/kg of complete feedingstuffs		
Turkeys for fattening	Until slaughter age	Endo-1,4-beta-xylanase: 4000 XU/kg complete feed endo-1,3-(4)-beta-glucanase: 900 BGU/kg complete feed		Not relevant

Other provisions and additional requirements for the labeling	
Specific conditions or restrictions for use (if appropriate)	In the direction for use of the additive and premixture, indicate the storage temperature, storage life, and stability to pelleting
Specific conditions or restrictions for handling (if appropriate)	-
Post-market monitoring (if appropriate)	-
Specific conditions for use in complementary feedingstuffs (if appropriate)	Recommended dosages per kilogram of complete feedingstuff for turkeys for fattening: endo-1,4-beta-xylanase: 4000 XU, endo-1,3(4)-beta-glucanase: 900 BGU

Maximum Residue Limit (MRL) (if appropriate)			
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues
-	-	-	-

ASSESSMENT

1. Introduction

The additive AveMix® XG 10 is an enzyme preparation of endo-1,4-beta-xylanase (xylanase; EC 3.2.1.8) and endo-1,3(4)-beta-glucanase (glucanase; EC 3.2.1.6), produced by two strains of *Trichoderma reesei* (MUCL 49755 and 49754, respectively). The product is produced in two forms, solid and liquid, with an activity of xylanase of 40 000 XU/g and of glucanase of 9 000 BGU/g. This product is currently authorised for its use in feed for chickens for fattening, laying hens and minor poultry species and weaned piglets as a zootechnical additive, under the functional group of digestibility enhancers. The applicant is now seeking the authorisation of the product as feed additive for turkeys for fattening at a recommended dose of 4 000 XU (xylanase units) and 900 BGU (glucanase units) per kg complete feed (delivered by 100 mg additive/kg feed).

The European Food Safety Authority issued two scientific opinions on the safety and efficacy of AveMix® XG 10 as a feed additive for chickens for fattening (EFSA, 2009, 2010), another one for its use in weaned piglets (EFSA, 2011) and a fourth on its use in laying hens and minor poultry species (EFSA, 2012). A full description of the formulations, manufacturing processes, purity, stability and homogeneity of the product has already been provided in a previous assessment (EFSA, 2009). The FEEDAP Panel considers that the safety aspects other than safety for the new target species have been covered in this previous assessment and would not be affected by the requested extension of use. Therefore, the present opinion focuses only on the safety and efficacy of this enzyme preparation for the new target species.

2. Evaluation of the analytical methods by the European Union Reference Laboratory (EURL)

The EURL considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[11]

3. Safety for turkeys for fattening

A total of 1 500 one-day-old Big-9 female turkeys were distributed in replicates of 31 or 32 birds and allocated to four dietary treatments (12 replicates per treatment).[12] On day 28 the number of birds per replicate was reduced to 25. Basal diets based on wheat and soya bean meal were supplemented with AveMix® XG 10 to provide 0/0, 3 000/675 (0.75×), 4 000/900 (1×) and 400 000/90 000 (100×) XU and BGU/kg feed, respectively (confirmed by analyses). Diets contained monensin until eight weeks of age and were offered as crumbs until day 28 and thereafter as pellets. The study lasted 84 days and performance of the birds was measured. Performance data were subject to analysis of variance (ANOVA) and a Dunnett test to compare the means.[13]

Mortality ranged from 0.8 % to 1.6 % without differences between the treatments (see Table 3). This figure does not include runt birds that were culled during the first two weeks (3, 3, 8 and 9 in the 0, 0.75×, 1× and 100× group, respectively). Mean body weight was 59 g initially and after 84 days was 7.36, 7.46, 7.52 and 7.46 kg in the four groups. Average daily gain was 87, 88, 89 and 88 g and the corresponding feed to gain ratio was 2.14, 2.10, 2.09 and 2.07 (feed to gain ratio values in the 1× and 100× were significantly different from the 0/0 group). The animals tolerated well a dose of 100× the recommended dose; thus, the Panel concludes that the additive is safe for the turkeys for fattening at the recommended dose.

[11] The full report is available on the EURL website: http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-FAD-2009-0062.pdf
[12] Technical dossier/Section III/Annex III.2.1 and supplementary information December 2012/Annex 1.
[13] Technical dossier/Supplementary information February 2013/Annex 2.

4. Efficacy for turkeys for fattening

Three performance trials conducted in three different countries were provided. The design of the trials is presented in Table 2 and a summary of the results in Table 3.

The third trial is the tolerance trial reported above. In all cases, one-day-old birds were used, and were under study for 84 days. Males were used in trials 1 and 2 and females in trial 3. The dietary treatments resulted from the supplementation of basal diets with AveMix® XG 10 (solid) at different dosages. The intended doses were confirmed by analyses. Diets in trial 1 and 2 were offered as pellets, in trial 3 as crumbs until day 28 and thereafter as pellets. General health status and mortality were monitored and performance of the animals was measured. Data was subject to an ANOVA followed by a Tukey (trial 1) or a Dunnett test (trials 2 and 3) in order to compare group means.

