

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Econor 50% premix for medicated feed for pigs
Econor 10% premix for medicated feed for pigs
Econor 1% premix for medicated feed for pigs
Econor 0.5% premix for medicated feed for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Econor contains valnemulin in the form of valnemulin hydrochloride.

	Econor 50%	Econor 10%	Econor 1%	Econor 0.5%
Active substance Valnemulin hydrochloride	532.5 mg/g	106.5 mg/g	10.65 mg/g	5.325 mg/g
equivalent to valnemulin base	500 mg/g	100 mg/g	10 mg/g	5 mg/g
Excipients	Hypromellose and talc	Hypromellose and talc Colloidal anhydrous silicum Isopropyl myristate Lactose	Hypromellose and talc Colloidal anhydrous silicum Isopropyl myristate Lactose	Hypromellose and talc Colloidal anhydrous silicum Isopropyl myristate Lactose

3. PHARMACEUTICAL FORM

Premix for medicated feedingstuff

4. PHARMACOLOGICAL PROPERTIES

4.1 Pharmacodynamic properties:

ATCvet code: QJ01XX94

Pharmacotherapeutic group: Antibacterial for systemic use

Valnemulin is an antibiotic belonging to the pleuromutilin group, which acts by the inhibition of the initiation of protein synthesis at the level of the bacterial ribosome.

Valnemulin has activity against a range of bacteria including those responsible for enteric and respiratory disease in pigs.

Valnemulin shows high activity against *Mycoplasma spp.* and spirochaetes such as *Brachyspira hyodysenteriae* and *Brachyspira pilosicoli*.

Species	MIC (Range) (µg/ml)	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
<i>Mycoplasma hyopneumoniae</i>	0.0009 – 0.125	0.0025	0.01
<i>Brachyspira hyodysenteriae</i>	0.025 – 4.0	0.2	1.0
<i>Brachyspira pilosicoli</i>	0.0156 – 2.0	0.0156	0.5
<i>Lawsonia intracellularis</i>	< 2.0 is the concentration likely to cause significant inhibition of intracellular growth		

Valnemulin has little activity against *Enterobacteriaceae*, such as *Salmonella spp.* and *Escherichia coli*.

4.2 Pharmacokinetic properties:

In pigs, after a single oral dose of radiolabelled material >90% absorption was demonstrated. Maximum plasma concentrations (C_{max}) of radio-labelled or ‘cold’ material were obtained 1-4 hours after dosing (T_{max}) with a plasma half-life (t_{1/2}), estimated from non-radioactive data, between 1 and 4½ hours. A linear relationship between concentration and dose administered was established.

After repeat dosing, slight accumulation occurred, but a steady state was achieved within 5 days.

Because of a marked ‘first pass’ effect, plasma concentrations are affected by the method of administration, but valnemulin is highly concentrated in tissues, particularly the lungs and liver, relative to plasma. Five days after the last of 15 doses of radiolabelled valnemulin administered to pigs, the concentration in liver was >6 times that in plasma. Two hours after withdrawal of Premix given in feed twice daily for 4 weeks at a dose of 15 mg/kg bodyweight/day, liver concentration was 1.58 µg/g and lung concentration 0.23 µg/g whereas concentrations in plasma were below the limit of detection.

In pigs valnemulin is extensively metabolised and excretion of parent molecule and metabolites occurs mainly via bile. 73% - 95% of the daily dose of total radioactivity was recovered from the faeces. The plasma half-life was 1.3 – 2.7 hours, and the majority of the total radio-activity administered was excreted within 3 days of the last administration.

5. CLINICAL PARTICULARS

5.1 Target species

Pigs

5.2 Indications for use

Econor 10% and 50%:

The treatment and prevention of swine dysentery.

The treatment of clinical signs of porcine proliferative enteropathy (ileitis).

The prevention of clinical signs of porcine colonic spirochaetosis (colitis) when the disease has been diagnosed in the herd.

Treatment and prevention of swine enzootic pneumonia. At the recommended dosage of 10 - 12 mg/kg bodyweight lung lesions and weight loss are reduced, but infection with *Mycoplasma hyopneumoniae* is not eliminated.

Econor 0.5% and 1%:

For the treatment and prevention of swine dysentery.

The treatment of clinical signs of porcine proliferative enteropathy (ileitis).

The prevention of clinical signs of porcine colonic spirochaetosis (colitis) when the disease has been diagnosed in the herd.

5.3 Contraindications

Do not administer the product to pigs receiving ionophores.

Valnemulin should not be administered to rabbits because of its toxicity in this species.

