Annex I

List of the names, pharmaceutical form, strength of the veterinary medicinal product, animal species, route of administration, withdrawal periods, applicant in the Member States

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Austria	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Bulgaria	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Cyprus	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Czech Republic	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	DECTOMAX 10 mg/ml Solution for Injection for Cattle, Sheep and Pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Denmark	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Estonia	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Greece	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Spain	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	DECTOMAX 10 mg/ml Solution for Injection for Cattle, Sheep and Pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

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Finland	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
France	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution injectable pour bovins, ovins et porcins	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Hungary	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

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Ireland	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Dectomax 10 mg/ml Solution for Injection for Cattle, Sheep and Pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

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Iceland	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

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Latvia	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

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Lithuania	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days..

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Malta	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
The Netherlands	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

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Norway	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Poland	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Portugal	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Romania	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Sweden	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Slovenia	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Dectomax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Member State EU/EEA	Applicant	Name	Pharmaceutical form	INN/Strength	Animal species	Route of administration	Recommended dose	Withdrawal periods
Slovakia	Pfizer Limited Veterinary Medical Research & Development Sandwich Kent CT13 9NJ United Kingdom	Prontax 10 mg/ml solution for injection for cattle, sheep and pigs	Solution for injection	Doramectin 10 mg/ml	Cattle, sheep and pigs	Cattle - subcutaneous Sheep and pigs - intramuscular	Cattle and sheep - 1 ml per 50 kg bodyweight Pigs - 1 ml per 33 kg bodyweight	**CATTLE:** Meat and offal: - withdrawal period: 54 days. Milk: - The product is not permitted for use in lactating cows used to produce milk for human consumption. Do not use in dry dairy cows including pregnant dairy heifers within 60 days prior to calving. **SHEEP:** Meat and offal: - withdrawal period: 63 days. Milk: - The product is not permitted for use in lactating sheep used to produce milk for human consumption. Do not use in dry dairy ewes including pregnant dairy ewe lambs within 70 days prior to lambing. **PIGS:** Meat and offal: - withdrawal period 56 days.

Annex II

Scientific conclusions and grounds for amendment of the summary of product characteristics, labelling and package leaflet

Overall summary of the scientific evaluation of Prontax 10 mg/ml solution for injection for cattle, sheep, and pigs and associated names

1. Introduction

Prontax 10 mg/ml solution for injection for cattle, sheep, and pigs and associated names is a sterile solution for injection containing doramectin 10 mg per ml. Doramectin is an antiparasitic agent, isolated from the fermentation of selected strains derived from the soil organism *Streptomyces avermitilis*. It is a macrocyclic lactone and is closely related to ivermectin. Both compounds share a wide spectrum of antiparasitic activity and produce a similar paralysis in nematodes and parasitic arthropods.

In cattle, the product is intended for the treatment and control of gastrointestinal roundworms, lungworms, eyeworms, warbles, lice and mange mites. In pigs, the product is intended for the treatment of mange mites, gastrointestinal roundworms, lungworms, kidney worms and sucking lice. It protects pigs against infection or reinfection with *Sarcoptes scabiei* for 18 days.

In sheep, the product is intended for the treatment and control of *Psoroptes ovis* (sheep scab mite) and for the treatment and control of gastrointestinal roundworms and nasal bots.

The applicant Pfizer Limited has submitted an application for a decentralised procedure for Dectomax 10 mg/ml solution for cattle, sheep, and pigs. The Reference Member State was Ireland and the Concerned Member States were Austria, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Greece, Spain, Finland, France, Hungary, Iceland, Latvia, Lithuania, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia and Sweden. The application was submitted in accordance with the Article 13(1) of the Directive 2001/82/EC (i.e. an application for a generic product). The reference products for this generic application were Dectomax 1% w/v solution for injection for cattle and sheep and Dectomax 10 mg/ml solution for injection for pigs.

During the procedure, there was disagreement between the Reference Member State and Concerned Member States on the data presented to support the environmental risk assessment and the proposed withdrawal period for cattle. Two Concerned Member States (the Netherlands and France) considered that the authorisation of Prontax 10 mg/ml solution for injection for cattle, sheep, and pigs may present a potential serious risk to the environment and risk to the consumer. Consequently the matter was referred to the CVMP.

The CVMP was asked to give its opinion on the concerns raised by the Concerned Member States and to conclude on the benefit/risk balance for Prontax 10 mg/ml solution for injection for cattle, sheep, and pigs.