Table 2: Summary of the design of the three performance trials in turkeys for fattening considered for the assessment

Trial	AveMix® XG 10 (U/kg)[1]		Diet composition	Breed (sex)	Total no of animals *(animals/replicate)* replicates/treatment[2]
	Intended	Analysed			
1[14]	0/0 2 000/450 4 000/900	–/– 2 214/528 4 350/1 008	Wheat, rye, soya bean meal	BUT 6 (♂)	600 *(10)* 20
2[15]	0/0 2 000/450 4 000/900	–/– 2 330/523 4 815/1 051	Wheat, barley, soya bean meal	BUT (♂)	360 *(12)* 10
3[16]	0/0 3 000/675 4 000/900 400 000/90 000	–/– 3 260/702 4 427/933 466 488/108 404	Wheat, soya bean meal	Big-9 (♀)	1500 *(12)* 31-32

[1] Values for xylanase/glucanase, analysed values for the non-supplemented diets were not provided.
[2] In trial 3 the number of animals per pen was reduced to 25 birds on day 28.

Table 3: Effect of AveMix® XG 10 on the performance of turkeys for fattening

Trial	AveMix® XG 10 (U/kg)[1]	Body weight (g)		Daily feed intake (g)	Feed to gain ratio	Mortality[2] (%)
		Initial	Final			
1	0/0	60.4	10 953[a]	253	1.95[a]	5.8
	2 000/450	60.4	11 015[ab]	250	1.92[b]	2.5
	4 000/900	60.4	11 199[b]	253	1.91[b]	4.0
2	0/0	61	10 457	250	2.02	0
	2 000/450	62	10 511	248	1.99	2.5
	4 000/900	60	10 542*	249	1.99	1.7
3	0/0	59	7 361	186	2.14	0.8
	3 000/675	59	7 464	185	2.10	1.6
	4 000/900	59	7 517	185	2.09*	1.6
	400 000/90 000	59	7 463	183	2.07*	1.1

[1] Intended dose for xylanase/glucanase.
[2] In trial 1 values do not consider the animals that died during the first week, in trial 3 values do not consider dead animals during the two initial weeks.
[a,b]Values in one column and within a given trial with different superscripts are significantly different ($P < 0.05$).
* Values are different from the control diet ($P < 0.05$).

[14] Technical dossier/Section IV/Annex IV.2.11 and supplementary information December 2012.
[15] Technical dossier/Section IV/Annex IV.2.12 and supplementary information February 2013/Annex 3.
[16] Technical dossier/Section IV/Annex IV.2.13 and supplementary information February 2013/Annex 2.

Mortality was low (< 6 %) and not related to the experimental treatments. The supplementation of the basal diet with AveMix® XG 10 at the recommended dose of 4 000 XU and 900 BGU/kg feed resulted in a higher final body weight in trials 1 and 2 and a better feed to gain ratio in trials 1 and 3. Therefore, the Panel concludes that the additive has the potential to improve the performance of turkeys for fattening at the recommended dose.

5. 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[17] and Good Manufacturing Practice.

CONCLUSIONS

The two formulations (liquid and solid) of the additive are considered to be equivalent regarding the safety and efficacy for the target species when used at the same level.

Based on the results obtained in a tolerance study with turkeys for fattening, in which birds tolerated well a 100-fold overdose of the recommended dose, the FEEDAP Panel concludes that the additive is safe for turkeys for fattening at the recommended dose.

Supplementation of feed with AveMix® XG 10 at the recommended dose (4 000 XU and 900 BGU/kg feed) resulted in a better performance of turkeys for fattening in three trials. Therefore, the Panel concludes that the additive has the potential to be efficacious in turkeys for fattening at this dose.

DOCUMENTATION PROVIDED TO EFSA

1. AveMix® XG 10 turkeys for fattening. May 2012. Submitted by AVEVE NV.
2. AveMix® XG 10 turkeys for fattening. Supplementary information. December 2012. Submitted by AVEVE NV.
3. AveMix® XG 10 turkeys for fattening. Supplementary information. February 2013. Submitted by AVEVE NV.
4. Comments from Member States received through the ScienceNet.

REFERENCES

EFSA (European Food Safety Authority), 2009. Safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) for use as feed additive for chickens for fattening. The EFSA Journal, 1094, 1–17.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2010. Modification of the terms of the authorisation of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as a feed additive for chickens for fattening. EFSA Journal, 8(12):1919, 10 pp.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2011. Safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as feed additive for weaned piglets. EFSA Journal, 9(6):2278, 11 pp.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2012. Safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as feed additive for laying hens and minor poultry species. EFSA Journal, 10(6): 2728, 10 pp.

[17] 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.