Review of the existing maximum residue levels for pinoxaden according to Article 12 of Regulation (EC) No 396/2005

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Abstract

According to Article 12 of Regulation (EC) No 396/2005, EFSA has reviewed the maximum residue levels (MRLs) currently established at European level for the pesticide active substance pinoxaden. To assess the occurrence of pinoxaden residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Commission Regulation (EU) No 188/2011, the MRLs established by the Codex Alimentarius Commission as well as the European authorisations reported by Member States and the UK (including the supporting residues data). Based on the assessment of the available data, MRL proposals were derived and a consumer risk assessment was carried out. Although no apparent risk to consumers was identified, some information required by the regulatory framework was missing. Hence, the consumer risk assessment is considered indicative only and some MRL proposals derived by EFSA still require further consideration by risk managers.

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Summary

Pinoxaden was approved on 1 July 2016 by means of Commission Implementing Regulation (EU) 2016/370 in the framework of Regulation (EC) No 1107/2009 as amended by Commission Implementing Regulations (EU) No 540/2011 and 541/2011.

As the active substance was approved after the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(1) of the aforementioned regulation.

As the basis for the MRL review, on 15 April 2020 EFSA initiated the collection of data for this active substance. In a first step, Member States and the UK were invited to submit by 15 May 2020 their national Good Agricultural Practices (GAPs) in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State Austria to identify the critical GAPs in the format of a specific GAP overview file. Subsequently, Member States and the UK were requested to provide residue data supporting the critical GAPs, within a period of 1 month, by 7 August 2020. On the basis of all the data submitted by Member States, the UK and by the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked the RMS to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The PROFile and evaluation report, together with Pesticide Residues Intake Model (PRIMO) calculations were provided by the RMS to EFSA on 16 September 2020. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report.

Based on the information provided by the RMS, Member States, the UK and the EURLs, and taking into account the conclusions derived by EFSA in the framework of Commission Regulation (EU) No 188/2011 and the MRLs established by the Codex Alimentarius Commission, EFSA prepared in December 2020 a draft reasoned opinion, which was circulated to Member States and the EURLs for consultation via a written procedure. Comments received by 27 January 2021 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of pinoxaden in plants was investigated in primary and rotational crops and the processing is not expected to modify the nature of residues. According to the results of the metabolism studies, the residue definition for risk assessment can be proposed as sum of M4 and M6 (both free and conjugated), expressed as pinoxaden. For enforcement, in view of the available information on residue trials and analytical methods, two residue definitions are presented for further consideration by risk managers: sum of M4 and M6 (both free and conjugated), expressed as pinoxaden (option 1); and sum of M4 and M6 (both free only), expressed as pinoxaden (option 2). These residue definitions are restricted to cereals only. A sufficiently validated single-residue method is available for the enforcement of the proposed residue definition option 1 at the combined limit of quantification (LOQ) of 0.03 mg/kg in dry commodities and 0.05 mg/kg in high water content commodities. For the option 2, the combined LOQ of 0.03 mg/kg in all four main plant matrices was demonstrated to be achievable by multi-residue methods. According to the EURLs, the combined LOQ of 0.03 mg/kg is achievable for RD-Mo options 1 and 2 in routine analyses. Analytical standards are commercially available for parent pinoxaden, but not for metabolites M4 and M6.

The available data are considered sufficient to derive two sets of MRL proposals according to the two options for the residue definition for enforcement, for all commodities under evaluation. Residue trials analysing simultaneously for monitoring option 2 and risk assessment residue definitions were not available; however, since only one risk assessment residue definition is proposed in this review, the input values for dietary burden and consumer exposure assessment derived from the residue definition option 1 cover both options. Nonetheless, residue trials analysing simultaneously for enforcement and risk assessment residue definitions are still desirable to derive robust conversion factors from enforcement to risk assessment for option 2.

Pinoxaden is authorised for use on crops that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. The dietary burdens calculated for all groups of livestock were found to exceed the trigger value of 0.1 mg/kg dry matter (DM). Behaviour of residues was therefore assessed in all commodities of animal origin.

The metabolism of pinoxaden residues in livestock was investigated in lactating goats and laying hens at dose rate covering the maximum dietary burdens calculated in this review. According to the results of these studies, the residue definition for enforcement and risk assessment in livestock commodities was proposed as M4 (free and conjugated), expressed as pinoxaden. An analytical
method, involving a hydrolysis step, for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in milk, and 0.02 mg/kg in animal tissues and eggs is available. According to the EURLs metabolite M4 (free only) can be monitored in milk and in liver at the LOQ of 0.01 mg/kg using a QuEChERS based method in routine analysis. Judging from the analytical behaviour of M4, an LOQ of 0.01 mg/kg is supposed to be achievable also for the other main groups of animal products (egg, muscle, kidney, fat).

Livestock feeding studies on lactating cows and laying hens were used to derive MRL and risk assessment values in animal tissues, milk and eggs. Since extrapolation from ruminants to pigs is acceptable, results of the livestock feeding study on ruminants were relied upon to derive the MRL and risk assessment values in pigs. Considering that a confirmatory method is still required for enforcement purposes, MRLs in livestock are considered tentative.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The highest chronic exposure represented 1% of the acceptable daily intake (ADI; Danish child) and the highest acute exposure amounted to 1% of the acute reference dose (ARfD; wheat). Apart from the MRLs evaluated in the framework of this review, internationally recommended CXLs have also been established for pinoxaden. CXLs for plants and animals were found to be covered by the MRLs derived from EU uses, and in consequence, consumer risk assessments with and without consideration of the existing CXLs resulted in the same estimated exposure.
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Background

Regulation (EC) No 396/2005\(^1\) (hereinafter referred to as ‘the Regulation’) establishes the rules governing the setting and the review of pesticide maximum residue levels (MRLs) at European level. Article 12(1) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide, within 12 months from the date of the inclusion or non-inclusion of an active substance in Annex I to Directive 91/414/EEC\(^2\) a reasoned opinion on the review of the existing MRLs for that active substance.

As pinoxaden was approved on 1 July 2016 by means of Commission Implementing Regulation (EU) 2016/370\(^3\) in the framework of Regulation (EC) No 1107/2009\(^4\) as amended by Commission Implementing Regulations (EU) No 540/2011\(^5\) and 541/2011\(^6\), EFSA initiated the review of all existing MRLs for that active substance.

By way of background information, in the framework of Commission Regulation (EU) No 188/2011 pinoxaden was evaluated by United Kingdom, designated as rapporteur Member State (RMS). Subsequently, a peer review on the initial evaluation of the RMS was conducted by EFSA, leading to the conclusions as set out in the EFSA scientific output (EFSA, 2013).

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC repealed by Regulation (EC) No 1107/2009. It should be noted, however, that, in the framework of Regulation (EC) No 1107/2009, only a few representative uses are evaluated, whereas MRLs set out in Regulation (EC) No 396/2005 should accommodate all uses authorised within the European Union (EU), and uses authorised in third countries that have a significant impact on international trade. The information included in the assessment report prepared under Regulation (EC) No 1107/2009 is therefore insufficient for the assessment of all existing MRLs for a given active substance.

To gain an overview of the pesticide residues data that have been considered for the setting of the existing MRLs, EFSA developed the Pesticide Residues Overview File (PROFile). The PROFile is an inventory of all pesticide residues data relevant to the risk assessment and MRL setting for a given active substance. This includes data on:

- the nature and magnitude of residues in primary crops;
- the nature and magnitude of residues in processed commodities;
- the nature and magnitude of residues in rotational crops;
- the nature and magnitude of residues in livestock commodities;
- the analytical methods for enforcement of the proposed MRLs.

As the basis for the MRL review, on 15 April 2020 EFSA initiated the collection of data for this active substance. In a first step, Member States and the UK\(^7\) were invited to submit by 15 May 2020 their Good Agricultural Practices (GAPs) that are authorised nationally, in a standardised way, in the format of specific GAP forms. In the framework of this consultation 19 Member States and the UK provided feedback on their national authorisations of pinoxaden. Based on the GAP data submitted, the designated RMS Austria was asked to identify the critical GAPs to be further considered in the assessment, in the

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\(^1\) Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

\(^2\) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32. Repealed by Regulation (EC) No 1107/2009.

\(^3\) Commission Implementing Regulation (EU) 2016/370 of 15 March 2016 approving the active substance pinoxaden, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, amending the Annex to Commission Implementing Regulation (EU) No 540/2011 and allowing the Member States to extend provisional authorisations granted for that active substance. OJ L 70, 16.3.2016, p. 7–11.

\(^4\) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

\(^5\) Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–86.

\(^6\) Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.

\(^7\) The United Kingdom withdrew from EU on 1 February 2020. In accordance with the Agreement on the Withdrawal of the UK from the EU, and with the established transition period, the EU requirements on data reporting also apply to the UK data collected until 31 December 2020.
format of a specific GAP overview file. Subsequently, in a second step, Member States and the UK were requested to provide residue data supporting the critical GAPs by 7 August 2020.

On the basis of all the data submitted by Member States, the UK and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked Austria to complete the PROFile and to prepare a supporting evaluation report. The PROFile and the supporting evaluation report, together with the Pesticide Residues Intake Model (PRIMO) calculations, were submitted to EFSA on 16 September 2020. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report.

Considering all the available information, and taking into account the MRLs established by the Codex Alimentarius Commission (CAC) (i.e. codex maximum residue limit; CXLs), EFSA prepared in December 2020 a draft reasoned opinion, which was circulated to Member States and EURLs for commenting via a written procedure. All comments received by 27 January 2021 were considered by EFSA during the finalisation of the reasoned opinion.

The evaluation report submitted by the RMS (Austria, 2020), taking into account also the information provided by Member States and the UK during the collection of data, and the EURLs report on analytical methods (EURLs, 2020) are considered as main supporting documents to this reasoned opinion and, thus, made publicly available.

In addition, further supporting documents to this reasoned opinion are the completeness check report (EFSA, 2020) and the Member States consultation report (EFSA, 2021). These reports are developed to address all issues raised in the course of the review, from the initial completeness check to the reasoned opinion. Furthermore, the exposure calculations for all crops reported in the framework of this review performed using the EFSA Pesticide Residues Intake Model (PRIMO) and the PROFile as well as the GAP overview file listing all authorised uses are key supporting documents and made publicly available as background documents to this reasoned opinion. A screenshot of the report sheet of the PRIMO is presented in Appendix C.

Terms of Reference

According to Article 12 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

- the inclusion of the active substance in Annex IV to the Regulation, when appropriate;
- the necessity of setting new MRLs for the active substance or deleting/modifying existing MRLs set out in Annex II or III of the Regulation;
- the inclusion of the recommended MRLs in Annex II or III to the Regulation;
- the setting of specific processing factors as referred to in Article 20(2) of the Regulation.

The active substance and its use pattern

Pinoxaden is the ISO common name for 8-(2,6-diethyl-p-tolyl)-1,2,4,5-tetrahydro-7-oxo-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-9-yl 2,2-dimethylpropionate (IUPAC).

The chemical structure of the active substance and its main metabolites are reported in Appendix F.

The EU MRLs for pinoxaden are established in Annexes IIIA of Regulation (EC) No 396/2005. CXLs for pinoxaden were also established by the CAC. There are no MRL changes occurred since the entry into force of the Regulation mentioned above.

For the purpose of this MRL review, all the uses of pinoxaden currently authorised within the EU as submitted by Member States and the UK during the GAP collection, have been reported by the RMS in the GAP overview file. The critical GAPs identified in the GAP overview file were then summarised in the PROFile and considered in the assessment. The details of the authorised critical GAPs for pinoxaden are given in Appendix A. The RMS did not report any use authorised in third countries that might have a significant impact on international trade.

Assessment

EFSA has based its assessment on the following documents:

- the PROFile submitted by the RMS;
- the PROFile prepared by EFSA;
- the evaluation report accompanying the PROFile (Austria, 2020);
the draft assessment report (DAR) and its addendum prepared under Council Directive 91/414/EEC (United Kingdom, 2005, 2013);
the conclusion on the peer review of the pesticide risk assessment of the active substance pinoxaden (EFSA, 2013);
the review report on active substance (European Commission, 2016);
the Joint Meeting on Pesticide residues (JMPR) Evaluation report (FAO, 2016);

The assessment is performed in accordance with the legal provisions of the uniform principles for evaluation and authorisation of plant protection products as set out in Commission Regulation (EU) No 546/2011 and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 1997a-g, 2000, 2010a,b, 2017; OECD, 2011, 2013).