Before addressing the issues of disagreement the following two changes to the initial application that were made during the decentralised procedure and the CVMP referral procedure should be noted:

- During the decentralised procedure the proposed product name was changed from Dectomax 10 mg/ml solution for injection for cattle, sheep and pigs to Prontax 10 mg/ml solution for injection for cattle, sheep and pigs[1]

[1] During the decentralised procedure it was agreed that the authorisation of the generic product under the name "Dectomax" will not be issued until the reference product under the name "Dectomax" has either been withdrawn or re-named.

- During this referral procedure in Ireland the marketing authorisations of the two reference products Dectomax 1% w/v solution for injection for cattle and sheep and Dectomax 10 mg/ml solution for injection for pigs were transferred from Pfizer Healthcare Ireland to Elanco Animal Health, Eli Lilly and Company Limited and the names of the reference products in Ireland were changed to Zearl 10 mg/ml solution for injection for cattle and sheep and Zearl 10 mg/ml solution for injection for pigs).

2. Assessment of the data submitted

The referral for Prontax 10 mg/ml solution for injection for injection for cattle, sheep and pigs relates to the potential serious risks raised by France and the Netherlands regarding the environmental risk assessment (ERA) and by the Netherlands regarding the proposed withdrawal period for cattle.

The potential serious risks regarding the environment identified by France and the Netherlands are risks to dung fauna and *Daphnia magna* in accordance with the proposed instructions for use and a risk identified by the Netherlands due to the bioaccumulation potential linked to the determination of the log K_{OW} by using a test method, which was not considered appropriate for the active ingredient.

The potential serious risk regarding the withdrawal period identified by the Netherlands relates to the proposed withdrawal period of 54 days for slaughter in cattle, which is considered rather short taking into account the residue levels at injection site demonstrated in other studies than the one used as pivotal study, and that none of the residue depletion studies was performed according to existing guidelines for injection site residues.

Environmental risk assessment

An ERA was performed by the applicant in accordance with the VICH guidelines for Phase I and Phase II assessment adopted by the CVMP (CVMP/VICH/592/98-FINAL, CVMP/VICH/790/03-final) as well as the CVMP guideline on Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH Guidelines GL6 and GL38 (CVMP/ERA/418282/2005-corr).

The ERA for pigs can stop at Phase I in accordance with the VICH guideline. A Phase II, Tier A assessment was required for cattle and sheep.

The n-octanol/water coefficient (log Pow) was determined as 4.4 using the shake flask method. This method is however not considered suitable for substances with a log Pow above 4. The CVMP considered that the test method for the determination of the n-octanol/water partition coefficient was not appropriate. The log Pow of 4.4 can therefore only be considered as an indicator of the actual value.

As a result of a log Pow ≥ 4 the assessment of bioaccumulation is required. However, no bioaccumulation study was provided; also no assessment of secondary poisoning was performed. The CVMP considered that the available data package does not allow the assessment of bioaccumulation and therefore, bioaccumulation of doramectin cannot be ruled out.

Several studies and published literature on the toxicity to dung fauna were available. The risk characterisation for dung fauna was performed using Predicted Environmental Concentrations (PECs) for dung, which were derived using the metabolism study provided. The concentration of total doramectin residues excreted in cattle faeces peaked at 5 days after administration (562 µg/kg) and declined thereafter, accounting for 239 µg/kg at 14 days. The concentration of parent drug in faeces peaked at 3 days after administration (319 µg/kg) with a concentration of 133 µg/kg at 14 days (last sampling point). No data on the nature and rates of metabolites are available. Therefore no PEC refinement based on metabolism is possible, the risk assessment is based on total residues.

Based on the Predicted No Effect Concentrations (PNECs) derived from the LC50 of 1.34 µg/kg soil for horn flies (*Haematobia irritans*) and the NOEC of 4.0 µg/kg soil for dung beetles (*Ontophagus gazelle*) the resulting risk quotients (RQs) for both species were high (41940 and 1405, respectively, based on the amount of total residues in dung at day 5 after administration), indicating a high acute risk to dung insects in Tier A. Consequently a Tier B assessment should be performed. However, it is recognised that no harmonised guidance on how to conduct Tier B assessment studies for dung insects is currently available.

