The new meloxicam range for cattle, pigs & horses

Melovem® 5 mg/ml
Melovem® 20 mg/ml
Melovem® 30 mg/ml
The new Melovem® range

+ Many indications for cattle, horses and pigs
+ Accurate dosing

Dopharma has obtained an EU-marketing authorisation for two new products:
+ Melovem® 20 mg/ml
+ Melovem® 30 mg/ml

Together with the already successful Melovem® 5 mg/ml, Dopharma now offers a unique meloxicam range.

With Melovem® 5 mg/ml it is possible to accurately treat animals with a low bodyweight. The higher concentrations however are very suitable for the treatment of larger animals, without the need to inject large volumes. Melovem® 20 mg/ml is authorised for cattle, pigs as well as horses and is licensed for intravenous administration. Melovem® 30 mg/ml is a unique registration in the EU: a high concentrated meloxicam injection indicated for cattle as well as pigs.

<table>
<thead>
<tr>
<th>Animal Species</th>
<th>Melovem® 5 mg/ml EU/2/09/098/001</th>
<th>Melovem® 20 mg/ml EU/2/09/098/002-004</th>
<th>Melovem® 30 mg/ml EU/2/09/098/005-007</th>
</tr>
</thead>
</table>
| **Indications** | • respiratory infections  
• diarrhoea  
• pain relief after dehorning | • respiratory infections  
• diarrhoea  
• pain relief after dehorning  
• acute mastitis | • respiratory infections  
• diarrhoea  
• pain relief after dehorning  
• acute mastitis |
| **Dosage** | 1 ml / 10 kg BW  
1 ml / 40 kg BW  
1 ml / 60 kg BW | 1 ml / 10 kg BW  
1 ml / 40 kg BW  
1 ml / 60 kg BW | 1 ml / 10 kg BW  
1 ml / 40 kg BW  
1 ml / 60 kg BW |
| **Administration** | s.c.  
s.c. / i.v.  
s.c. | s.c.  
s.c. / i.v.  
s.c. | s.c.  
s.c. / i.v.  
s.c. |
| **WT meat and offal** | 15 days  
15 days  
15 days | 15 days  
15 days  
15 days | 15 days  
15 days  
15 days |
| **WT milk** | -  
5 days  
5 days | -  
5 days  
5 days | -  
5 days  
5 days |

<table>
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<tr>
<th>Animal Species</th>
<th>Melovem® 5 mg/ml EU/2/09/098/001</th>
<th>Melovem® 20 mg/ml EU/2/09/098/002-004</th>
<th>Melovem® 30 mg/ml EU/2/09/098/005-007</th>
</tr>
</thead>
</table>
| **Indications** | • musculo-skeletal disorders  
• colic | • non-infective locomotor diseases  
• pain relief associated with castration  
• non-infective locomotor diseases  
• acute mastitis  
• non-infective locomotor diseases  
• acute mastitis | • non-infective locomotor diseases  
• acute mastitis  
• non-infective locomotor diseases  
• acute mastitis |
| **Dosage** | 1 ml / 12.5 kg BW  
1 ml / 50 kg BW  
1 ml / 75 kg BW | 1 ml / 12.5 kg BW  
1 ml / 50 kg BW  
1 ml / 75 kg BW | 1 ml / 12.5 kg BW  
1 ml / 50 kg BW  
1 ml / 75 kg BW |
| **Administration** | i.m.  
i.m.  
i.m. | i.m.  
i.m.  
i.m. | i.m.  
i.m.  
i.m. |
| **WT meat and offal** | 5 days  
5 days  
5 days | 5 days  
5 days  
5 days | 5 days  
5 days  
5 days |

* See SPC for details
Inflammation

The body’s response to cell injury

Inflammation is the body’s response to cell injury caused by stimuli of various origin e.g. trauma, infection or irritants. When a cell membrane becomes damaged phospholipids are released starting the arachidonic acid cascade. As a result prostaglandins, thromboxanes and leucotrienes are formed in inflamed tissues.

Two isoforms of the enzyme cyclooxygenase, COX-1 and COX-2, are responsible for the production of prostaglandins and thromboxanes. The enzyme lipoxygenase is responsible for the production of leucotrienes.

**COX-1**
COX-1 is a constitutive form of cyclooxygenase or a so called housekeeping enzyme and has a mainly homeostatic function. It is responsible for the production of cytoprotective prostaglandins and has an important role in the protection of the gastric mucosa. Furthermore COX-1 has an important role in controlling renal blood flow and platelet aggregation.

**COX-2**
COX-2 is an inducible form of cyclooxygenase and is mainly responsible for the elevated level of prostaglandins in inflamed tissues. These pro-inflammatory prostaglandins are largely responsible for the undesirable effects of the inflammatory reaction such as pain and fever.