More detailed information on the available data and on the conclusions derived by EFSA can be retrieved from the list of end points reported in Appendix B.

1. Residues in plants

1.1. Nature of residues and methods of analysis in plants

1.1.1. Nature of residues in primary crops

The metabolism of pinoxaden was investigated after foliar treatment in cereals (wheat) (United Kingdom, 2005, 2013) and assessed in the framework of the peer review (EFSA, 2013). In total, three studies were conducted with wheat: in one study, pinoxaden was radiolabelled in the pyrazole ring of the molecule; in the second study, it was radiolabelled in the phenyl ring; and in the third study, the radiolabelled positions were the phenyl and the oxadiazepine rings.

Parent pinoxaden was rapidly metabolised and it was not found in any sample at harvest. The major components identified in grain were metabolites M4 and M6, representing (together) up to 30% (0.07 mg eq./kg) of the total radioactive residues (TRRs), at harvest. However, 20-45% TRR (depending on the study and label position) in grain was not extracted with solvents. Subsequent acid hydrolysis of whole grain samples released nearly all remaining radioactivity, indicating that a significant portion was present as conjugated metabolite M4 (up to 50% TRR), and to a lesser extent, as conjugated M6 (up to 8%). Metabolite M4 was the major metabolite identified in forage (up to 30% TRR; 0.13 mg eq./kg) and straw (up to 37% TRR; 0.33 mg eq./kg) at harvest. A number of other metabolites were identified in grain, forage and straw, but they were not found at significant levels.

1.1.2. Nature of residues in rotational crops

Pinoxaden is authorised on cereals, which may be grown in rotation. According to the soil degradation studies performed in the framework of the peer review (EFSA, 2013), parent pinoxaden exhibits low persistence (DT90 less than 5 days) in soil. Under aerobic soil conditions, it forms its relevant soil metabolites M2 and M3. Both metabolites exhibit DT90 values exceeding 100 days, and therefore metabolism studies in rotational crops are required.

One confined rotational crop study with pinoxaden radiolabelled on the phenyl and oxadiazepine rings was available for this review (United Kingdom, 2005; EFSA, 2013). Pinoxaden was applied at a rate of 1 × 60.3 g a.s./ha (phenyl-labelled) and 1 × 65.5 g a.s./ha (oxadiazepine-labelled) onto bare soil. Lettuce (leafy vegetables) and radish (roots) crops were planted at nominal plant-back intervals (PBI) of 29 and 120 days after treatment (DAT). Spring wheat was drilled 29, 120 and 361 DAT and winter wheat was planted at 168 DAT.

Residues in the three planted crops declined over time. Total radioactive residues in radish (tops and roots, both labels) and lettuce (both labels) at PBI 120 were too low (≤ 0.001 mg eq./kg) to allow for further characterisation. In spring wheat, total residues in grain (both labels) were very low (≤ 0.007 mg eq./kg) at all PBIs and no further characterisation was performed in grain. Similarly, for forage and fodder of spring wheat at PBI 360 and forage and grain of winter wheat, further identification of residues was not performed.

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8 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
Parent pinoxaden was not found in any sample, and of the detected metabolites only M3 slightly exceeded 0.01 mg eq./kg (49% TRR) in wheat forage at the shortest plant back interval of 29 days. The peer review concluded that residues were not significant in rotational crops as a result of the representative uses. Since the authorised uses considered under this MRL review are the same as the representative ones, the same conclusion is applicable here.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of pinoxaden was investigated in the framework of the peer review (United Kingdom, 2013; EFSA, 2013). The study was conducted with radiolabelled pinoxaden on the phenyl ring and simulating representative hydrolytic conditions for pasteurisation (20 min at 90°C, pH 4), boiling/brewing/baking (60 min at 100°C, pH 5) and sterilisation (20 min at 120°C, pH 6). Parent pinoxaden was stable (86% of applied radioactivity (AR) still present at parent) to hydrolysis under standard conditions of pasteurisation. Under baking/brewing/boiling, it degraded slightly (parent 72% AR) to form metabolite M2 (20% AR). Degradation increased with temperature and pH: parent pinoxaden represented 54% of AR under sterilisation and metabolite M2 40% AR (see Appendix B.1.1. for more details). According to the metabolic pattern observed in primary crops (Section 1.1.1), significant residues of parent pinoxaden are not expected in the raw commodities, and thus the results of this study are considered as supportive to the assessment.

Specific studies to address the processing of the major metabolites identified in the metabolism studies (M4 and M6) are not available. In the EFSA conclusion, a case was made based on validation data of the analytical method using acid hydrolysis at 100°C for 60 min. It was deemed that M4 and M6 were stable under the standard hydrolysis conditions simulating food processing (EFSA, 2013). Additionally, EURLs indicated in its evaluation report (EURLs, 2020) that metabolites M4 and M6 were stable under typical hydrolysis conditions applied for the cleavage of conjugates and esters. Altogether, it is concluded that processing is not expected to have a significant impact on the composition of residues in plant matrices.

1.1.4. Methods of analysis in plants

In the framework of the peer review (United Kingdom 2005; EFSA, 2013), a single residue method based on liquid chromatography with tandem mass spectrometry (LC–MS/MS) involving a hydrolysis step for the determination of free and conjugated forms of metabolites M4 and M6 was validated for dry commodities (wheat and barley grain), high water content commodities (wheat and barley whole plant) and matrices difficult to analyse (wheat straw) with an limit of quantification (LOQ) of 0.01 mg/kg for each metabolite in dry commodities, and 0.02 mg/kg for each metabolite in high water content and cereal straw. For completeness, the method was also validated for M2 and M10. The independent laboratory validation (ILV) was available, but no confirmation method, which was identified as data gap in the EFSA conclusion (EFSA, 2013). To address this data gap, an update of the LC–MS/MS analytical method including a second transition was submitted under this review (Austria, 2020). The confirmation method was validated for the determination of free and conjugated forms of M4 and M6 in high water content (lettuce), high acid content (orange), high oil content (oilseed rape) and dry commodities (barley grain, lentils), as well as in matrices difficult to analyse (wheat straw), with LOQ of 0.01 mg/kg for each metabolite. EFSA considers that the data gap set in the conclusion for the confirmatory method is addressed.

The free forms of metabolites M4 and M6 can be determined by multiresidue QuEChERS based LC–MS/MS in high water content (lettuce), high acid content (orange), high oil content (rape seed) and dry commodities (barley grain) with an LOQ of 0.01 mg/kg for each metabolite (United Kingdom, 2013). At the time of the peer review, the ILV was not available (EFSA, 2013). An ILV of the QuEChERS method on high water content (lettuce) and dry commodities (wheat grain) has been submitted in the framework of this MRL review (Austria, 2020) and it is considered sufficient for the four main matrix groups.

1.1.5. Stability of residues in plants

The storage stability of metabolites M2, M4, M6 and M10 in wheat whole plant, grain and straw was investigated in the framework of the peer review (United Kingdom, 2013; EFSA, 2013).

In high water content, dry/high protein content commodities and no group (wheat straw), the available studies demonstrated the storage stability of metabolites M4 and M6 for a period of
28 months when stored at -18°C. The storage stability for M2 and M10 was the same as for M4 and M6 under the same conditions. This information on M2 and M10 is included here only for completeness. Additional storage stability studies are not needed for the current authorised uses.

1.1.6. Proposed residue definitions

The metabolism of pinoxaden was investigated in the cereal crop group only. Particular considerations for rotational crops are not needed, and degradation under hydrolytic conditions to form new compounds is not expected based on the evidence submitted (EFSA, 2013).

Free and conjugated forms of metabolites M4 and M6 were the predominant species identified in cereals and therefore, the peer review set the residue definition for risk assessment for cereals as sum of M4 and M6 (both free and conjugated), expressed as pinoxaden. The residue definition for risk assessment set in the EFSA conclusion is still valid for this MRL review.

For enforcement, the same residue definition as for risk assessment was provisionally set in the EFSA conclusion (EFSA, 2013). As the inclusion of conjugates for enforcement is not amenable for routine monitoring, two simpler proposals were considered: a) free forms of both M4 and M6, and b) free M6 alone. At the time of the peer review, residue trials analysing only free forms of metabolites M4 and M6 were not available. Hence, the peer review could not reach a final agreement (EFSA, 2013).

Residue trials analysing free forms of M4 and M6 have been submitted in the framework of this MRL review (Austria, 2020) and the appropriateness of the alternative residue definitions could be compared. When the sum of free and conjugated M4 and M6 was measured, residues in wheat and barley grain were above the LOQ in 41 out 43 trials (95% of positive findings) (see Appendix B.1.2.1 for more details), with M4 up to fivefold the levels of M6. In contrast, the sum of free forms of M4 and M6 was detected at levels > LOQ in only 3 out of the 16 trials (19% of positive findings) available for wheat grain (see Appendix B.1.2.1 for more details). Nonetheless, although the derived MRLs will not capture the conjugated metabolites and will be significantly lower, if the residue definition for enforcement is limited to free M4 and M6, this definition is still related to the residue definition for risk assessment.

Regarding free M6 alone, the peer review postulated that M6 does not readily form conjugates, and then it would be possible to measure it using analytical methods with or without hydrolysis step. However, the new data submitted showed that the presence of M6 as conjugated forms is not negligible. Furthermore, this residue definition is not readily linked to the residue definition for risk assessment, and therefore, EFSA concludes that free M6 alone is not a good marker for enforcement.

The discussion is then related to whether to include the conjugated forms of M4 and M6 in the residue definition. EFSA is of the opinion that to include them gives a more robust residue definition. However, to allow the use of multi-residue methods, the RMS Austria (Austria, 2020) proposed not to include the conjugates for enforcement. Two options for the enforcement residue definition are thus presented here for further consideration by risk managers: **RD-Mo option 1**: sum of M4 and M6 (both free and conjugated), expressed as pinoxaden; and **RD-Mo option 2**: sum of M4 and M6 (both free only), expressed as pinoxaden. Both options are restricted to cereals. It is also noted that the residue definition for enforcement set in Regulation (EC) No 396/2005 is pinoxaden.

A single-residue analytical method for the enforcement of the RD-Mo option 1 at the combined LOQ of 0.03 mg/kg in dry commodities and 0.05 mg/kg in high water content commodities is available (EFSA, 2013; Austria, 2020). A multi-residue analytical method (QuEChERS based) for the enforcement of the RD-Mo option 2 at the combined LOQ of 0.03 mg/kg in all four main plant matrices is available (EFSA, 2013; Austria, 2020). According to the EURs, the combined LOQ of 0.03 mg/kg is achievable for RD-Mo option 2 by using a QuEChERS based method in routine analyses (EURs, 2020). During Mss consultation, EURs proposed that the combined LOQ of 0.03 mg/kg is also achievable for RD-Mo option 1 (EFSA, 2021). EURs informed EFSA about the commercial availability of the analytical standard for parent pinoxaden. However, metabolites M4 and M6 are not commercially available (EFSA, 2021).

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

To assess the magnitude of pinoxaden residues resulting from the reported GAPs, EFSA considered all residue trials reported by the RMS in its evaluation report (Austria, 2020) as well as the residue trials evaluated in the framework of the peer review (EFSA, 2013). All residue trial samples considered...
in this framework were stored in compliance with the conditions for which storage stability of residues was demonstrated. Decline of residues during storage of the trial samples is therefore not expected.

The number of residue trials and extrapolations were evaluated in accordance with the European guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (European Commission, 2017).

As stated in Section 1.1.6, two options for the residue definition for enforcement are proposed, namely sum of M4 and M6 (both free and conjugated), expressed as pinoxaden (RD-Mo option 1) and sum of M4 and M6 (both free only), expressed as pinoxaden (RD-Mo option 2). The two different data sets supporting each option are presented in two separate tables, i.e. Appendices B.1.2.1 and B.1.2.2, respectively.

RD-Mo option 1: for all crops under evaluation, available residue trials were sufficient to derive MRL and risk assessment values, noting that residue data from wheat and barley trials were combined in each climate zone to derive a more robust MRL (EFSA, 2015). For wheat forage (feed item), the overdosed trials available were tentatively used for dietary burden calculation purposes. As MRLs for commodities of animal origin are proposed at the LOQ, GAP compliant trials for wheat forage are only desirable. Risk assessment values of this data set were used for the dietary burden and exposure assessment calculations.