The risk characterisation for the aquatic environment was conducted based on an EC50 of 0.1 µg/l and a NOEC of 0.025 derived from an acute toxicity study of doramectin in Daphnia (*D. magna).* Based on Predicted Environmental Concentrations for surface water PECsw of 0.0005 µg doramectin/l surface water (run-off scenario) and PECsw of 0.209 µg doramectin/l surface water (direct excretion) an acute risk for Daphnia was identified in Tier A for both exposure scenarios with risk quotients (RQ) of 5 and 2090, respectively. After refinement of PECsw using the FOCUS model as recommended by CVMP guideline CVMP/ERA/418282/2005, it was concluded that aquatic organisms were not at risk from doramectin entering surface water bodies via run-off.
Further PEC refinement for the direct excretion scenario considering that peak excretion of total residues occurred on day 5 after administration and accounted for 7.8% of the administered dose, as well as based on sediment partitioning lead to a PECsw-refined-direct of 0.00049 µg/l, resulting in a RQ for Daphnia (4.9) still higher than 1. As the risk for daphnids could not be ruled out by PEC refinements Tier B assessment should be performed according VICH Guideline 38 for which a *Daphnia magna* reproduction study is required. However, this study is not available and cannot be requested in this referral.

Conclusions regarding the environmental impact

The applicant provided a targeted Phase II environmental risk assessment. The outcome of the ERA for cattle indicates that the RQs are higher than 1 in the Tier A assessment in two cases, namely daphnids (following direct excretion scenario) and dung fauna. According to the VICH Guideline 38 Phase II, a Tier B assessment is required. In the first case, the risk to daphnids could not be ruled out by performing several PEC refinements for the direct excretion scenario. A *Daphnia magna* reproduction study for conducting a Tier B assessment was not submitted in the ERA.

For the dung fauna, results of the Tier A assessment showed a very high RQ indicating an unacceptable acute risk. The supplementary data provided did not allow ruling out a medium to long-term risk to dung insects. As no harmonised guidance on how to conduct Tier B assessment studies for dung insects is currently available, risk mitigation measures to reduce exposure are considered necessary to overcome the identified risk.

In terms of bioaccumulation the log Pow value is not considered to be robust given the method employed (shake flask). The current data package does not allow the assessment of bioaccumulation and therefore, bioaccumulation of doramectin cannot be ruled out.

In respect to the environmental impact for the use of Prontax 10 mg/ml solution for injection in sheep the CVMP considered that according to the CVMP guidance, only cattle are concerned with the scenario "direct excretion into surface water". Therefore, this scenario was not considered for sheep. For the run-off scenario, as the highest PECcattle (0.84 µg/kg) is higher than the highest PECsheep (0.48 µg/kg), the conclusion from the cattle can be extrapolated to sheep. Aquatic organisms were considered not at risk from doramectin entering surface water bodies via run-off from use in sheep.

There are no specific studies available on dung fauna in sheep. In absence of data, it is proposed that the risk to dung fauna from sheep dung should be viewed as similar to the risk arising from treatment of cattle.

In order to address the identified risks for aquatic organisms and dung fauna as well as any remaining uncertainty regarding bioaccumulation the following risk mitigation measures are recommended:

The following text is proposed in section 4.5 (special precautions for use):

Doramectin is very toxic to dung fauna and aquatic organisms and may accumulate in sediments.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of doramectin (and products of the same anthelmintic class) in cattle and sheep.

The risk to aquatic ecosystems will be reduced by keeping treated cattle away from water bodies for two to five weeks after treatment.

The following text should be included in section 5.3 of the SPC (environmental properties):

Like other macrocyclic lactones, doramectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of doramectin may take place over a period of several weeks. Faeces containing doramectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.

Doramectin is very toxic to aquatic organisms and may accumulate in sediments.

Withdrawal period for cattle

The following MRLs have been established in the EU for the active substance doramectin (Table 1 of the Annex to Regulation (EU) No 37/2010 for all mammalian food producing species:

Muscle: 40 µg/kg

Fat: 150 µg/kg

Liver: 100 µg/kg

Kidney: 60 µg/kg

A withdrawal period of 63 days has been established for cattle for the reference product. Since the authorisation of the reference product the MRLs for the active substance, doramectin, were increased (to the levels shown above) and residue data were submitted to support a shorter withdrawal period for cattle.

Seven residue studies were made available and assessed by the CVMP for the evaluation of the withdrawal period for cattle.

All except one were GLP studies and were carried out with the same formulation (plus or minus radioactive tracer). Two of the residue studies were carried out using a different route of administration than the intended use of the product and were therefore not considered relevant for the evaluation.

Injection site was the tissue with the slowest rate of residue depletion and therefore results from the injection site are the basis from which derive the withdrawal period.