**NSAIDs**
Non-Steroidal Anti-inflammatory Drugs (NSAIDs) inhibit the cyclooxygenase enzymes. Toxicity of NSAIDs is predominately related to COX-1 inhibition.
Meloxicam

One of the most widely used NSAIDs in animals

+ Long acting
+ Potent anti-inflammatory drug\(^1\)
+ Preferential COX-2 inhibitor; low ulcerogenic potential\(^1\)
+ Analgetic effect

Meloxicam is a COX-2 preferential NSAID of the oxicam class. This means that meloxicam mainly inhibits COX-2 thereby exerting anti-inflammatory, anti-exudative, analgetic, and antipyretic effects.\(^2,4\)

Administered in the registered dose, meloxicam has only a minor effect on COX-1.

+ Antipyretic effect
+ Anti-endotoxic effect
+ Administration is tolerated well\(^2,3\)
+ Better animal welfare

Its marked anti-endotoxic activity has also been shown: meloxicam inhibits the production of thromboxane B2, induced by intravenous administered \textit{E. coli} endotoxin in calves and pigs and the intramammary administration of \textit{E. coli} endotoxin in lactating cows.\(^5,6,7\)
Meloxicam

Pharmacokinetic properties

+ Long plasma half-life; long acting
+ Good bioavailability

After intramuscular or subcutaneous administration, meloxicam is usually well absorbed. Species differences occur. In general, the volume of distribution is low for NSAIDs in most species. This is probably caused by the extreme binding to plasma proteins (more than 98%); meloxicam is no exception to this phenomenon.

Duration of action
The therapeutic effect of NSAIDs exceeds the elimination half-life. NSAIDs penetrate readily into inflamed tissue because of increased vascular permeability. Furthermore as a result of an acidic environment in inflamed tissue, NSAIDs are slowly cleared from inflammatory exudate (“ion trapping”). In cattle it has been shown that a single subcutaneous dose of meloxicam was clinically effective for 3 days.

Despite the difference between duration of action and elimination half-life, the half-life can be used to compare different NSAIDs.

<table>
<thead>
<tr>
<th>Animal Species</th>
<th>Meloxicam</th>
<th>Flunixine</th>
<th>Ketoprofen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>26 h* (sc) 17.5 h* (im)</td>
<td>4 h (iv)</td>
<td>2.5 h (im)</td>
</tr>
<tr>
<td>Pig</td>
<td>2.5 h (im)</td>
<td>5 h (im)</td>
<td>2 h (im)</td>
</tr>
<tr>
<td>Horse</td>
<td>8.5 h (iv)</td>
<td>2 h (iv)</td>
<td>1 h (iv)</td>
</tr>
</tbody>
</table>

* Elimination half-life in cattle for young stock and dairy cattle respectively.
Melovem® 5 mg/ml

Composition: meloxicam 20 mg/ml, benzyl alcohol 80 mg/ml.

Uses:

Contraindications:
- Do not use in animals suffering from impaired hepatic, cardiac or renal function and haemorrhagic disorders, or where there is evidence of ulcerogenic gastrointestinal lesions. Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.

Special precautions for use in animals
- Do not use in pregnant animals.
- Do not use in pregnant animals.

Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.

Withdrawal periods
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.
- Do not use in pregnant animals.

References
5. Arimura S, Hirose H, Hiraoka M, Horie H. Pharmacokinetics of meloxicam in cows with mastitis – metritis – agalactia syndrome with appropriate antibiotic therapy. - Use during pregnancy or lactation Cattle. Use can be used during pregnancy. lation. With this veterinary medicinal product does not require any special temperature storage condition. Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products. Any unsuitable veterinary medicinal products or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements. Marketing authorisation number: EU/2019/001-007 Marketing authorisation holder: Dopharma Research B.V., Zalum 26, 4941 VK, Raamsdonkse, The Netherlands.

Melovem® 30 mg/ml

Composition: meloxicam 30 mg/ml, benzyl alcohol 80 mg/ml.

Uses:
- For the relief of post-operative pain following dehorning in calves. Pigs: For use in non-infectious locomotor disorders to reduce the symptoms of lameness and inflammation. For adjunctive therapy in the treatment of purulent septicemia and trauma (mucous-membrane-ulcerative syndrome) with appropriate antibiotic therapy. - Use during pregnancy or lactation Cattle. Use can be used during pregnancy. lation. With this veterinary medicinal product does not require any special temperature storage condition. Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products. Any unsuitable veterinary medicinal products or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements. Marketing authorisation number: EU/2019/001-007 Marketing authorisation holder: Dopharma Research B.V., Zalum 26, 4941 VK, Raamsdonkse, The Netherlands.

Melovem® 20 mg/ml

Composition: meloxicam 20 mg/ml, benzyl alcohol 80 mg/ml.

Uses:
- For the relief of post-operative pain following dehorning in calves. Pigs: For use in non-infectious locomotor disorders to reduce the symptoms of lameness and inflammation. For adjunctive therapy in the treatment of purulent septicemia and trauma (mucous-membrane-ulcerative syndrome) with appropriate antibiotic therapy. - Use during pregnancy or lactation Cattle. Use can be used during pregnancy. lation. With this veterinary medicinal product does not require any special temperature storage condition. Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products. Any unsuitable veterinary medicinal products or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements. Marketing authorisation number: EU/2019/001-007 Marketing authorisation holder: Dopharma Research B.V., Zalum 26, 4941 VK, Raamsdonkse, The Netherlands.