RD-Mo option 2: available residue trials on wheat, and, by extrapolation to barley, were sufficient to derive MRLs for all crops under evaluation. Regarding risk assessment values, it is noted that residue trials analysing simultaneously for enforcement and risk assessment residue definitions were not available. EFSA acknowledges that this is a data requirement needed to derive robust conversion factors from enforcement to risk assessment; however, in this case the risk assessment could be finalised using the input values derived in Table B.1.2.1. for dietary burden and consumer exposure assessment, and thus trials analysing simultaneously for enforcement and risk assessment residue definitions are considered only desirable.

1.2.2. Magnitude of residues in rotational crops

There were no studies investigating the magnitude of residues in rotational crops available for this review. Nevertheless, based on the confined rotational crop study and considering the fact that pinoxaden was applied to a bare soil (interception of active substance by the plants is expected in practice), it can be concluded that pinoxaden residue levels in rotational commodities are not expected to exceed 0.01 mg/kg, provided that pinoxaden is applied in compliance with the GAPs reported in Appendix A. At higher application rates, consideration might be given to the levels of the toxicologically relevant metabolite M3 that was the major metabolite in the confined rotational crop studies.

1.2.3. Magnitude of residues in processed commodities

The effect of industrial processing and/or household preparation on the levels of metabolites M4 and M6 was assessed on studies conducted on barley and wheat (United Kingdom, 2013; EFSA, 2013). An overview of all available processing studies is available in Appendix B.1.2.4.

In the studies, raw and processed commodities were analysed using methods involving a hydrolysis step and thus determining total (free and conjugated) fractions of the analytes. In the EFSA conclusion, processing factors were summarised separately for metabolites M4 and M6. Processing factors have been recalculated in this review according to the enforcement residue definition option 1: sum of M4 and M6 (both free and conjugated), expressed as pinoxaden. Conversion factors from enforcement to risk assessment in processed commodities are not needed for option 1 since residue definitions for monitoring and risk assessment are the same. Robust processing factors (fully supported by data) could be derived for barley brewing malt, beer, pot/pearl and dry brewer’s grain, and wheat whole meal flour, whole meal bread, white flour, dry milled by-products and dry distiller’s grain. Processing factors according to residue definition RD-Mo option 2 could not be calculated as results for the free fractions of the metabolites were not available. However, since residues in the raw commodities according to this residue definition were below 0.1 mg/kg (see Section B.1.2.2), processing studies are in principle not required for option 2.

Further processing studies are not required as they are not expected to affect the outcome of the risk assessment. However, if more robust processing factors were to be required by risk managers, in particular for enforcement purposes, additional processing studies would be needed.
1.2.4. Proposed MRLs

The available data are considered sufficient to derive two sets of MRL proposals according to the two options for the residue definition for enforcement, for all commodities under evaluation. Residue trials analysing simultaneously for monitoring option 2 and risk assessment residue definitions were not available; however, since only one risk assessment residue definition is proposed in this review, the input values for dietary burden and consumer exposure assessment derived from the residue definition option 1 cover both options. Nonetheless, residue trials analysing simultaneously for enforcement and risk assessment residue definitions are still desirable to derive robust conversion factors from enforcement to risk assessment for option 2.

Tentative MRLs were also derived for feed crops (wheat forage and wheat, rye and barley straw) in view of the future need to set MRLs in feed items, except for wheat forage according to RD-Mo option 2.

2. Residues in livestock

Pinoxaden is authorised for use on wheat, barley and rye that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance (OECD, 2013), which has now also been agreed upon at European level. The input values for all relevant commodities are summarised in Appendix D.1. The dietary burdens calculated for all groups of livestock were found to exceed the trigger value of 0.1 mg/kg dry matter (DM). Behaviour of residues was therefore assessed in all commodities of animal origin.

As abovementioned (see Section 1.2.1), the input values derived in Table B.1.2.1 were used for the dietary burden calculation. It is highlighted that for wheat forage, the residue data available were coming from overdosed trials. The animal intake of pinoxaden residues via this commodity is thus overestimated. Since wheat forage was found to be the major contributor in all diets, except in sheep (lamb), the calculated dietary burden represents a worst-case scenario.

2.1. Nature of residues and methods of analysis in livestock

The metabolism of pinoxaden residues in livestock was investigated in lactating goats and laying hens at dose rates covering the maximum dietary burdens calculated in this review (United Kingdom, 2005). These studies were assessed in the framework of the peer review (EFSA, 2013). In one of the studies conducted with lactating goat, animals were dosed with metabolite M4 radiolabelled in the pyrazol ring of the molecule. In the other study on goat, as well as in the study on laying hens, animals were dosed with parent pinoxaden radiolabelled in the phenyl ring of the molecule.

From the residue trials supporting the authorised uses, it is unlikely that animals will be exposed to significant levels of parent pinoxaden through the consumption of barley, rye or wheat. Animals are however potentially exposed to metabolites M4 and M6. Consequently, the metabolism studies on goat and hen conducted with parent pinoxaden are less relevant and described here as supportive to the assessment. Parent pinoxaden was not found in any tissues, milk or eggs. Metabolite M2 was the main component of the radioactive residues found in goat tissues (up to 90% TRR, 2.67 mg eq./kg in kidney) and milk (88% TRR, 0.013 mg eq./kg). Metabolite M4 was only a minor metabolite in goat tissues (up to 1.6% TRR) and milk (1.7%). In hens, M4 was the major residue in fat (30% TRR, 0.05 mg eq./kg), meat (44% TRR, 0.026 mg eq./kg) and egg yolk (24% TRR, < 0.01 mg eq./kg). It was also detected at significant levels in liver. Metabolite M6 was also found in tissues and egg yolk, being the predominant residue in liver (45% TRR, 0.28 mg eq./kg). The main components identified in egg white were metabolites M2 (46%, < 0.01 mg eq./kg) and M4 (27% TRR, < 0.01 mg eq./kg).

In the metabolism study on goat dosed with radiolabelled M4, unchanged M4 was the major residue identified in liver and kidney (up to 55% TRR, 0.026 mg eq./kg) and in urine and faeces (90–98% TRR), indicating that metabolism of M4 was very limited. Total radioactive residues in milk, fat and muscle were below 0.01 mg eq./kg despite the exaggerated dose administered, and thus no further characterisation was carried out in these tissues.

Metabolite M4 was the dominant residue in the goat study conducted with radiolabelled M4 (the most relevant study) and there is no evidence from the studies on ruminants that M4 was further metabolised to form M6. Metabolism of M6 was not separately studied in ruminants but based on the similarity of both M6 and M4 in terms of molecule structure and polarity, a similar behaviour of M6 compared to M4 can be expected (EFSA, 2013). For poultry, metabolism studies with radiolabelled M4 and M6 are not available but based on the results of the available study with parent pinoxaden, M4 and M6 are the most relevant components of the residue.
The peer review did not set residue definitions for livestock but indicated that M4 would be the most suitable component for ruminant matrices. From the residue trials in plants evaluated in this review, it is expected that dietary exposure of animals to M6 residues would be approximately from two to five times lower than that to M4. No exposure to M2 is expected, as pinoxaden is not present in the feed items, and M4 is not metabolised further to form M2. Bearing this in mind, the overdose rate of the animal metabolism studies compared to the maximum dietary burdens calculated in this review, and the results of the feeding studies (see below), the residue definitions for enforcement and risk assessment in livestock can be proposed as M4 (free and conjugated), expressed as pinoxaden. The residue is not fat soluble. Since residues are expected to remain far below the LOQ for enforcement, this residue definition could be simplified to M4 free only.

It is stressed that if additional uses are authorised in the future, the inclusion of metabolite M6 in the residue definition for risk assessment might be reconsidered, mostly for poultry.

An analytical method, involving a hydrolysis step, for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in milk, and 0.02 mg/kg in animal tissues and eggs is available (EFSA, 2013). A confirmatory method is still required (data gap). In case of future needs, the method could also be applied to metabolite M6 at the same LOQs, in the same matrices (confirmation also missing for M6). According to the EURLs, metabolite M4 (free only) can be monitored in milk and in liver at the LOQ of 0.01 mg/kg using a QuEChERS based method in routine analysis. Judging from the analytical behaviour of M4, an LOQ of 0.01 mg/kg is supposed to be achievable also for the other main groups of animal products (egg, muscle, kidney, fat) (EURLs, 2020). It is reiterated that the analytical standard of metabolite M4 is not commercially available.

The storage stability of metabolites M4 (and M6) was demonstrated for a period of 3 months at –20°C in muscle, liver, milk and eggs (United Kingdom, 2005, 2013; EFSA, 2013).

2.2. Magnitude of residues in livestock

Although from the lactating goats and laying hens metabolism studies (performed at 7N and 255N rates compared to the maximum dietary burdens calculated in this review), it could be possible to conclude that residues in livestock commodities would remain below the LOQs for enforcement, some uncertainty in terms of residue levels remains as the metabolism of M4 and M6 was not investigated in poultry and M6 in ruminants. Therefore, the results of the feeding studies performed with dairy cows and laying hens and submitted in the framework of the peer review (United Kingdom, 2013) are presented here and considered in the assessment. In these studies, metabolite M4 was administered using three different dosing levels at 1 (1X), 3 (9X) and 10 (28X) mg/kg feed for dairy cows and 0.5 (1X), 1.5 (3X) and 5 (10X) mg/kg feed for laying hens. In both studies, dosing levels were equivalent to 0.04, 0.12 and 0.4 mg/kg body weight (bw) per day. Samples were analysed for residues of free and conjugated M4 and M6. Samples of the cow study were stored in compliance with the conditions for which storage stability was demonstrated. Poultry tissues and eggs samples were stored for up to 99 days, slightly higher than the maximum demonstrated storage period (3 months). In both cases, decline of residues during storage of the trial samples is not expected.

No residues of M4 or M6 above the LOQ of 0.01 mg/kg for milk, and 0.02 mg/kg for animal tissues and eggs were found in any sample from the highest dosing level of 0.4 mg/kg bw per day. Consequently, samples from the lower dose treatment groups were not analysed in the cow or hen study, and it is not required. Since extrapolation from ruminants to pigs is acceptable, results of the livestock feeding study on ruminants can be applied also to pigs.

The results of the feeding studies confirm the findings of the metabolism, and MRLs and risk assessment values are proposed at the enforcement LOQs for all livestock commodities. Considering that a confirmatory method is still required for enforcement purposes, MRLs in livestock are considered tentative.

3. Consumer risk assessment

In the framework of this review, only the uses of pinoxaden reported by the RMS in Appendix A were considered; however, the use of pinoxaden was previously also assessed by the JMPR (FAO, 2016). The CXLs, resulting from this assessment by JMPR and adopted by the CAC, are now international recommendations that need to be considered by European risk managers when establishing MRLs. For animals, the EU and JMPR residue definitions are the same. For plants however, the EU RD-Mo option 1 includes also metabolite M6 (free and conjugated), which was not
reviewed by JMPR. In the JMPR evaluation (FAO, 2016), it is stated that metabolite M4 (free and conjugated) represented the majority of the residues in primary crops (up to sevenfold the residues of metabolite M6 in the field trials) and thus the contribution of M6 was disregarded by JMPR. Since as abovementioned (see Sections 1.1.1 and 1.1.6), metabolite M4 (free and conjugated) was the major component of the residue in the metabolism studies and in the field trials evaluated in this assessment, EU residue definitions monitoring option 1 and risk assessment may be considered comparable to JMPR enforcement and risk assessment residue definitions. EU RD-Mo option 2 includes only the free forms of M4 and M6 and thus it is not considered compatible with CXL.

To include the CXLs in the calculations of the consumer exposure, CXLs were compared with the EU MRL proposals for option 1 in compliance with Appendix E and all data relevant to the consumer exposure assessment have been collected from JMPR evaluations. CXLs for plants and animals were found to be covered by the MRLs derived from EU uses, and in consequence, consumer risk assessments with and without consideration of the existing CXLs resulted in the same estimated exposure.

The exposure calculation is considered to cover also option 2 as a single residue definition for risk assessment is proposed in this review.

Chronic and acute exposure calculations were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018, 2019). Input values were derived according to the internationally agreed methodologies (FAO, 2009). All input values included in the exposure calculations are summarised in Appendix D. The exposure values calculated were compared with the toxicological reference values for pinoxaden, derived by the European Commission under Reg. (EU) 2016/370. The highest chronic exposure was calculated for Danish (DK) child, representing 1% of the acceptable daily intake (ADI), and the highest acute exposure was calculated for wheat, representing 1% of the acute reference dose (ARfD). Based on these calculations, EFSA concludes that EU-MRLs and CXLs for the uses assessed in this review are unlikely to pose a risk to consumer’s health.

