Penethamate:
A specialist technology designed for mastitis

Unique pharmacokinetic profile

The active of Mamyzin®, penethamate hydriodide, is a prodrug of Penicillin G.

Unlike salts of penicillin, penethamate
• Is not ionized at blood pH, because it is a weak basis (pKa=8.4)
• Possesses a high lipid solubility

This profile substantially enhances the penetration of Mamyzin® through lipid membranes, and therefore its migration into target tissues.

Unique ion trapping mechanism

Superior excretion into milk

Mamyzin® concentrates where it’s needed, in the udder.
Penethamate: A specialist technology designed for mastitis

**Mamyzin® is udder tissue preferential**

The rapid uptake of Mamyzin results in peak concentration in milk within 4-6 hours.

![Mamyzin concentration in udder over time (IM administration of 15-7.5-7.5mg/kg)](image)

**High concentrations in target tissues**

Mamyzin achieves levels of penicillin in milk which are over ten times higher than those obtained from sodium benzylpenicillin or procaine penicillin.

![Milk concentrations of Mamyzin® and Procaine Penicillin following IM injection of 10,000 IU/kg](image)

Penethamate is a time dependent bactericidal antibiotic with a spectrum of activity primarily against non-penicillinase producing gram positive cocci.

Penethamate treatment is effective against mastitis caused by streptococci such as Streptococcus uberis, Streptococcus dysgalactiae and Streptococcus agalactiae and penicillin-sensitive staphylococci such as Staphylococcus aureus, and Corynebacteria.
Penethamate: The drug of choice for Gram positive mastitis

Low MIC values...

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>C: Clinical</th>
<th>S: Subclinical</th>
<th>n</th>
<th>MIC 90 (µg/ml)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus</td>
<td>S+C</td>
<td>29</td>
<td></td>
<td>0.07</td>
<td>1</td>
</tr>
<tr>
<td>(Including Str. dysgalactiae, Str. agalactiae and Str. Uberis)</td>
<td>S+C</td>
<td>251</td>
<td></td>
<td>0.12</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>170</td>
<td></td>
<td>0.12</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>S+C</td>
<td>29</td>
<td></td>
<td>0.12</td>
<td>4</td>
</tr>
<tr>
<td>Non penicillinase producing</td>
<td>C</td>
<td>239</td>
<td></td>
<td>0.06</td>
<td>5</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>S+C</td>
<td>585</td>
<td></td>
<td>≤0.07</td>
<td>6</td>
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<tr>
<td></td>
<td>S+C</td>
<td>40</td>
<td></td>
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<tr>
<td></td>
<td>S+C</td>
<td>48</td>
<td></td>
<td>0.08</td>
<td>8</td>
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<tr>
<td>Actinomyces pyogenes</td>
<td>C</td>
<td>16</td>
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<td>0.06</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>103</td>
<td></td>
<td>0.03</td>
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</tr>
</tbody>
</table>


Effective intracellular killing of mastitis pathogens

Mamyzin® is capable of entering mammary epithelial cells and is effective at killing intracellular mastitis pathogens at concentrations achieved in milk following the recommended dosage.

Transmission electron micrographs of mastitis pathogens internalized into mammary epithelial cells before and after addition of penethamate hydriodide. Streptococcus uberis (a, b), Streptococcus dysgalactiae subsp. dysgalactiae (c, d) and Staphylococcus aureus (e, f) before (a, c, and e) and after treatment with penethamate hydriodide (32 µg/mL, b, d and f). Arrows indicate viable bacteria.

... easily achieved in milk

Following IM administration, the concentration of penethamate in the milk rises to up to 800 ng/ml. This represents approximately 10 times the maximum MIC quoted in the literature.

Mamyzin concentration in udder over time
**Mamyzin® achieves high cure rates**

- **In clinical mastitis**
  - Mamyzin® achieves up to 81.2% cure rates in gram-positive mastitis.\(^5\)
  - Mamyzin® has demonstrated up to 87.7% cure rates against Strep. uberis mastitis.\(^5\)

- **In subclinical mastitis**
  - Treatment of subclinical mastitis with Mamyzin® results in bacteriological cure in 59.5% of quarters and 52.2% of cows.\(^6\)

**Mamyzin® improves milk quality**

- **Milk Somatic Cell Count (all 4 quarters)**
  - Treatment of clinical mastitis with Mamyzin® is followed by a marked reduction of SCC.\(^7\)
  - Quarters that were cured following a treatment with Mamyzin® showed a significant and sustained decrease of SCC.\(^6\)
Mamyzin®
in the treatment of heifer mastitis

- **Reduced risk of mastitis**

89 dairy heifers from herds with high prevalence of Streptococcus spp. mastitis. 54 were treated with a single dose of 15 mg/kg Mamyzin® 7 days before expected calving date; 35 were untreated (controls).

Heifers treated with Mamyzin showed a reduced incidence of mastitis at calving (p<0.05). Treated heifers had almost half the risk of mastitis as control heifers.8

- **Increased milk yield**

Sixty dairy heifers from herds with high prevalence of Staphylococcus aureus mastitis. Treated at parturition with 10g of Mamyzin and then with 5g 24 h later. The control group received no treatment.

There were fewer intramammary infections in the first 3 weeks after calving in Mamyzin®-treated heifers. These heifers also produced significantly more milk during the first 15 weeks of lactation than untreated heifers (up to 323 kg more milk in the first 200 d of lactation).9
Mamyzin’s exceptional properties make it a highly effective treatment of clinical and subclinical mastitis caused by gram positive bacteria.

- Crosses the blood–milk barrier for high penetration into udder tissue
- Reaches persistently higher concentrations in the udder than other penicillins
- Achieves excellent cure rates against target pathogens with rapid reduction of SCC
- Once-daily intramuscular injection conveniently treats all 4 quarters