

## SCIENTIFIC OPINION

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# Safety and efficacy of Coxar<sup>®</sup> (nicarbazin) for turkeys for fattening

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP),  
Guido Rychen, Gabriele Aquilina, Giovanna Azimonti, Vasileios Bampidis,  
Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli,  
Gerhard Flachowsky, Boris Kolar, Maryline Kouba, Marta López Alonso,  
Secundino López Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Maria Saarela,  
Roberto Edoardo Villa, Robert John Wallace, Pieter Wester, Paul Brantom, Ingrid Halle,  
Patrick van Beelen, Orsolya Holczknecht, Maria Vittoria Vettori and Jürgen Gropp

### Abstract

Coxar<sup>®</sup> is safe for turkeys for fattening at the use level of 100 mg nicarbazin/kg complete feed, with a margin of safety of about 1.25. Nicarbazin, when ingested, is rapidly split in its two components 2-hydroxy-4,6-dimethylpyrimidine (HDP) and dinitrocarbanilide (DNC), which behave independently. HDP-related residues are much lower than those of DNC. DNC is the marker residue. Liver is the target tissue. Nicarbazin is not genotoxic. The primary toxicity resulting from the oral use of nicarbazin is renal toxicity. The lowest no observed adverse effect level (NOAEL) identified in a 52-week study in rat using DNC+HDP is 20 mg DNC + 8 mg HDP/kg body weight (bw) per day based on the absence of microcrystals in urine and related microscopic renal observations. The use of 100 mg nicarbazin from Coxar<sup>®</sup>/kg complete feed for turkeys for fattening will not pose a risk to consumers, provided that maximum contents in nicarbazin of 0.1% *p*-nitroaniline (PNA) and 0.4% methyl(4-nitrophenyl) carbamate (M4NPC) would be respected. No withdrawal time is required. Residue data comply with the established maximum residue limits (MRLs). Nicarbazin is not a skin or eye irritant and not a skin sensitiser. These conclusions also apply to the additive Coxar<sup>®</sup>. Inhalation toxicity of nicarbazin is limited; the granulated additive has a low dusting potential. No risk for users is identified. Based on the available data, the FEEDAP Panel cannot conclude on the safety of Coxar<sup>®</sup> for the environment. The efficacy of 100 mg nicarbazin from Coxar<sup>®</sup>/kg feed was demonstrated in three anticoccidial sensitivity tests (AST), but only in one floor pen study. The floor pen study with 75 mg nicarbazin failed to demonstrate evidence of efficacy. No final conclusions on the efficacy of nicarbazin from Coxar<sup>®</sup> for turkeys for fattening can be drawn.

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**Correspondence:** [feedap@efsa.europa.eu](mailto:feedap@efsa.europa.eu)

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

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## Summary

Following a request from 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 Coxar® (nicarbazin) when used as a feed additive for turkeys for fattening.

Coxar® is considered safe for turkeys for fattening at the use level of 100 mg nicarbazin/kg complete feed, with a margin of safety of about 1.25. Nicarbazin has no antimicrobial activity; no incompatibilities or interactions with feedingstuffs, carriers, or other approved additives are expected.

Nicarbazin, when ingested, is rapidly split in its two components 2-hydroxy-4,6-dimethylpyrimidine (HDP) and dinitrocarbanilide (DNC), which behave independently. DNC residues decline rapidly from tissues following nicarbazin withdrawal. HDP-related residues are much lower than those derived from DNC. DNC appears as the marker residue. Liver is the target tissue. The metabolic pathways in the turkey are similar to those in the chicken and rat.

Nicarbazin is not genotoxic. The primary toxicity resulting from the oral use of nicarbazin is renal toxicity. The lowest no observed adverse effect level (NOAEL) identified in a 52-week study in rat using DNC+HDP was 20 mg DNC + 8 mg HDP/kg body weight (bw) per day based on the absence of microcrystals in urine and related microscopic renal observations.

The use of Coxar® at the highest proposed dose (100 mg nicarbazin/kg complete feed) will not pose a risk to persons consuming animal products from turkeys for fattening, provided that maximum contents in nicarbazin of 0.1% *p*-nitroaniline (PNA) and 0.4% methyl(4-nitrophenyl) carbamate (M4NPC) would be respected. No withdrawal time is required for Coxar® in turkeys for fattening. Residue data comply with the established maximum residue limits (MRLs).

Nicarbazin is not a skin or eye irritant and not a skin sensitiser. These conclusions also apply to the additive Coxar®. Inhalation toxicity of nicarbazin is limited. Due to low dusting potential of the granulated additive, the risk for users is negligible.

No final conclusions on the safety of nicarbazin for the environment can be made since: (i) DNC refined predicted environmental concentrations (PECs) shows uncertainties linked to the very high persistence of the compound, (ii) DNC might accumulate in the sediment compartment, and (iii) DNC can potentially bioaccumulate and may cause secondary poisoning.

The efficacy of 100 mg nicarbazin from Coxar®/kg feed was demonstrated in three anticoccidial sensitivity tests (AST), but only in one floor pen study. The floor pen study with 75 mg nicarbazin failed to demonstrate evidence of efficacy. No final conclusions on the efficacy of nicarbazin from Coxar® for turkeys for fattening can be drawn.