Conclusions

The metabolism of pinoxaden in plants was investigated in primary and rotational crops and the processing is not expected to modify the nature of residues. According to the results of the metabolism studies, the residue definition for risk assessment can be proposed as sum of M4 and M6 (both free and conjugated), expressed as pinoxaden. For enforcement, in view of the available information on residue trials and analytical methods, two residue definitions are presented for further consideration by risk managers: sum of M4 and M6 (both free and conjugated), expressed as pinoxaden (option 1); and sum of M4 and M6 (both free only), expressed as pinoxaden (option 2). These residue definitions are restricted to cereals only. A sufficiently validated single-residue method is available for the enforcement of the proposed residue definition option 1 at the combined LOQ of 0.03 mg/kg in dry commodities and 0.05 mg/kg in high water content commodities. For the option 2, the combined LOQ of 0.03 mg/kg in all four main plant matrices was demonstrated to be achievable by multi-residue methods. According to the EURLs, the combined LOQ of 0.03 mg/kg is achievable for RD-Mo options 1 and 2 in routine analyses. Analytical standards are commercially available for parent pinoxaden, but not for metabolites M4 and M6.

The available data are considered sufficient to derive two sets of MRL proposals according to the two options for the residue definition for enforcement, for all commodities under evaluation. Residue trials analysing simultaneously for monitoring option 2 and risk assessment residue definitions were not available; however, since only one risk assessment residue definition is proposed in this review, the input values for dietary burden and consumer exposure assessment derived from the residue definition option 1 cover both options. Nonetheless, residue trials analysing simultaneously for enforcement and risk assessment residue definitions are still desirable to derive robust conversion factors from enforcement to risk assessment for option 2.

Pinoxaden is authorised for use on crops that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. The dietary burdens calculated for all groups of livestock were found to exceed the trigger value of 0.1 mg/kg DM. Behaviour of residues was therefore assessed in all commodities of animal origin.

The metabolism of pinoxaden residues in livestock was investigated in lactating goats and laying hens at dose rate covering the maximum dietary burdens calculated in this review. According to the results of these studies, the residue definition for enforcement and risk assessment in livestock commodities was proposed as M4 (free and conjugated), expressed as pinoxaden. An analytical
method, involving a hydrolysis step, for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in milk, and 0.02 mg/kg in animal tissues and eggs is available. According to the EURLs metabolite M4 (free only) can be monitored in milk and in liver at the LOQ of 0.01 mg/kg using a QuEChERS based method in routine analysis. Judging from the analytical behaviour of M4, an LOQ of 0.01 mg/kg is supposed to be achievable also for the other main groups of animal products (egg, muscle, kidney, fat).

Livestock feeding studies on lactating cows and laying hens were used to derive MRL and risk assessment values in animal tissues, milk and eggs. Since extrapolation from ruminants to pigs is acceptable, results of the livestock feeding study on ruminants were relied upon to derive the MRL and risk assessment values in pigs. Considering that a confirmatory method is still required for enforcement purposes, MRLs in livestock are considered tentative.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The highest chronic exposure represented 1% of the ADI (Danish child) and the highest acute exposure amounted to 1% of the ARfD (wheat). Apart from the MRLs evaluated in the framework of this review, internationally recommended CXLs have also been established for pinoxaden. CXLs for plants and animals were found to be covered by the MRLs derived from EU uses, and in consequence, consumer risk assessments with and without consideration of the existing CXLs resulted in the same estimated exposure.

Recommendations

MRL recommendations for option 1 (sum of M4 and M6 (both free and conjugated), expressed as pinoxaden) were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 1). All MRL values listed as ‘Recommended’ in the table are sufficiently supported by data and are therefore proposed for inclusion in Annex II to the Regulation. The remaining MRL values listed in the table are not recommended for inclusion in Annex II because they require further consideration by risk managers (see Table 1 footnotes for details). In particular, all tentative MRLs need to be confirmed by the following data:

1) Confirmatory method for all livestock commodities. Nonetheless, risk managers may decide to simplify the residue definition for enforcement to M4 free only. In this case, they may consider requesting a fully validated method determining only free M4.

Minor deficiencies were also identified in the assessment, but these deficiencies are not expected to impact either on the validity of the MRLs derived or on the national authorisations. The following data are therefore considered desirable but not essential:

- GAP compliant residue trials on wheat forage supporting the southern use (relevant if MRLs are set for feed items).

In order to assist risk managers in the decision-making process, EFSA has considered an alternative list of MRLs for plants commodities according to a simplified residue definition including only free forms of metabolites M4 and M6 (RD-MO option 2). The MRLs for plants according to this option are also considered as sufficiently supported by data (see Table B.1.2.2 for the MRLs values). However, if risk managers decide to go for this option, the following points need to be taken into account:

- A minimum of eight residue trials analysing simultaneously for enforcement and risk assessment residue definitions supporting the authorised northern and southern uses on wheat, rye and barley are desirable in order to derive CFs from enforcement to risk assessment.
- Residue trials on wheat forage analysing simultaneously for enforcement and risk assessment residue definitions (relevant for the dietary burden calculations) are desirable.
- Specific validation details of the QuEChERS method for straw are desirable.
- EU-MRLs derived according to this second option are not considered compatible with CXLs.

Finally, EFSA underlines that according to EURLs, the analytical standard of metabolites M4 and M6 are not commercially available.
### Table 1: Summary table

| Code number | Commodity | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review MRL (mg/kg) | Comment |
|-------------|-----------|------------------------|----------------------|----------------------------------|---------|
| **Enforcement residue definitions (existing): pinoxaden** | | | | | |
| 500010 | Barley grain | 1 | 0.7 | 0.7 | Recommended<sup>(a)</sup> |
| 500070 | Rye grain | 1 | – | 0.7 | Recommended<sup>(b)</sup> |
| 500090 | Wheat grain | 1 | 0.7 | 0.7 | Recommended<sup>(a)</sup> |
| **Enforcement residue definition (plants, proposed option 1):** sum of M4 and M6 (both free and conjugated), expressed as pinoxaden | | | | | |
| 500010 | Barley grain | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 500070 | Rye grain | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 500090 | Wheat grain | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| **Enforcement residue definition (animals, proposed):** M4 (free and conjugated), expressed as pinoxaden | | | | | |
| 1011010 | Swine meat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1011020 | Swine fat (free of lean meat) | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1011030 | Swine liver | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1011040 | Swine kidney | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1012010 | Bovine meat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1012020 | Bovine fat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1012030 | Bovine liver | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1012040 | Bovine kidney | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1013010 | Sheep meat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1013020 | Sheep fat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1013030 | Sheep liver | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1013040 | Sheep kidney | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1014010 | Goat meat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1014020 | Goat fat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1014030 | Goat liver | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1014040 | Goat kidney | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1015010 | Horse meat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1015020 | Horse fat | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1015030 | Horse liver | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1015040 | Horse kidney | – | – | 0.02* | Further consideration needed<sup>(c)</sup> |
| 1016010 | Poultry meat | – | 0.02* | 0.02* | Further consideration needed<sup>(d)</sup> |
| 1016020 | Poultry fat | – | 0.02* | 0.02* | Further consideration needed<sup>(d)</sup> |

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**Enforcement residue definitions (existing):** pinoxaden

**Enforcement residue definition (plants, proposed option 1):** sum of M4 and M6 (both free and conjugated), expressed as pinoxaden

**Enforcement residue definition (animals, proposed):** M4 (free and conjugated), expressed as pinoxaden

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<sup>(a)</sup> Further consideration needed

<sup>(b)</sup> Further consideration needed

<sup>(c)</sup> Further consideration needed

<sup>(d)</sup> Further consideration needed
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### Code number Commodity Existing EU MRL (mg/kg) Existing CXL (mg/kg) Outcome of the review MRL (mg/kg) Comment

| Code number | Commodity            | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review | MRL (mg/kg) | Comment |
|-------------|----------------------|------------------------|----------------------|-----------------------|-------------|---------|
| 1016030     | Poultry liver        | –                      | 0.02*                | Further consideration needed | 0.02*       | (d)     |
|             |                      |                        |                      |                       |             |         |
| 1020010     | Cattle milk          | –                      | –                    | Further consideration needed | 0.01*       | (c)     |
|             |                      |                        |                      |                       |             |         |
| 1020020     | Sheep milk           | –                      | –                    | Further consideration needed | 0.01*       | (c)     |
|             |                      |                        |                      |                       |             |         |
| 1020030     | Goat milk            | –                      | –                    | Further consideration needed | 0.01*       | (c)     |
|             |                      |                        |                      |                       |             |         |
| 1020040     | Horse milk           | –                      | –                    | Further consideration needed | 0.01*       | (c)     |
|             |                      |                        |                      |                       |             |         |
| 1030000     | Birds’ eggs          | See Reg. (EC) No 839/2008 | 0.02*                | Further consideration needed | 0.02*       | (d)     |

MRL: maximum residue level; CXL: codex maximum residue limit.

*: Indicates that the MRL is set at the limit of quantification.

(a): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; existing CXL is covered by the recommended MRL (combination H-III in Appendix E).

(b): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination H-I in Appendix E).

(c): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified (assuming the existing residue definition); no CXL is available (combination F-I in Appendix E).

(d): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified (assuming the existing residue definition); existing CXL is covered by the tentative MRL (combination F-III in Appendix E).

(e): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).
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**Abbreviations**

a.i. active ingredient
a.s. active substance
ADI acceptable daily intake
AR applied radioactivity
ARfD acute reference dose
BBCH growth stages of mono- and dicotyledonous plants
bw body weight
CAC Codex Alimentarius Commission
CF conversion factor for enforcement residue definition to risk assessment residue definition
CXL codex maximum residue limit
DAR draft assessment report
DAT    days after treatment
DB    dietary burden
DM    dry matter
DT$_{90}$ period required for 90% dissipation (define method of estimation)
EC    emulsifiable concentrate
EMS    evaluating Member State
eq    residue expressed as a.s. equivalent
EURLs European Union Reference Laboratories for Pesticide Residues (former CRLs)
FAO    Food and Agriculture Organization of the United Nations
GAP    Good Agricultural Practice
HR    highest residue
IEDI    international estimated daily intake
IESTI    international estimated short-term intake
InChIKey    International Chemical Identifier Key
ILV    independent laboratory validation
ISO    International Organisation for Standardization
IUPAC    International Union of Pure and Applied Chemistry
K$_{ow}$ n-Octanol/Water Partition Coefficient
LC-MS/MS liquid chromatography with tandem mass spectrometry
LOQ    limit of quantification
Mo    monitoring
MRL    maximum residue level
MS    Member States
NEDI    national estimated daily intake
NESTI    national estimated short-term intake
NTMDI    national theoretical maximum daily intake
OECD    Organisation for Economic Co-operation and Development
PBI    plant-back interval
PF    processing factor
PHI    preharvest interval
PRIMo (EFSA) Pesticide Residues Intake Model
PROFile (EFSA) Pesticide Residues Overview File
QuEChERS Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RA    risk assessment
RAC    raw agricultural commodity
RD    residue definition
RMS    rapporteur Member State
SANCO    Directorate-General for Health and Consumers
SEU    southern European Union
SMILES simplified molecular-input line-entry system
STMR    supervised trials median residue
TMDI    theoretical maximum daily intake
TRR    total radioactive residue
WHO    World Health Organization

Review of the existing MRLs for pinoxaden
Appendix A – Summary of authorised uses considered for the review of MRLs

### A.1. Authorised outdoor uses in northern EU

| Crop and/or situation | MS or country | F or G or I(a) | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)(d) | Remarks |
|-----------------------|--------------|----------------|------------------------------------|-------------|----------------|---------------------------------|-------------|---------|
| Barley                | NL, UK, AT, FI, DE, FR, LT, PL | F | Grass weeds | EC | 50 g/L Foliar treatment – spraying | 27–39 | 1–1 | – | 60 g a.i./ha | n.a. | FR: PHI of 60 days |
| Rye                   | NL, AT, FI, DE, FR, LT | F | Grass weeds | EC | 50 g/L Foliar treatment – spraying | 27–39 | 1–1 | – | 60 g a.i./ha | n.a. | FR: PHI of 60 days |
| Wheat                 | NL, EE, AT, FI, DE, LT, PL | F | Grass weeds | EC | 50 g/L Foliar treatment – spraying | 27–39 | 1–1 | – | 60 g a.i./ha | n.a. | |