5.4 Undesirable effects (frequency and seriousness)

Medication of pigs with Econor has led to the occurrence of adverse reactions in the European Union. Of the cases reported in 1999-2000, the majority occurred in Denmark and Sweden (one case each in Finland and Ireland). In these countries, the incidence ranged from 0.03 to 1.76% of all pigs treated. On affected farms, one third of the pigs treated were affected, with a mortality of 1%. Affected pigs are pyrexia, exhibit inappetence, and in severe cases become incoordinated, ataxic and may become recumbent. A percentage of such pigs may also suffer oedema or erythema (posterior in distribution), and palpebral oedema. The reaction has been studied in controlled trials in susceptible animals. Mortality was less than 1%, but might be increased as a result of secondary infections.

In the case of an adverse reaction, immediate withdrawal of medication is recommended. Severely affected pigs should be removed to clean dry pens and given symptomatic treatment, including treatment for concurrent disease.

An epidemiological survey has indicated that there is likely to be an association between the susceptibility to adverse reactions and the Danish and Swedish Landrace breeds, and their crossbreds thereof, especially younger pigs.

Valnemulin is well-accepted in feed, but administered at concentrations above 200 mg valnemulin / kg feed may result in transient reduction in food consumption associated with unpalatability during the first few days of feeding.

5.5 Special precaution(s) for use

None

5.6 Use during pregnancy and lactation

Whilst studies in rats and mice have not produced any evidence of teratogenic effect, the safety in pregnant and lactating sows has not been established.

5.7 Interaction with other medicinal products and other forms of interaction

Valnemulin has been shown to interact with ionophores such as monensin, salinomycin and narasin and may result in signs indistinguishable from an ionophore toxicosis. Animals should not receive products

containing monensin, salinomycin or narasin, during or at least 5 days before or after treatment with valnemulin. Severe growth depression, ataxia, paralysis or death may result.

5.8 Posology and method of administration

In feed use.

The uptake of medicated feed depends on the clinical condition of the animal. In order to obtain the correct dosage the concentration of Econor has to be adjusted. Inclusion levels may also need to be increased in older pigs or pigs on restricted feed to achieve target dosage.

Indication	Dosage (active substance)	Application period of medicated feed as the sole daily ration	Application in feed
<u>Treatment of</u> Swine Dysentery	3-4 mg/kg bodyweight/day	Minimum of 7 days and up to 4 weeks or until signs of disease disappear	Incorporation of 75 mg active substance per kg feed with: Econor 50% - 150 mg / kg feed Econor 10% - 750 mg / kg feed Econor 1% - 7.5 g / kg feed Econor 0.5% - 15 g / kg feed

This dose level is effective in the treatment of clinical disease, but higher dosages or longer duration of treatment may be necessary for complete elimination of infection. It is important to institute medication as early as possible in an outbreak of swine dysentery. If there is no response to treatment within 5 days, the diagnosis should be re-established.

Indication	Dosage (active substance)	Application period of medicated feed as the sole daily ration	Application in feed
<u>Treatment of</u> Clinical signs of Porcine Proliferative Enteropathy (ileitis)	3-4 mg/kg bodyweight/day	2 weeks or until signs of disease disappear	Incorporation of 75 mg active substance per kg feed with: Econor 50% - 150 mg / kg feed Econor 10% - 750 mg / kg feed Econor 1% - 7.5 g / kg feed Econor 0.5% - 15 g / kg feed

This dose level is effective under normal situation in the treatment of clinical signs of disease, but higher dosages or longer duration of treatment may be necessary for complete elimination of infection. It is important to institute medication as early as possible in an outbreak of porcine proliferative enteropathy. If there is no response to treatment within 5 days, the diagnosis should be re-established. For severely affected animals which fail to respond to treatment within 3-5 days, parenteral treatment should be considered.

Indication	Dosage (active substance)	Application period of medicated feed as the sole daily ration	Application in feed
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<u>Prevention of</u>			Incorporation of 25 mg active substance per kg feed with:
Swine Dysentery	1.0 – 1.5 mg/kg bodyweight/day	minimum of 7 days and up to 4 weeks	Econor 50% - 50 mg / kg feed Econor 10% - 250 mg / kg feed Econor 1% - 2.5 g / kg feed Econor 0.5% - 5 g / kg feed
Clinical signs of Porcine Colonic Spirochaetosis (colitis)		4 weeks	

Long term preventative use of valnemulin should be avoided by improving management practice and thorough cleansing and disinfection. Consideration should be given to the eradication of infection from the farm.

