BALANCED CHOICE

xefo®
(Lornoxicam)

AN NSAID WITH A BALANCED COX-1 & COX-2 INHIBITORY EFFECT
A balanced cox-1 and cox-2 inhibitor

Relative selectivity of agents as inhibitors of cox-1 and cox-2

Approximately isopotent inhibition of cox-1 and cox-2 by Lornoxicam (in vitro)

Metabolism and Bioavailability of Lornoxicam

- Peak plasma levels: 1 - 2 h
- Bioavailability: 90%
- With food intake: ≤ 70%
- Plasma binding: 99%
- Plasma t1/2: 3 h
- Elimination urine: 33%
- Elimination faeces: 66%
- Liver metabolism: 100%

Plasma concentration time curve for Lornoxicam

- Lornoxicam’s shorter half-life results in a more rapid clearance and reduced risk of accumulation.
- Completely metabolised to inactive derivatives, for reduced accumulation.
A balanced COX-1 and COX-2 inhibitory molecule with high analgesic potency

**Efficacy superior to Diclofenac and Naproxen** (7,8,9,10)

![Decrease in Ritchie Arthritic Index from baseline (%)](image)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Decrease in Ritchie Arthritic Index from baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lornoxicam, 8 mg bid</td>
<td>-20</td>
</tr>
<tr>
<td>Diclofenac, 50 mg bid</td>
<td>-15</td>
</tr>
<tr>
<td>Lornoxicam, 8 mg bid</td>
<td>-30</td>
</tr>
<tr>
<td>Naproxen, 500 mg tid</td>
<td>-25</td>
</tr>
</tbody>
</table>

**Lornoxicam vs. Tramadol in post-operative pain** (12)

![Total pain relief](image)

Xefo IM is significantly superior to Tramadol IM in the treatment of post-operative pain

Patients receiving a single dose of Xefo IM 16 mg experienced significantly greater total pain relief than patients receiving Tramadol 100 mg 8 hours following the initial dose after arthroscopic reconstruction of the anterior cruciate ligament.

**Xefo has fewer adverse events than Tramadol** (12)

![Adverse events](image)

Significantly fewer adverse events with Xefo compared with Tramadol for post-operative pain (p=0.003)

Distribution of adverse events during treatment with Xefo Vial (IM) (single 16 mg dose followed by 8 mg) or Tramadol (IM) (100 mg tid) for 3 days after anterior cruciate ligament repair.

**Lornoxicam vs. Rofecoxib in Osteoarthritis** (11)

![Reduction in pain (%)](image)

<table>
<thead>
<tr>
<th>Pain type</th>
<th>Reduction in pain (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain at rest</td>
<td>42.0</td>
</tr>
<tr>
<td>Pain on movement</td>
<td>45.3</td>
</tr>
<tr>
<td>Pain at night</td>
<td>42.5</td>
</tr>
</tbody>
</table>

**Lornoxicam** exceeds Rofecoxib in reducing pain on movement, at rest and at night.
Balance between Efficacy and Safety

NSAIDs which inhibit both the cox-1 & cox-2, maintain the thrombotic and vasomotor balances (13)

Prostacyclin
- Vasodilation
- Anti-thrombosis

COX-2
- Thromboxane
- Vasoconstriction
- Thrombosis

COX-1
- Thromboxane
- Vasoconstriction
- Thrombosis

American Heart Association (14)

Stepped Care Approach to Pharmacologic Therapy for Musculoskeletal Symptoms With Known Cardiovascular Disease or Risk Factors for Ischemic Heart Disease

- Acetaminophen, ASA, tramadol, narcotic analgesics (short term)
- Nonacetylated salicylates

Non COX-2 selective NSAIDs

Select patients
at low risk of
thrombotic events

Prescribe lowest dose
required to control symptoms

Add ASA 81 mg and PPI to
patients at increased risk of
thrombotic events *

* Addition of ASA may not be sufficient protection against thrombotic events

- Regular monitoring for sustained hypertension (or worsening of prior blood pressure control), edema, worsening renal function, or gastrointestinal bleeding
- If these occur, consider reduction of the dose or discontinuation of the offending drug, a different drug, or alternative therapeutic modalities, as dictated by clinical circumstances

From the market representing more than 1.5 million patient years of treatment, there is no evidence that lornoxicam is associated with an increased cardiovascular risk - Danish Heart Foundation (15)

Balance between Efficacy and Safety

Changes in kidney parameters under various NSAID’S (16, 17)

The influence of Lornoxicam on kidney laboratory values are within acceptable limits-and less pronounced than that of comparator drugs (16,17)

Changes in liver parameters under various NSAID’S (16, 17)

No dosage adjustment is needed in liver impairment, unless severe (16,17)

Gastrointestinal tolerability of Lornoxicam compared to that of Naproxen in healthy male volunteers (18)

Lornoxicam 8mg bid. caused significantly less mucosal injury than Naproxen 500mg bid. in the stomach/duodenal bulb, as well as in the mild/distal duodenum (18)
**Simple Dosing**

- 8 mg Lornoxicam, once or twice daily, (Tablet or Injection)
- No dose adjustment across age range.

**Perioperative - Injections**

<table>
<thead>
<tr>
<th>Drug</th>
<th>IM Dose</th>
<th>IM Dose</th>
<th>IM Dose</th>
<th>IM Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xefo</td>
<td>8 mg</td>
<td>8 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Dosage Equivalence between Xefo and Opioids**

<table>
<thead>
<tr>
<th></th>
<th>mg</th>
<th>mg</th>
<th>mg</th>
<th>mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>20 IM</td>
<td>8/16 IM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pethidine</td>
<td>50 IV</td>
<td>8 IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>100 tid IM</td>
<td>8 tid IM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Dose Equivalence between Xefo and other NSAIDs**

<table>
<thead>
<tr>
<th></th>
<th>mg</th>
<th>mg</th>
<th>mg</th>
<th>mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac</td>
<td>50 tid / 75 IM</td>
<td>8 bid / 8 IM</td>
<td>8 bid / 8 IM</td>
<td>8 bid / 8 IM</td>
</tr>
<tr>
<td>Naproxene</td>
<td>500 tid</td>
<td>8 bid</td>
<td>8 bid / 8 IM</td>
<td>8 bid / 8 IM</td>
</tr>
<tr>
<td>Aspirin</td>
<td>650</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>400</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>50 tid</td>
<td>4 tid</td>
<td>4 tid</td>
<td>4 tid</td>
</tr>
</tbody>
</table>

**BALANCED CHOICE**

- Strong and effective pain killer
- Improved safety and tolerability
- Simple dosing
- FOR ACUTE AND CHRONIC PAIN

- LOW BACK PAIN
- EXTRA ARTICULAR INFLAMMATORY PAIN
- MUSCLE PAIN
- POST – OPERATIVE PAIN
- DENTAL PAIN
- PAIN CAUSED BY INJURIES

References
9. Bugge C. A randomized parallel group trial with Chlortenoxicam (Lornoxicam) and Naproxen in patients with pain due to metastatic bone tumours. Clinical Study Report CT 17, 1993;Nycomed Pharma, Denmark.
15. Heart Statistic 2000/2001 Danish Heart Foundation.

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www.cts.co.il