MRL: maximum residue level; MS: Member State; EC: emulsifiable concentrate; a.s.: active substance; a.i.: active ingredient.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.
### A.2. Authorised outdoor uses in southern EU

| Crop and/or situation | MS or country | F G or I<sup>(a)</sup> | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)<sup>(d)</sup> | Remarks |
|-----------------------|---------------|------------------------|------------------------------------|-------------|----------------|-------------------------------|-----------------|---------|
| Barley                | ES, FR        | F                      | Grass weeds                        | EC          | 50 g/L        | Foliar treatment – spraying   | 60 g a.i./ha     | FR: PHI of 60 days |
| Rye                   | ES            | F                      | Grass weeds                        | EC          | 50 g/L        | Foliar treatment – spraying   | 60 g a.i./ha     | n.a.    |
| Wheat                 | ES            | F                      | Grass weeds                        | EC          | 60 g/L        | Foliar treatment – spraying   | 60 g a.i./ha     | n.a.    |
| Wheat (for forage)    | HR            | F                      | Grass weeds                        | EC          | 50 g/L        | Foliar treatment – spraying   | 40 g a.i./ha     | 1       |

**Remarks:**
- MRL: maximum residue level; MS: Member State; EC: emulsifiable concentrate; a.s.: active substance; a.i.: active ingredient.
- (a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
- (b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.
- (c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
- (d): PHI: minimum preharvest interval.
Appendix B – List of end points

B.1. Residues in plants

B.1.1. Nature of residues and methods of analysis in plants

B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

| Primary crops (available studies) | Crop groups | Crop(s)                             | Application(s) | Sampling (DAT) | Comment/Source                                                                 |
|----------------------------------|-------------|-------------------------------------|----------------|----------------|--------------------------------------------------------------------------------|
| Cereals/grass                    | Wheat (winter and spring) | Foliar: 1 × 68.5 g a.s./ha BBCH 13  | 0, 14, 42, 209, 264 | Radiolabelled active substance: $^{14}$C-pyrazol pinoxaden (EFSA, 2013)      |
|                                  |             | Foliar: 1 × 64 g a.s./ha BBCH 49    | 0, 7, 14, 28, 55 | $^{14}$C-phenyl pinoxaden (EFSA, 2013)                                    |
|                                  |             | Foliar: 1 × 62 g a.s./ha             | 0, 14, 670, 7, 14, 28, 67 | $^{14}$C-phenyl pinoxaden $^{14}$C-oxadiazepine pinoxaden (EFSA, 2013) |
|                                  |             | Foliar: 1 × 66 g a.s./ha             |                  |                  |                                                                                  |
|                                  |             | BBCH 37-39 (both applications)       |                  |                  |                                                                                  |

| Rotational crops (available studies) | Crop groups | Crop(s)                             | Application(s) | PBI (DAT) | Comment/Source                                                                 |
|--------------------------------------|-------------|-------------------------------------|----------------|-----------|--------------------------------------------------------------------------------|
| Root/tuber crops                     | radish      | Bare soil: 1 × 60.3 g a.s./ha Bare soil: 1 × 65.5 g a.s./ha | 30, 120, 29, 120 | $^{14}$C-phenyl pinoxaden $^{14}$C-oxadiazepine pinoxaden (EFSA, 2013) |
| Leafy crops                          | Lettuce     | Bare soil: 1 × 60.3 g a.s./ha Bare soil: 1 × 65.5 g a.s./ha | 30, 120, 29, 120 | $^{14}$C-phenyl pinoxaden $^{14}$C-oxadiazepine pinoxaden (EFSA, 2013) |
| Cereal (small grain)                 | Spring wheat| Bare soil: 1 × 60.3 g a.s./ha Bare soil: 1 × 65.5 g a.s./ha | 30, 120, 36529, 120, 361 | $^{14}$C-phenyl pinoxaden $^{14}$C-oxadiazepine pinoxaden (EFSA, 2013) |
|                                    | Winter wheat| Bare soil: 1 × 60.3 g a.s./ha Bare soil: 1 × 65.5 g a.s./ha | 177168 | $^{14}$C-phenyl pinoxaden $^{14}$C-oxadiazepine pinoxaden (EFSA, 2013) |
### Processed commodities (hydrolysis study)

| Conditions                              | Stable? | Comment/Source                                      |
|-----------------------------------------|---------|-----------------------------------------------------|
| Parent pinoxaden                        |         |                                                     |
| Pasteurisation (20 min, 90°C, pH 4)     | Yes     | Pinoxaden (86.3%), M2 (5.3%) (EFSA, 2013)           |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | Yes/partially | Pinoxaden (72.3%), M2 (20.2%) (EFSA, 2013)          |
| Sterilisation (20 min, 120°C, pH 6)     | No      | Pinoxaden (53.5%), M2 (39.7) (EFSA, 2013)           |
| Metabolites M4 and M6                   |         |                                                     |
| Degradation under hydrolytic conditions to form new compounds is not expected based on the evidence submitted (EFSA, 2013). |         |                                                     |
## Review of the existing MRLs for pinoxaden

### Can a general residue definition be proposed for primary crops?

| No | Metabolism only investigated in cereal crop group |
|----|-----------------------------------------------|

### Rotational crop and primary crop metabolism similar?

| Yes | Residues are not significant in rotational crops for the current authorised uses, and the residue definition for plants does not require a particular consideration for rotational crops. At higher application rates, consideration might be given to the toxicologically relevant metabolite M3 that was the major metabolite in the confined rotational crop studies. |
|----|------------------------------------------------|

### Residue pattern in processed commodities similar to residue pattern in raw commodities?

| Yes | Degradation under hydrolytic conditions to form new compounds is not expected based on the evidence submitted (EFSA, 2013). |
|----|------------------------------------------------|

### Plant residue definition for monitoring (RD-Mo)

Cereal crop group (option 1): sum of M4 and M6 (both free and conjugated), expressed as pinoxaden

Cereal crop group (option 2): sum of M4 and M6 (both free only), expressed as pinoxaden

### Plant residue definition for risk assessment (RD-RA)

Cereal crop group: sum of M4 and M6 (both free and conjugated), expressed as pinoxaden

### Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)

**Free and conjugated forms** of metabolites M4 and M6 (EFSA, 2013; Austria, 2020):

- Single residue method LC–MS/MS
- LOQ = 0.01 mg/kg, each metabolite, in dry commodities, and 0.02 mg/kg, each metabolite, in high water content commodities and cereal straw.
- Combined LOQ = 0.03 mg/kg for sum of M4 and M6 in dry commodities and 0.05 mg/kg for sum of M4 and M6 in high water content commodities and cereal straw.
- Confirmation method (LC-MS/MS, 2 MRM transitions monitored) for M4 and M6 available in four main matrices and cereal straw.
- ILV (LC–MS/MS) available for M4 and M6 in high water content and dry commodities.

**Free forms** of metabolites M4 and M6 (EFSA, 2013; Austria, 2020; EURLs, 2020):

- Multiresidue QuEChERS (LC–MS/MS)
- LOQ = 0.01 mg/kg, each metabolite, in high water content, high acid content, high oil content and dry commodities.
- Confirmation by monitoring 1 additional MRM transition
- ILV available for high water content and dry commodities (sufficient for four main matrices).
- No specific validation for straw (desirable).
- Combined LOQ = 0.03 mg/kg for sum of M4 and M6 in high water content, high acid content, high oil content and dry commodities in routine analysis.

**Note:** a.s.: active substance; DAT: days after treatment; PBI: plant-back interval; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.
### B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category     | Commodity          | T (°C) | Stability period | Compounds covered | Comment/Source                  |
|-----------------------------------|--------------|--------------------|--------|-----------------|-------------------|--------------------------------|
|                                   | High water content | Wheat whole plant | –18    | 28 Months       | Metabolites M4 and M6 | (EFSA, 2013)                   |
|                                   | High oil content     | –                  | –      | –               | –                 | Not available and not required. |
|                                   | High protein content | Wheat grain      | –18    | 28 Months       | Metabolites M4 and M6 | (EFSA, 2013)                   |
|                                   | High starch content   | –                  | –      | –               | –                 | Not available and not required. |
|                                   | High acid content     | –                  | –      | –               | –                 | Not available and not required. |
|                                   | Processed products    | –                  | –      | –               | –                 | Not available and not required. |
|                                   | Others                | Wheat straw       | –18    | 28 Months       | Metabolites M4 and M6 | (EFSA, 2013)                   |
### B.1.2. Magnitude of residues in plants

#### B.1.2.1. Summary of residues data from the supervised residue trials – Primary crops (RD-Mo option 1)

| Commodity       | Region/Indoor(a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source                                                                 |
|-----------------|------------------|-----------------------------------------------------------------|--------------------------------------------------------------------------------|
| **RD-Mo option 1:** sum of M4 and M6 (both free and conjugated), expressed as pinoxaden | | Combined data set on residue trials on wheat (10) and barley (12) compliant with GAP. Eleven trials were performed with two instead of one application, but this is deemed acceptable as residues in grain were driven by the last application (EFSA, 2013; Austria, 2020). MRL\_OECD = 0.23 | |
| Wheat grains    | NEU              | < 0.03; 3 x 0.04; 3 x 0.05; 3 x 0.06; 4 x 0.08; 3 x 0.09; 2 x 0.10; 0.11; 0.14; 0.20 | |
| Barley grains   | SEU              | < 0.03; 0.04; 3 x 0.05; 0.06; 0.08; 4 x 0.09; 3 x 0.13; 0.14; 0.18; 0.25; 2 x 0.26; 0.44; 0.54 | |
| Rye grains      | SEU              | < 0.05; 0.06; 0.13; 0.18; 0.54 | Overdose trials on wheat whole plant performed with 1.5N rate; PHI 0 (Austria, 2020) used on tentative basis. MRL\_OECD = 1.04 | |
| **SEU**         |                  |                                                                  | 1.00\(^{(d),(e)}\) (tentative) 0.54 0.13 |
| **Wheat forage**|                  |                                                                  | MRL\_OECD = 1.04 |
| **SEU**         |                  |                                                                  | 0.50\(^{(e)}\) (tentative) 0.35 0.16 |
| **Wheat straw** |                  |                                                                  | MRL\_OECD = 1.37 |
| **Barley straw**|                  |                                                                  | 1.50\(^{(e)}\) (tentative) 1.16 0.26 |
| **Rye straw**   |                  |                                                                  | |

GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; MRL: maximum residue level; Mo: residue levels expressed according to the monitoring residue definition; RA: residue levels expressed according to risk assessment residue definition. *: Indicates that the MRL is proposed at the limit of quantification.

(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.

(b): Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(c): Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(d): Tentative MRL from overdosed trials (relevant for dietary burden calculations).

(e): A tentative MRL is derived in view of the future need to set MRLs in livestock feed items.
### B.1.2.2. Summary of residues data from the supervised residue trials – Primary crops (RD-Mo option 2)

| Commodity          | Region Indoor(a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source                                                                 | Calculated MRL (mg/kg) | HR(b) (mg/kg) | STMR(c) (mg/kg) |
|--------------------|------------------|---------------------------------------------------------------|---------------------------------------------------------------------------------|------------------------|---------------|-----------------|
| Wheat grains       | NEU              | **Mo:** 7 × < 0.03; 0.03                                       | Residue trials on wheat compliant with GAP. QuEChERS method used allowing the determination of only free forms of M4 and M6 (Austria, 2020). Extrapolation to barley is applicable. MRL$_{OECD}$ = 0.04 | 0.04                   | (d)           | (d)             |
| Barley grains      |                  | **RA:** –                                                      |                                                                                  |                        |               |                 |
| Rye grains         | SEU              | **Mo:** 6 × < 0.03; 0.05                                       | Residue trials on wheat compliant with GAP. It is noted that three trials were performed at BBCH 35. QuEChERS method used allowing the determination of only free forms M4 and M6 (Austria, 2020). Extrapolation to barley is applicable. MRL$_{OECD}$ = 0.07 | 0.07                   | (d)           | (d)             |
| Wheat forage       | SEU              | **Mo:** –                                                      | No GAP compliant trials available.                                              | –                      | (d)           | (d)             |
| Wheat straw        | NEU              | **Mo:** 0.03; 0.04; 0.09; 0.15; 0.16; 0.23 0.24; 0.52          | Residue trials on wheat compliant with GAP. QuEChERS method used allowing the determination of only free forms M4 and M6 (Austria, 2020). Extrapolation to barley is applicable. MRL$_{OECD}$ = 0.81 | 0.90(e) (tentative)   | (d)           | (d)             |
| Barley straw       |                  | **RA:** –                                                      |                                                                                  |                        |               |                 |
| Rye straw          | SEU              | **Mo:** < 0.03; 0.03; 0.1; 0.15; 0.21; 0.26; 0.4; 0.48         | Residue trials on wheat compliant with GAP. It is noted that three trials were performed at BBCH 35. QuEChERS method used allowing the determination of only free forms M4 and M6 (Austria, 2020). Extrapolation to barley is applicable. MRL$_{OECD}$ = 0.87 | 0.90(e) (tentative)   | (d)           | (d)             |

GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; MRL: maximum residue level.