Indication	Dosage (active substance)	Application period of medicated feed as the sole daily ration	Application in feed
<u>Treatment and Prevention of</u> Swine Enzootic Pneumonia	10 – 12 mg/kg bodyweight/day	Up to 3 weeks	Incorporation of 200 mg active substance per kg feed with : Econor 50% - 400 mg/kg feed Econor 10% - 2 g/kg feed

Secondary infection by organisms such as *Pasteurella multocida* and *Actinobacillus pleuropneumoniae* may complicate enzootic pneumonia and require specific medication.

Mixing Instructions:

The product has been shown to be stable to the pelleting process at temperatures of 75°C. Aggressive pelleting conditions such as temperatures in excess of 80°C, and the use of abrasive substances for pre-mixture should be avoided.

Econor 50%

mg Econor 50% premix/kg feed = Dosage required (mg/kg) x 2 x bodyweight (kg)/Daily feed intake (kg).
To achieve good mixture and homogeneity of incorporation, the use of pre-mixture is required. The required quantity of product is thoroughly mixed with a feed ingredient of similar physical nature (e.g. wheat middlings) in the proportion: 1 part Econor 50% premix to 20 parts feed ingredient.

Econor 10%

mg Econor 10% premix/kg feed = Dosage required (mg/kg) x 10 x bodyweight (kg)/Daily feed intake (kg).

To achieve good mixture and homogeneity of incorporation, the use of a pre-mixture is recommended. The required quantity of product is thoroughly mixed with a feed ingredient of similar physical nature (e.g. wheat middlings) in the proportion: 1 part Econor 10% premix to 10 parts feed ingredient.

Econor 1%

mg Econor 1% premix/kg feed = Dosage required (mg/kg) x 100 x bodyweight (kg)/Daily feed intake (kg).

To achieve good mixture and homogeneity of incorporation, especially when product is incorporated at a rate less than 5 kg/tonne feed, the use of a pre-mixture is recommended. The required quantity of product is thoroughly mixed with a feed ingredient of similar physical nature (e.g. wheat middlings) in the proportion: 1 part Econor 1% premix to 10 parts feed ingredient.

Econor 0.5%

mg Econor 0.5% premix/kg feed = Dosage required (mg/kg) x 200 x bodyweight (kg)/Daily feed intake (kg).

5.9 Overdose

Toxic signs have not been seen in pigs given 5 times the recommended dose.

5.10 Special warnings for each target species

Adverse drug reactions have occurred following the use of Econor. Their occurrence may be principally restricted to the Scandinavian countries and appears to be mainly associated with breed mixes that include Danish and/or Swedish Landrace. Extreme care should therefore be taken in the use of Econor in pigs of Scandinavian origin especially of the Danish and Swedish Landrace breeds, and their crossbreeds thereof.

5.11 Withdrawal period

1 day

5.12 Special precautions to be taken by the person administering the veterinary medicinal product to animals.

When mixing the product and handling the final feed containing the product, direct contact with the skin and mucous membranes should be avoided. In case of accidental ingestion, seek medical advice immediately and show the product label. People with known hypersensitivity to valnemulin should administer the product with caution.

6. PHARMACEUTICAL PARTICULARS

6.1 Major Incompatibilities

None known

6.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years

Shelf-life when incorporated into meal feed and protected from light and moisture: 3 months

Shelf-life when incorporated into pelleted feed and protected from light and moisture: 3 weeks

6.3 Special precautions for storage

Store below 25°C.

In case of aluminium-lined bags, store product in the original container.

In case of polyethylene bags, store the product in the original container within the outer carton and protected from light and moisture.

Part-used containers should be tightly closed following dispensing.

6.4 Nature and contents of container

Econor 10%, Econor 50%:

1 x 1 kg and 1 x 25 kg low density polyethylene bags packed in cardboard carton,
1 x 1 kg and 1 x 25 kg aluminium-lined plastic bags.

Econor 1%:

1 x 1 kg, 1 x 2.5 kg and 1 x 25 kg low density polyethylene bags packed in cardboard carton,
1 x 1 kg, 1 x 2.5 kg and 1 x 25 kg aluminium-lined plastic bags.

Econor 0.5%:

1 x 5 kg and 1 x 25 kg aluminium-lined plastic bags.

6.5 Special precautions for the disposal of unused medicinal product or waste materials, if any

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. NAME OR CORPORATE NAME AND ADDRESS OR REGISTERED PLACE OF BUSINESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Animal Health Austria GmbH
Biochemiestrasse 10
A-6250 Kundl
Austria

Prohibition of sale, supply and / or use:

Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.

Marketing Authorisation number(s)

EU/2/98/010/001-024

Date of first authorisation/renewal of the authorisation

12 March 1999 / <*Date of Commission Decision*>

Date of revision of the text

<*Date of Commission Decision*>