One of the residue studies did not include sampling at the injection site and was therefore not considered for the establishment of the withdrawal period.

The four remaining studies are summarised below.

A GLP tissue depletion study from 1989 was performed in calves (3 groups of 4 animals) following a single subcutaneous administration of doramectin at the recommended dose of 200 µg/kg bw.

Doramectin residues were below muscle MRL at the injection site 35 days after treatment.

The study is not in accordance with the CVMP Note for guidance on the approach towards harmonisation of withdrawal periods (EMEA/CVMP/036/95/final) and the guideline on injection site residues (EMEA/CVMP/542/03-FINAL) as the injection site was not sampled as recommended in the current guideline (i.e. with a separate core plus its surrounding tissue).

A GLP tissue depletion study from 1991 was performed in calves (18 animals) following a single subcutaneous administration of doramectin at the recommended dose of 200 µg/kg bw.

The study is not in accordance with the Note for guidance on injection site residues (EMEA/CVMP/542/03-FINAL) as the injection site was not sampled as recommended in the current guideline (i.e. with a separate core plus surrounding tissue) and the sample weight was low, only between 201-359 g.

Residues were found to be highly variable between animals. Doramectin residues were above the muscle MRL at the injection site in all animals at 35 days after administration, which is the last timepoint for which there is data.

A non-GLP tissue depletion study from 2003 was performed in cattle (24 animals) following a single subcutaneous administration of doramectin at the recommended dose of 200 µg/kg bw. The study report provided is very brief and the animal weights were not provided. The sample sizes of injection sites were not reported and surrounding ring samples were not collected. Injection sites at 35 and 56 days were not assayed.

Injection site residues were highly variable between animals. Individual doramectin residues were still above the muscle MRL at the injection site 49 days after administration, which is the last timepoint for which there is data.

A GLP tissue depletion study from 2002 performed in cattle (34 animals) following two subcutaneous administrations of doramectin at the recommended dose of 200 µg/kg bw with an interval of 7 days between doses.

Two subcutaneous administrations were performed instead of one leading to more injection sites. The groups included more animals than the minimum number recommended in the withdrawal period guideline (EMEA/CVMP/036/95/final): 6 animals per groups instead of 4. The weights of animals were below 250 kg. Only injection sites (500-600 g) were sampled.

The study was well conducted but not fully in accordance with the guideline on injection site residues (EMEA/CVMP/542/03-FINAL) since a surrounding ring sample was not collected. It is noted that the study (2002) predates the introduction of that guideline (2005). It cannot be excluded that actual injection sites were missed in this study.

The individual doramectin residues were below the MRL at the injection sites at 35 days after treatment.

This study was considered the most appropriate study on which to base a withdrawal period for meat and offal in cattle, although all relevant data should be taken into account in the assessment. Although this study was well conducted other studies cannot be disregarded unless there is a sound reason for doing so (e.g. evidence of mistakes). In particular the Committee considered that findings in other studies showing residues above the MRLs for muscle at the last measured timepoints of 35 and 49 days could not be ignored.

In addition, the studies showed high variability of residues in injection site samples and none fully comply with current guidelines.

Significant differences between studies were observed (range from 5 to 68-fold) which cannot be explained by different sample weights of injection sites.

Based on the data from the last study a withdrawal period of 54 days could be calculated. However, in view of the variability seen across the studies, the fact that none of the studies were in full compliance with the current guideline, and that in a number of studies residue levels remained above the MRL at the last timepoint, it was considered appropriate to add a safety margin of 30% to compensate for the uncertainties associated with the overall data package. This results in a withdrawal period of 70 days.

The Committee noted that the final version of the product information achieved during the Coordination Group procedure at day 210 includes specific warnings concerning conditions of use in dairy cattle. This was not part of this referral and therefore not considered by the CVMP.

Benefit-risk assessment

Prontax 10 mg/ml solution for injection for cattle, sheep and pigs contains doramectin as active ingredient. The application has been presented in accordance with Article 13(1) of Directive 2001/82/EC as amended, i.e. it is a generic application.

Benefit assessment

Benefits have not been subject of this referral; they were considered in the preceding decentralised procedure.

Direct benefits

The product has the same indications as the reference product. In cattle, the product is intended for the treatment and control of gastrointestinal roundworms, lungworms, eyeworms, warbles, lice and mange mites. In pigs, the product is intended for the treatment of mange mites, gastrointestinal roundworms, lungworms, kidney worms and sucking lice. It protects pigs against infection or reinfection with *Sarcoptes scabiei* for 18 days.