*: Indicates that the MRL is proposed at the limit of quantification.
Mo: residue levels expressed according to the monitoring residue definition; RA: residue levels expressed according to risk assessment residue definition.
(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.
(b): Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.
(c): Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.
(d): Residue trials analysing simultaneously for enforcement and risk assessment residue definitions are not available. For dietary burden and consumer exposure assessment, the input value derived in Table B.1.2.1 were used.
(e): A tentative MRL is derived in view of the future need to set MRLs in livestock feed items.
B.1.2.3. Residues in rotational crops

**Overall summary**

Residues in rotational and succeeding crops expected based on confined rotational crop study?

| | No |
|---|---|

Based on the confined rotational crop study, significant residues are not expected in succeeding crops for the current authorised uses, provided that pinoxaden is applied in compliance with the GAPs reported in Appendix A.

Residues in rotational and succeeding crops expected based on field rotational crop study?

| | Not triggered |
|---|---|

No study available and not required

GAP: Good Agricultural Practice.

B.1.2.4. Processing factors

| Processed commodity | Number of valid studies (a) | Processing Factor (PF) | Comment/ Source |
|---|---|---|---|
| **RD-Mo option 1:** sum of M4 and M6 (both free and conjugated), expressed as pinoxaden | | | |
| Barley, brewing malt | 4 | 1.4; 1.3; 1.3; 1.4 | 1.3 (EFSA, 2013; Austria, 2020) |
| Barley, beer | 4 | 0.2; 0.2; 0.2; 0.1 | 0.2 (EFSA, 2013; Austria, 2020) |
| Barley, pot/pearl | 4 | 0.4; 0.4; 0.5; 0.5 | 0.5 (EFSA, 2013; Austria, 2020) |
| Barley, dry brewer’s grain | 4 | 0.9; 0.9; 0.9; 1.1 | 1 (EFSA, 2013; Austria, 2020) |
| Wheat, whole-meal flour | 4 | 1.3; 1.0; 0.9; 1.1 | 1.1 (EFSA, 2013; Austria, 2020) |
| Wheat, whole-meal bread | 4 | 0.6; 0.7; 0.5; 0.7 | 0.6 (EFSA, 2013; Austria, 2020) |
| Wheat, white flour | 4 | < 0.3; 0.3; 0.3; 0.3 | < 0.3 (EFSA, 2013; Austria, 2020) |
| Wheat, dry milled by-products (incl. bran) | 4 | 5.1; 4.4; 3.6; 4.1 | 4.3 (EFSA, 2013; Austria, 2020) |
| Wheat, dry distiller’s grain | 4 | 1.3; 1.0; 0.8; 0.9 | 0.9 (EFSA, 2013; Austria, 2020) |

| **RD-Mo option 2:** sum of M4 and M6 (both free only), expressed as pinoxaden | | | --- |
| No data available and not required (b) |

PF: Processing factor: (Residue level in processed commodity expressed according to RD-Mo/ Residue level in raw commodity expressed according to RD-Mo);

(a): Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).

(b): No processing studies available analysing free forms (only) of metabolites M6 and M4. However, they are not required as residues in raw commodity were below 0.1 mg/kg according to RD-Mo option 2.
### B.2. Residues in livestock

#### Relevant groups (subgroups)

| Relevant groups (subgroups) | Dietary burden expressed in mg/kg bw per day | Most critical subgroup\(^{(a)}\) | Most critical commodity\(^{(b)}\) | Trigger exceeded (Y/N) | Comments |
|-----------------------------|--------------------------------------------|----------------------------------|---------------------------------|------------------------|----------|
| Cattle (all)                | Median 0.011, Maximum 0.023               | Dairy cattle                     | Wheat forage                    | Yes                    | –        |
| Cattle (dairy only)         | Median 0.011, Maximum 0.023               | Dairy cattle                     | Wheat forage                    | Yes                    | –        |
| Sheep (all)                 | Median 0.017, Maximum 0.041               | Lamb                             | Wheat straw                     | Yes                    | –        |
| Sheep (ewe only)            | Median 0.013, Maximum 0.035               | Ram/Ewe                         | Wheat forage                    | Yes                    | –        |
| Swine (all)                 | Median 0.008, Maximum 0.016               | Swine (breeding)                | Wheat forage                    | Yes                    | –        |
| Poultry (all)               | Median 0.014, Maximum 0.026               | Poultry layer                   | Wheat forage                    | Yes                    | –        |
| Fish                        | –                                          | –                                | –                               | –                      | –        |

bw: body weight; DM: dry matter.

\(^{(a)}\): When one group of livestock includes several subgroups (e.g. poultry 'all' including broiler, layer and turkey), the result of the most critical subgroup is identified from the maximum dietary burdens expressed as 'mg/kg bw per day'.

\(^{(b)}\): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as 'mg/kg bw per day'.

### B.2.1. Nature of residues and methods of analysis in livestock

#### B.2.1.1. Metabolism studies, methods of analysis and residue definitions in livestock

| Livestock (available studies) | Animal          | Dose (mg/kg bw per day) | Duration (days) | Comment/Source                                                                                     |
|-------------------------------|-----------------|-------------------------|-----------------|---------------------------------------------------------------------------------------------------|
| Laying hen                    | 6.62            | 4                       | 255N compared to the maximum dietary burden calculated for layer poultry. Radiolabelled active substance: \(^{14}\)C-phenyl pinoxaden (EFSA, 2013) |
| Lactating ruminants           | 3.5             | 4                       | 85N compared to the maximum dietary burden calculated for sheep (lamb). Radiolabelled active substance: \(^{14}\)C-phenyl pinoxaden (EFSA, 2013) |
|                               | 0.29            | 4                       | 7N compared to the maximum dietary burden calculated for sheep (lamb). Radiolabelled active substance: \(^{14}\)C-pyrazol M4 (EFSA, 2013) |
| Pig                           | –               | –                       | Not available and not required (extrapolated from ruminants) |

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Time needed to reach a plateau concentration in milk and eggs (days)

| Milk: not relevant | The metabolism studies were dosed for 4 days and residues were low in eggs and milk. In feeding studies residues of M4 and M6 were below the LOQ for milk and eggs. |
| Eggs: not relevant |

Metabolism in rat and ruminant similar

Can a general residue definition be proposed for animals?

Animal residue definition for monitoring (RD-Mo)

Animal residue definition for risk assessment (RD-RA)

Fat soluble residues

Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)

| Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs) |
| Milk, eggs, muscle, fat, kindly and liver (EFSA, 2013): |
| • Single residue method LC–MS/MS |
| • LOQ = 0.01 mg/kg for metabolite M4 (free and conjugated) in milk, and 0.02 mg/kg in eggs and tissues. Same LOQs for metabolite M6 (free and conjugated) in same matrices. |
| • Confirmatory method missing (data gap) |
| • ILV available for both M4 and M6 in muscle, fat, milk and eggs. |
| • QuEChERS based (LC–MS/MS) for enforcement of M4 (free only) with LOQ 0.01 mg/kg in liver and milk, and of M6 (free only) with LOQ 0.01 mg/kg in milk and 0.02 mg/kg in liver, in routine analysis (EURL, 2020). |

LOQ: limit of quantification; LC–MS/MS: liquid chromatography with tandem mass spectrometry; ILV: independent laboratory validation; LogK_{ow}: Log n-Octanol/Water Partition coefficient.

B.2.1.2. Stability of residues in livestock

| Animal products (available studies) |
| Animal | Commodity | T (°C) | Stability period | Compounds covered | Comment/Source |
| --- | --- | --- | --- | --- | --- |
| Poultry | Muscle | –20 | 3 Months | Metabolite M4 | EFSA (2013) |
| Bovine | Fat | – | – | – | Not available and not required |
| Bovine | Liver | –20 | 3 Months | Metabolite M4 | EFSA (2013) |
| Bovine | Kidney | – | – | – | Not available and not required |
| Bovine | Milk | –20 | 3 Months | Metabolite M4 | EFSA (2013) |
| Poultry | Eggs | –20 | 3 Months | Metabolite M4 | EFSA (2013) |
### B.2.2. Magnitude of residues in livestock

#### B.2.2.1. Summary of the residue data from livestock feeding studies

Calculations performed with Animal model 2017\(^9\)

| Animal commodity | Residues at the closest feeding level (mg/kg) | Estimated value at 1N MRL proposal (mg/kg) | MRL proposal (mg/kg) |
|------------------|---------------------------------------------|-------------------------------------------|---------------------|
|                  | Mean | Highest | STMR\(_{Mo}\)\(^{(a)}\) (mg/kg) | HR\(_{Mo}\)\(^{(b)}\) (mg/kg) |
| **Cattle (all)** | -    | -       | 0.02  | 0.02 |
| Muscle           | < 0.02 | < 0.02 | 0.02  | 0.02 | 0.02* (tentative)\(^{(d)}\) |
| Fat              | < 0.02 | < 0.02 | 0.02  | 0.02 | 0.02* (tentative)\(^{(d)}\) |
| Liver            | < 0.02 | < 0.02 | 0.02  | 0.02 | 0.02* (tentative)\(^{(d)}\) |
| Kidney           | < 0.02 | < 0.02 | 0.02  | 0.02 | 0.02* (tentative)\(^{(d)}\) |

**Cattle (dairy only)** — Closest feeding level (0.04 mg/kg bw; 1.7 N rate)\(^{(c)}\)

| Milk\(^{(e)}\) | < 0.01 | n.a. | 0.01 | 0.01* (tentative)\(^{(d)}\) |

**Sheep (all)**\(^{(f)}\) — Closest feeding level (0.04 mg/kg bw; 1.0 N rate)\(^{(c)}\)

| Muscle | Fat | Liver | Kidney | |
|--------|-----|-------|--------|-----|
| < 0.02 | < 0.02 | 0.02  | 0.02  | |
| 0.02  | 0.02  | 0.02  | 0.02  |

**Sheep (ewe only)**\(^{(f)}\) — Closest feeding level (0.04 mg/kg bw; 1.1 N rate)\(^{(c)}\)

| Milk\(^{(e)}\) | < 0.01 | n.a. | 0.01 | 0.01* (tentative)\(^{(d)}\) |

**Swine (all)**\(^{(f)}\) — Closest feeding level (0.04 mg/kg bw; 2.5 N rate)\(^{(c)}\)

| Muscle | Fat | Liver | Kidney | |
|--------|-----|-------|--------|-----|
| < 0.02 | < 0.02 | 0.02  | 0.02  | |
| 0.02  | 0.02  | 0.02  | 0.02  |

**Poultry (all)** — Closest feeding level (0.04 mg/kg bw; 1.6 N rate)\(^{(c)}\)

| Muscle | Fat | Liver | |
|--------|-----|-------|-----|
| < 0.02 | < 0.02 | 0.02  | |
| 0.02  | 0.02  | 0.02  |

**Poultry (layer only)** — Closest feeding level (0.04 mg/kg bw; 1.6 N rate)\(^{(c)}\)

| Eggs\(^{(g)}\) | < 0.02 | < 0.02 | 0.02  | 0.02  |
|----------------|--------|--------|-------|-------|

MRL: maximum residue level; STMR: supervised trials median residue; HR: highest residue; Mo: monitoring; bw: body weight; *
*: Indicates that the MRL is proposed at the limit of quantification.

n.a.: not applicable.
n.r.: not reported.

(a): Median residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the median dietary burden.

(b): Highest residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the maximum dietary burden.

(c): Closest feeding level and N dose rate related to the maximum dietary burden.

(d): Tentative MRL in the absence of confirmatory method for all livestock commodities.

