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Safety and efficacy of Monimax® (monensin sodium and nicarbazin) for turkeys for fattening

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Abstract

Monimax® is considered safe for turkeys for fattening at the highest use level of 50 mg monensin sodium and 50 mg nicarbazin/kg complete feed. The margin of safety is about 1.5. The simultaneous use of Monimax® and certain antibiotic drugs (i.e. tiamulin) is contraindicated. Nicarbazin (equimolar complex of dinitrocarbanilide (DNC) and 2-hydroxy-4,6-dimethylpyrimidine (HDP)) has no antimicrobial activity. For both compounds of Monimax®, the metabolic pathways in the chicken are similar to those in the turkey and rat. Monimax® does not represent a genotoxic risk. No safety concerns would arise from the nicarbazin impurities *p*-nitroaniline and methyl(4-nitrophenyl) carbamate. The lowest no observed effect level (NOEL) identified for monensin sodium in a developmental study in rabbits was 0.3 mg monensin sodium/kg body weight (bw) per day for maternal toxicity in rabbits. 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 bw per day. No significant interaction between monensin sodium and nicarbazin is expected from toxicological studies. The use of Monimax® at the highest proposed dose will not pose a risk to persons consuming animal products from treated turkeys for fattening. No withdrawal time is required for Monimax® in turkeys for fattening. Residue data comply with the established maximum residue limits (MRLs) for monensin and DNC. Monensin sodium presents a hazard by inhalation and may also be associated with dermal toxicity. Monimax® is not a skin irritant; however, no data are available for the eye irritation potential of monensin. Monimax® is not a skin sensitiser. Based on the available data, the FEEDAP Panel cannot conclude on the safety of Monimax® for the environment. Monimax® has the potential to control coccidiosis in turkeys for fattening at a minimum concentration of 40 mg monensin sodium and 40 mg nicarbazin/kg complete feed.

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Keywords: coccidiostat, Monimax, monensin sodium, nicarbazin, safety, efficacy, turkeys for fattening

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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 Monimax® (monensin sodium and nicarbazin), when used as a feed additive for turkeys for fattening.

Monimax® is considered safe for turkeys for fattening at the highest use level of 50 mg monensin sodium and 50 mg nicarbazin/kg complete feed. The margin of safety is about 1.5. The simultaneous use of Monimax® and certain antibiotic drugs (i.e. tiamulin) is contraindicated. Monensin has a selective antimicrobial activity against Gram-positive bacterial species while many Enterobacteriaceae are naturally resistant. Induction of cross-resistance with clinically relevant antimicrobials or increased shedding of enteropathogenic bacteria are not reported. Nicarbazin has no antimicrobial activity.

Monensin sodium is absorbed at a limited extent and excreted rapidly, it is extensively metabolised and gives rise to demethylated, oxidised and decarboxylated metabolites. Nicarbazin, when ingested, is rapidly split in its two components 2-hydroxy-4,6-dimethylpyrimidine (HDP) and dinitrocarbanilide (DNC) which behave independently. Liver is the target tissue. DNC residues decline rapidly from tissues following nicarbazin withdrawal. DNC appears as the marker residue. HDP-related residues are much lower than those derived from DNC. For both compounds of Monimax®, the metabolic pathways in the turkey are similar to those in the chicken and rat.

The FEEDAP Panel concludes that the active substances in Monimax®, monensin sodium and nicarbazin, do not represent a genotoxic risk. No safety concerns would arise from the nicarbazin impurities *p*-nitroaniline (PNA) and methyl(4-nitrophenyl) carbamate (M4NPC). Monensin sodium has no structural alert for carcinogenesis. Monensin sodium is not a reproductive or developmental toxicant. The lowest no observed effect level (NOEL) identified in the developmental study in rabbits is 0.3 mg monensin sodium/kg body weight (bw) per day for maternal toxicity in rabbits. The primary toxicity resulting from the oral use of nicarbazin is renal toxicity. The absence of similar findings after treatment with DNC and HDP confirms that this equimolar association of compounds is better tolerated than nicarbazin at equivalent doses. 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 bw per day based on the absence of microcrystals in urine and related microscopic renal observations. No significant interaction between monensin sodium and nicarbazin is expected from toxicological studies.

The use of Monimax® at the highest proposed dose (50 mg monensin sodium and 50 mg nicarbazin/kg complete feed) will not pose a risk to persons consuming animal products from treated turkeys for fattening. No safety concern would arise from the impurity PNA if the maximum content in nicarbazin of 0.1% is respected. The impurity M4NPC is considered safe for the consumer provided that a maximum concentration of 0.4% in nicarbazin is not exceeded. No withdrawal time is required for Monimax® in turkeys for fattening. Residue data comply with the established maximum residue limits (MRLs) for monensin and DNC.

The monensin sodium contained in Monimax® presents a hazard by inhalation. Monimax® is not a skin irritant; however, no data are available for the eye irritation potential of monensin. Monimax® may also act as a dermal toxicant due to its monensin component. Monimax® is not a skin sensitiser.

The use of monensin sodium from Monimax® in complete feed for turkeys for fattening does not pose a risk for the aquatic compartment and sediment, while a risk cannot be excluded for the terrestrial compartment. A final conclusion on the risk resulting from the use of nicarbazin from Monimax® cannot be made because (i) DNC refined predicted environmental concentrations (PECs) show 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. No concerns would arise for the HDP moiety of nicarbazin excreted from chickens fed Monimax®. Based on the available data, the FEEDAP Panel cannot conclude on the safety of Monimax® for the environment.

The FEEDAP Panel concludes that Monimax® has the potential to control coccidiosis in turkeys for fattening at a minimum concentration of 40 mg monensin sodium and 40 mg nicarbazin/kg complete feed.