In sheep, the product is intended for the treatment and control of *Psoroptes ovis* (sheep scab mite) and for the treatment and control of gastrointestinal roundworms and nasal bots.

The internal and external parasites indicated for this product are recognised as causing significant loss of production and negatively impact on animal welfare.

The product is applied by a single subcutaneous or intramuscular injection.

Indirect benefits

Additional benefits of this product are the same as the reference product.

The product has claims for persistent efficacy ranging from 18 to 42 days. The need for repeat treatments is reduced relative to other anthelmintic products.

The product has dual action against endo- and ecto-parasites and may reduce the number of treatments with different pharmaceutical products.

Risk assessment

As for the benefits, quality of the product was not discussed by CVMP as part of this referral.

In general terms, as for the benefits, that except for the risks identified in particular by the referral (ERA and withdrawal period in cattle) all other risks are expected to be the same as for the reference product and have not been discussed in any detail by CVMP.

In terms of environmental safety, in addition to the fact that the current data package does not allow to rule out bioaccumulation of doramectin, a risk to the aquatic compartment has been identified based on available toxicity data (acute toxicity for *Daphnia magna*) as well as a risk to dung fauna exposed to residue-containing dung when the product is used in accordance with the recommended posology. Therefore, appropriate risk mitigation measures are considered necessary, as specified in the product information.

In terms of consumer safety, a withdrawal period for meat and offal in cattle of 70 days is recommended.

Conclusions on the benefit-risk balance

The benefit-risk evaluation is deemed to be positive provided that (1) the recommended risk mitigation measures are added to the product literature regarding risk to aquatic organisms and dung fauna and (2) the withdrawal period for meat and offal in cattle should be set at 70 days.

Grounds for amendments of the product information

Whereas:

- On the basis of environmental risk assessment data submitted with the application it was considered that in order to address the identified risks for aquatic organisms and dung fauna as well as any remaining uncertainty regarding bioaccumulation risk mitigation measures should be applied;
- On the basis of the residue depletion data in cattle submitted with the application is was considered that a 70-day withdrawal period should be established in cattle meat and offal;

the CVMP concluded that the objections raised by the Netherlands and France should not prevent the granting of a marketing authorisation for Prontax 10 mg/ml solution for injection for cattle, sheep and pigs and associated names (see annex I) as the overall benefit-risk balance for the product is positive subject to the recommended changes in the product information set out in annex III.

Annex III

Amendments in the relevant sections of the summary of product characteristics, labelling and package leaflet

The valid Summary of Product Characteristics, Labelling and Package Leaflet are the final versions achieved during the Coordination Group procedure with the following amendments:

Add the following text in the relevant sections of the product information:

Summary of Product Characteristics

4.5 Special precaution for use

…….

Other precautions

Doramectin is very toxic to dung fauna and aquatic organisms and may accumulate in sediments.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of doramectin (and products of the same anthelmintic class) in cattle and sheep.

The risk to aquatic ecosystems will be further reduced by keeping treated cattle away from water bodies for two to five weeks after treatment.

4.11 Withdrawal Period(s)

CATTLE:

Meat and offal: 70 days

…….

5.3 Environmental properties

Like other macrocyclic lactones, doramectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of doramectin may take place over a period of several weeks. Faeces containing doramectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.

Doramectin is very toxic to aquatic organisms and may accumulate in sediments.

…….

Labelling:

8. Withdrawal period

CATTLE:

Meat and offal: 70 days

…….

9. Special warnings, if necessary

Doramectin is very toxic to dung fauna and aquatic organisms and may accumulate in sediments.

Like other macrocyclic lactones, doramectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of doramectin may take place over a period of several weeks. Faeces containing doramectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of doramectin (and products of the same anthelmintic class) in cattle and sheep.

The risk to aquatic ecosystems will be further reduced by keeping treated cattle away from water bodies for two to five weeks after treatment.

…….

Package leaflet:

10. Withdrawal period

CATTLE:

Meat and offal: 70 days

…….

12. Special warnings

Doramectin is very toxic to dung fauna and aquatic organisms and may accumulate in sediments.

Like other macrocyclic lactones, doramectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of doramectin may take place over a period of several weeks. Faeces containing doramectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of doramectin (and products of the same anthelmintic class) in cattle and sheep.

The risk to aquatic ecosystems will be further reduced by keeping treated cattle away from water bodies for two to five weeks after treatment.

…….