(e): For milk, mean was derived from samplings performed from day 2 to day 28 (daily mean of 3 cows).

(f): Since extrapolation from cattle to other ruminants and swine is acceptable, results of the livestock feeding study on ruminants were relied upon to derive the MRL and risk assessment values in sheep and swine.

(g): For eggs, mean and highest residues were derived from samplings performed from day 1 to day 28 (daily mean or daily highest of 15 laying hens).

\(^9\) [https://ec.europa.eu/food/plant/pesticides/max_residue_levels/guidelines_en](https://ec.europa.eu/food/plant/pesticides/max_residue_levels/guidelines_en)
### B.3. Consumer risk assessment

| ARfD | 0.1 mg/kg bw (European Commission, 2016) |
|------|------------------------------------------|
| Wheat: 1% of ARfD |
| Not assessed in this review. |

| NESTI (% ARfD) |
|----------------|
| Not assessed in this review. |

#### Assumptions made for the calculations

The calculation is based on the highest residue levels expected in raw agricultural commodities, except for bulk commodities (cereals) for which the median residue levels were considered.

CXLs and EU residue definitions for enforcement are only considered compatible for option 1. For this option, CXLs and EU MRLs proposal were compared. CXLs were found to be covered by the proposed EU-MRLs for option 1, and thus consumer risk assessments with and without consideration of the existing CXLs resulted in the same estimated exposure. The exposure calculation is considered to cover also option 2 as the residue definition for risk assessment is the same as for option 1.

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| ADI | 0.1 mg/kg bw per day (European Commission, 2016) |
|-----|-----------------------------------------------|
| Not assessed in this review. |

| NTMDI, according to (to be specified) |
|---------------------------------------|
| Not assessed in this review. |

| Highest IEDI, according to EFSA PRIMO (rev.3.1) |
|-----------------------------------------------|
| 1% ADI (DK child) |
| Not assessed in this review. |

#### Assumptions made for the calculations

The calculation is based on the median residue levels derived for raw agricultural commodities. The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation.

CXLs and EU residue definitions for enforcement are only considered compatible for option 1. For this option, CXLs and EU MRLs proposal were compared. CXLs were found to be covered by the proposed EU-MRLs for option 1, and thus consumer risk assessments with and without consideration of the existing CXLs resulted in the same estimated exposure. The exposure calculation is considered to cover also option 2 as the residue definition for risk assessment is the same as for option 1.

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**ARfD:** acute reference dose; **bw:** body weight; **NESTI:** national estimated short-term intake; **PRIMO:** (EFSA) Pesticide Residues Intake Model; **WHO:** World Health Organization; **IESTI:** international estimated short-term intake.

**ADI:** acceptable daily intake; **bw:** body weight; **NEDI:** national estimated daily intake; **PRIMO:** (EFSA) Pesticide Residues Intake Model; **WHO:** World Health Organization; **TMDI:** theoretical maximum daily intake; **NTMDI:** national theoretical maximum daily intake; **IEDI:** international estimated daily intake.
Consumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/02/2003).

**Metabolite(s)**

- Not assessed in this review.

**ADI (mg/kg bw per day)**

- Not assessed in this review.

**Intake of groundwater metabolites (% ADI)**

- Not assessed in this review.

### B.4. Proposed MRLs

| Code number | Commodity       | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL (mg/kg) | Outcome of the review | Comment                  |
|-------------|-----------------|-------------------------|----------------------|-------------|-----------------------|--------------------------|
| 500010      | Barley grain    | 1                       | 0.7                  | 0.7         | Recommended            |                          |
| 500070      | Rye grain       | 1                       | –                    | 0.7         | Recommended            |                          |
| 500090      | Wheat grain     | 1                       | 0.7                  | 0.7         | Recommended            |                          |

**Enforcement residue definition (existing):** pinoxaden

**Enforcement residue definition (plants, proposed option 1):** sum of M4 and M6 (both free and conjugated), expressed as pinoxaden

| Code number | Commodity       | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL (mg/kg) | Outcome of the review | Comment                  |
|-------------|-----------------|-------------------------|----------------------|-------------|-----------------------|--------------------------|
| 1011010     | Swine meat      | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1011020     | Swine fat (free of lean meat) | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1011030     | Swine liver     | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1011040     | Swine kidney    | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1012010     | Bovine meat     | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1012020     | Bovine fat      | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1012030     | Bovine liver    | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1012040     | Bovine kidney   | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1013010     | Sheep meat      | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1013020     | Sheep fat       | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1013030     | Sheep liver     | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1013040     | Sheep kidney    | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1014010     | Goat meat       | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1014020     | Goat fat        | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1014030     | Goat liver      | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1014040     | Goat kidney     | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |
| 1015010     | Horse meat      | –                       | –                    | 0.02*       | Further consideration needed | Data gap # 1             |

**Enforcement residue definition (animals, proposed):** M4 (free and conjugated), expressed as pinoxaden

Data gap # 1
| Code number | Commodity         | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL (mg/kg) | Comment                                      |
|-------------|-------------------|-------------------------|----------------------|-------------|----------------------------------------------|
| 1015020     | Horse fat         | –                       | –                    | 0.02*       | Further consideration needed<sup>(c)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1015030     | Horse liver       | –                       | –                    | 0.02*       | Further consideration needed<sup>(c)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1015040     | Horse kidney      | –                       | –                    | 0.02*       | Further consideration needed<sup>(c)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1016010     | Poultry meat      | –                       | 0.02*                | 0.02*       | Further consideration needed<sup>(d)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1016020     | Poultry fat       | –                       | 0.02*                | 0.02*       | Further consideration needed<sup>(d)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1016030     | Poultry liver     | –                       | 0.02*                | 0.02*       | Further consideration needed<sup>(d)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1020010     | Cattle milk       | –                       | –                    | 0.01*       | Further consideration needed<sup>(c)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1020020     | Sheep milk        | –                       | –                    | 0.01*       | Further consideration needed<sup>(c)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1020030     | Goat milk         | –                       | –                    | 0.01*       | Further consideration needed<sup>(c)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1020040     | Horse milk        | –                       | –                    | 0.01*       | Further consideration needed<sup>(c)</sup>   |
|             |                   |                         |                      |             | Data gap # 1                                |
| 1030000     | Birds’ eggs       | See Reg. (EC) No 839/2008 | –                    | 0.02*       | Further consideration needed<sup>(d)</sup>   |
|             | Other commodities | –                       | –                    | –           | Further consideration needed<sup>(e)</sup>   |
|             | of plant and/or   |                         |                      |             |                                              |
|             | animal origin     |                         |                      |             |                                              |

MRL: maximum residue level; CXL: codex maximum residue limit.

*: Indicates that the MRL is set at the limit of quantification.

(a): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; existing CXL is covered by the recommended MRL (combination H-III in Appendix E).

(b): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination H-I in Appendix E).

(c): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified (assuming the existing residue definition); no CXL is available (combination F-I in Appendix E).

(d): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified (assuming the existing residue definition); existing CXL is covered by the tentative MRL (combination F-III in Appendix E).

(e): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).
**Appendix C – Pesticide Residue Intake Model (PRIMo)**

**PRIMo(EU_CXL)**

LOQs (mg/kg) range from: 0.01 to 0.02

ADI (mg/kg bw per day): 0.1

ARfD (mg/kg bw): 0.1

Source of ADI: European Commission, EFSA PRIMo revision 3.1; 2019/03/19

Year of evaluation: Year of evaluation:

No of diets exceeding the ADI: ---

### Calculated exposure (% of ADI)

| Commodity/group of commodities | Exposure resulting from | Highest contributor to MS diet | And contributor to MS diet | 3rd contributor to MS diet | Commodity/group of commodities MRLs set at the LOQ (in % of ADI) | Commodity/group of commodities not under assessment (in % of ADI) |
|--------------------------------|------------------------|-------------------------------|---------------------------|---------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| MRLs set at the LOQ (in % of ADI) | conclusion of chronic risk assessment (in % of ADI) |
| *Appendix C – Pesticide Residue Intake Model (PRIMo)* | | | | | | |

### Normal mode

#### Chronic risk assessment: JMPR methodology (IEDI/TMDI)

| Commodity/group of commodities | Exposure resulting from | Highest contributor to MS diet | And contributor to MS diet | 3rd contributor to MS diet | Commodity/group of commodities MRLs set at the LOQ (in % of ADI) | Commodity/group of commodities not under assessment (in % of ADI) |
|--------------------------------|------------------------|-------------------------------|---------------------------|---------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| *Appendix C – Pesticide Residue Intake Model (PRIMo)* | | | | | | |

#### Input values

#### Supplementary results – acute risk assessment

#### Details – acute risk assessment/children

#### Details – acute risk assessment/adults

### Summary

The estimated long-term dietary intake (TMDI=IEDI/TMDI) was below the ADI. The long-term intake of residues of pinoxaden is unlikely to present a public health concern.

## References

[TMDI=NED/TMDI]

[TMDI=NED/TMDI]

[Normal mode]

### Calculated exposure (% of ADI)

| Commodity/group of commodities | Exposure resulting from | Highest contributor to MS diet | And contributor to MS diet | 3rd contributor to MS diet | Commodity/group of commodities MRLs set at the LOQ (in % of ADI) | Commodity/group of commodities not under assessment (in % of ADI) |
|--------------------------------|------------------------|-------------------------------|---------------------------|---------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| *Appendix C – Pesticide Residue Intake Model (PRIMo)* | | | | | | |

### Normal mode

#### Chronic risk assessment: JMPR methodology (IEDI/TMDI)

| Commodity/group of commodities | Exposure resulting from | Highest contributor to MS diet | And contributor to MS diet | 3rd contributor to MS diet | Commodity/group of commodities MRLs set at the LOQ (in % of ADI) | Commodity/group of commodities not under assessment (in % of ADI) |
|--------------------------------|------------------------|-------------------------------|---------------------------|---------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| *Appendix C – Pesticide Residue Intake Model (PRIMo)* | | | | | | |

### Input values

#### Supplementary results – acute risk assessment

#### Details – acute risk assessment/children

#### Details – acute risk assessment/adults

### Summary

The estimated long-term dietary intake (TMDI=IEDI/TMDI) was below the ADI. The long-term intake of residues of pinoxaden is unlikely to present a public health concern.

## References

[TMDI=NED/TMDI]

[TMDI=NED/TMDI]

[Normal mode]
### Acute risk assessment/children

The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.

#### Results for children

| IESTI | Highest % of ARfD/ADI | Commodities | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | IESTI | Highest % of ARfD/ADI | Commodities | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) |
|-------|------------------------|-------------|--------------------------|---------------------|-------|------------------------|-------------|--------------------------|---------------------|
| 1%    | Wheat                  | 0.70/0.09   | 1.3                      |                     | 0.8%  | Wheat                  | 0.70/0.09   | 0.76                      |
| 1%    | Milk: Cattle           | 0.01/0.01   | 1.2                      |                     | 0.4%  | Rye                    | 0.70/0.09   | 0.44                      |
| 0.6%  | Rye                    | 0.70/0.09   | 0.57                     |                     | 0.4%  | Barley                 | 0.70/0.09   | 0.44                      |
| 0.5%  | Barley                 | 0.70/0.09   | 0.51                     |                     | 0.4%  | Milk: Cattle           | 0.01/0.01   | 0.39                      |
| 0.3%  | Poultry: Muscle/meat   | 0.02/0.02   | 0.34                     |                     | 0.2%  | Milk: Goat             | 0.01/0.01   | 0.18                      |
| 0.2%  | Eggs: Chicken          | 0.02/0.02   | 0.25                     |                     | 0.2%  | Milk: Sheep            | 0.01/0.01   | 0.15                      |
| 0.2%  | Swine: Muscle/meat     | 0.02/0.02   | 0.24                     |                     | 0.2%  | Milk: Sheep            | 0.01/0.01   | 0.11                      |
| 0.2%  | Milk: Milk             | 0.01/0.01   | 0.24                     |                     | 0.1%  | Milk: Muscle           | 0.02/0.02   | 0.10                      |
| 0.2%  | Bovine: Liver          | 0.02/0.02   | 0.16                     |                     | 0.1%  | Lactose: Milk          | 0.02/0.02   | 0.09                      |
| 0.1%  | Bovine: Muscle/meat    | 0.02/0.02   | 0.14                     |                     | 0.1%  | Milk: Milk             | 0.02/0.02   | 0.09                      |
| 0.1%  | Equine: Muscle/meat    | 0.02/0.02   | 0.12                     |                     | 0.09% | Milk: Milk             | 0.02/0.02   | 0.09                      |
| 0.1%  | Sheep: Muscle/meat     | 0.02/0.02   | 0.11                     |                     | 0.09% | Milk: Milk             | 0.02/0.02   | 0.09                      |
| 0.08% | Bovine: Kidney         | 0.02/0.02   | 0.08                     |                     | 0.09% | Milk: Milk             | 0.02/0.02   | 0.08                      |
| 0.04% | Bovine: Fat tissue     | 0.02/0.02   | 0.04                     |                     | 0.09% | Milk: Milk             | 0.02/0.02   | 0.08                      |
| 0.04% | Milk: Sheep            | 0.01/0.01   | 0.04                     |                     | 0.06% | Milk: Milk             | 0.02/0.02   | 0.06                      |

Expand/collapse list

#### Results for adults

No exceedance of the toxicological reference value was identified for any unprocessed commodity.

### Acute risk assessment/adults/general population

The acute risk assessment is based on the ARfD.

#### Results for adults

No of commodities for which ARfD/ADI is exceeded (IESTI):

| IESTI | Highest % of ARfD/ADI | Commodities | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) |
|-------|------------------------|-------------|--------------------------|---------------------|
| 0.5%  | Wheat/milling (wholemeal)-l | 0.70/0.09   | 0.50                      |
| 0.3%  | Wheat/milling (flour)    | 0.70/0.03   | 0.33                     |
| 0.3%  | Rye/baked               | 0.70/0.09   | 0.33                     |
| 0.3%  | Barley/baked            | 0.70/0.09   | 0.32                     |
| 0.2%  | Barley/milling (wholemeal)-bwb | 0.70/0.09 | 0.16                    |

Expand/collapse list

#### Results for children

No exceedance of the toxicological reference value was identified for any unprocessed commodity.

### Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short term intake of residues of pinoxaden is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.
### Appendix D – Input values for the exposure calculations

#### D.1. Livestock dietary burden calculations

| Feed commodity       | Median dietary burden | Maximum dietary burden |
|----------------------|-----------------------|------------------------|
|                      | Input value (mg/kg)   | Comment                | Input value (mg/kg) | Comment |
| **Risk assessment residue definition:** sum of M4 and M6 (both free and conjugated), expressed as pinoxaden |
| Barley straw         | 0.26                  | STMR                   | 1.16               | HR      |
| Rye straw            | 0.26                  | STMR                   | 1.16               | HR      |
| Triticale forage     | 0.13                  | STMR                   | 0.54               | HR      |
| Triticale hay        | 0.38                  | STMR × default PF (2.9)(a) | 1.57               | HR × default PF (2.9)(a) |
| Triticale straw      | 0.26                  | STMR                   | 1.16               | HR      |
| Wheat forage         | 0.13                  | STMR                   | 0.54               | HR      |
| Wheat hay (fodder dry)| 0.46                  | STMR × default PF (3.5)(a) | 1.89               | HR × default PF (3.5)(a) |
| Wheat straw          | 0.26                  | STMR                   | 1.16               | HR      |
| Barley grain         | 0.09                  | STMR                   | 0.09               | STMR    |
| Rye grain            | 0.09                  | STMR                   | 0.09               | STMR    |
| Triticale grain      | 0.09                  | STMR                   | 0.09               | STMR    |
| Wheat grain          | 0.09                  | STMR                   | 0.09               | STMR    |
| Brewer’s grain dried | 0.09                  | STMR × PF (1)          | 0.09               | STMR × PF (1) |
| Distiller’s grain dried | 0.08                  | STMR × PF (0.9)       | 0.08               | STMR × PF (0.9) |
| Wheat gluten meal    | 0.16                  | STMR × default PF (1.8)(a) | 0.16               | STMR × default PF (1.8)(a) |
| Wheat milled by-pdts | 0.39                  | STMR × PF (4.3)       | 0.39               | STMR × PF (4.3) |

STMR: supervised trials median residue; HR: highest residue; PF: processing factor.

*: Indicates that the input value is proposed at the limit of quantification.

(a): In the absence of processing factors supported by data, default the processing factor of was included in the calculation to consider the potential concentration of residues in these commodities.

#### D.2. Consumer risk assessment

| Commodity          | Chronic risk assessment | Acute risk assessment |
|--------------------|-------------------------|-----------------------|
|                    | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment |
| **Risk assessment residue definition (plants):** sum of M4 and M6 (both free and conjugated), expressed as pinoxaden |
| Barley grains      | 0.09                    | STMR                  | 0.09                | STMR    |
| Rye grains         | 0.09                    | STMR                  | 0.09                | STMR    |
| Wheat grains       | 0.09                    | STMR                  | 0.09                | STMR    |
| **Risk assessment residue definition (animals):** M4 (free and conjugated), expressed as pinoxaden |
| Swine meat         | 0.02*                   | STMR muscle (tentative) | 0.02*              | HR muscle (tentative) |
| Swine fat          | 0.02*                   | STMR (tentative)      | 0.02*              | HR (tentative) |
| Swine liver        | 0.02*                   | STMR (tentative)      | 0.02*              | HR (tentative) |
| Swine kidney       | 0.02*                   | STMR (tentative)      | 0.02*              | HR (tentative) |
| Bovine and equine meat | 0.02*                   | STMR muscle (tentative) | 0.02*              | HR muscle (tentative) |
| Bovine and equine fat | 0.02*                   | STMR (tentative)      | 0.02*              | HR (tentative) |
| Commodity                  | Chronic risk assessment | Acute risk assessment |
|---------------------------|-------------------------|-----------------------|
|                           | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment               |
| Bovine and equine liver   | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |
| Bovine and equine kidney  | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |
| Sheep and goat meat       | 0.02*                   | STMR muscle (tentative)| 0.02*               | HR muscle (tentative) |
| Sheep and goat fat        | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |
| Sheep and goat liver      | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |
| Sheep and goat kidney     | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |
| Poultry meat              | 0.02*                   | STMR muscle (tentative)| 0.02*               | HR muscle (tentative) |
| Poultry fat               | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |
| Poultry liver             | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |
| Cattle and horse milk     | 0.01*                   | STMR (tentative)      | 0.01*               | STMR (tentative)      |
| Sheep and goat milk       | 0.01*                   | STMR (tentative)      | 0.01*               | STMR (tentative)      |
| Birds eggs                | 0.02*                   | STMR (tentative)      | 0.02*               | HR (tentative)        |

*: Indicates that the input value is proposed at the limit of quantification. CXLs were covered by the proposed EU-MRLs according to RD-Mo option 1.
Appendix E – Decision tree for deriving MRL recommendations

Evaluation of the GAPs and available residues data at EU level

- GAP or DB > 0.1 mg/kg GM in EU?
  - Yes: GAPs waiting for approval
  - No: GAPs evaluated

- Is RD-RA derived for this commodity?
  - Yes: MRL and RA derived in Section 3?
    - Yes: MRL fully supported by data?
      - Yes: MRLs recommended
      - No: MRLs not recommended
    - No: Consumer risk assessment for GAPs evaluated at EU level – EU scenarios
  - No: MRLs recommended

Consumer risk assessment for GAPs evaluated at EU level – EU scenarios

- Not considered for the RA
- Current EU MRL is included in the RA
- Tentative median/highest values are included in the RA
- Tentative median/highest values are included in the RA

- Risk identified?
  - Yes: Risk identified?
    - Yes: Fall-back MRL available?
      - Yes: MRLs recommended
      - No: MRLs not recommended
    - No: MRLs recommended
  - No: MRLs recommended

Recommendations resulting from EU authorisations and import tolerances

- A: Specific LOQ or default MRL?
- B: Specific LOQ or default MRL?
- C: Specific LOQ or default MRL?
- D: Maintain current EU MRL?
- E: Specific LOQ or default MRL?
- F: Establish tentative EU MRL?
- G: Specific LOQ or default MRL?
- H: MRLs are recommended.

Comparison with OMs
Comparison of the EU recommendation with the existing CXL

CXL available? Yes

RD comparable? Yes

CXL higher? Yes

Consumer risk assessment with consideration of the existing CXL

Input values for the RA remain unchanged.

CXL included in the RA.

Risk identified?

Yes

CXL supported by data?

Yes

Input values for the RA remain unchanged.

CXL included in the RA.

Risk identified?

Yes

Input values for the RA remain unchanged.

CXL included in the RA.

Risk identified?

Yes

Recommendations with consideration of the existing CXL

Maintain EU recommendation indicating that no CXL is available.

Maintain EU recommendation indicating that CXL is not compatible.

Maintain EU recommendation indicating that CXL is covered.

Maintain EU recommendation; higher CXL is not safe for consumer.

Maintain current CXL or EU recommendation?

Maintain EU recommendation; higher CXL is not safe for consumer.

CXL is recommended; EU recommendation is covered as well.
### Appendix F – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|--------------------------------|-----------------------------------------------|---------------------------------|
| **Pinoxaden**                  | 8-(2,6-diethyl-p-tolyl)-1,2,4,5-tetrahydro-7-oxo-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-9-yl 2,2-dimethylpropionate | ![Structural formula for Pinoxaden](image) |
|                               | CC(C)(C)(−O)OC1−C(C(−O)N2CCOCN2C1)c1c(CC)c(C)c1CC | ![Structural formula for Pinoxaden](image) |
|                               | MGOHCFMYLBAPRN-UHFFFAOYSA-N | ![Structural formula for Pinoxaden](image) |
| **M2, NOA 407854**            | 8-(2,6-diethyl-4-methylphenyl)tetrahydro-7H-pyrazolo[1,2-d][1,4,5]oxadiazepine-7,9(8H)-dione | ![Structural formula for M2](image) |
|                               | CCc1cc(CC)c1C1C(−O)N2CCOCN2C1=O | ![Structural formula for M2](image) |
|                               | XTDSHACLOHQSIG-UHFFFAOYSA-N | ![Structural formula for M2](image) |
| **M3, NOA 447204**            | 8-(2,6-diethyl-4-methylphenyl)-8-hydroxytetrahydro-7H-pyrazolo[1,2-d][1,4,5]oxadiazepine-7,9(8H)-dione | ![Structural formula for M3](image) |
|                               | CCc1cc(CC)c1C1(O)(C(−O)N2CCOCN2C1=O | ![Structural formula for M3](image) |
|                               | XTDSHACLOHQSIG-UHFFFAOYSA-N | ![Structural formula for M3](image) |
| **M4, SYN 505164**            | 8-[2,6-diethyl-(hydroxymethyl)phenyl]-9-hydroxy-1,2,4,5-tetrahydro-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-7-one | ![Structural formula for M4](image) |
|                               | CCc1cc(CC)c1C1−C(−O)N2CCOCN2C1=O | ![Structural formula for M4](image) |
|                               | WGVDNRLFQTNMIF-UHFFFAOYSA-N | ![Structural formula for M4](image) |
| **M6, SYN 502836**            | 3,5-diethyl-4-(9-hydroxy-7-oxo-1,2,4,5-tetrahydro-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-8-yl)benzoic acid | ![Structural formula for M6](image) |
|                               | O−C(O)c1cc(CC)c(C=2(−O)N3CCOCN3C−2O)c(CC)c1 | ![Structural formula for M6](image) |
|                               | IGUXRAORWEOEM-UHFFFAOYSA-N | ![Structural formula for M6](image) |
| **M10, SYN 505887**           | 8-[2,6-diethyl-(hydroxymethyl)phenyl]-8-hydroxytetrahydro-7H-pyrazolo[1,2-d][1,4,5]oxadiazepine-7,9(8H)-dione | ![Structural formula for M10](image) |
|                               | CCc1cc(CC)c1C1(O)(C(−O)N2CCOCN2C1=O | ![Structural formula for M10](image) |
|                               | MXC3NNVICXCNEB-UHFFFAOYSA-N | ![Structural formula for M10](image) |

**IUPAC**: International Union of Pure and Applied Chemistry; **SMILES**: simplified molecular-input line-entry system; **InChiKey**: International Chemical Identifier Key.

(a): The metabolite name in bold is the name used in the conclusion.

(b): ACD/Name 2019.1.3 ACD/Labs 2019 Release (File version N05E41, Build 111418, 3 September 2019).

(c): ACD/ChemSketch 2019.1.3 ACD/Labs 2019 Release (File version C05H41, Build 111302, 27 August 2019).