Ketorolac Injection

<table>
<thead>
<tr>
<th>0223944</th>
<th>SANDOZ CANADA INCORPORATED*</th>
<th>KETOROLAC TROMETHAMINE INJECTION USP</th>
<th>KETOROLAC TROMETHAMINE 30 MG / ML 1 ml amp</th>
</tr>
</thead>
<tbody>
<tr>
<td>0216244</td>
<td>HOFFMAN LAROCHE LTD</td>
<td>KETOROLAC TROMETHAMINE INJECTION USP</td>
<td>TORADOL IM 10 MG / ML 1 ml amp</td>
</tr>
</tbody>
</table>

*Sandoz is the only source of ketorolac tromethamine 30 ml/ml injection in Canada

Indications:
- Short term management (not to exceed 2 days) of moderate to severe acute pain, including pain following major abdominal, orthopaedic and gynecological operative procedures.
- Treatment of cancer pain in palliative care patients

Efficacy of IM ketorolac for acute pain: **NNT 10 mg = 5.7; 30 mg = 3.4; 60 = 1.8** (number needed to treat for one person to experience at least 50% pain relief over 4 to 6 hours)

Suggested alternatives for IM Ketorolac:

1. Oral Options; if patient is able to eat and drink

<table>
<thead>
<tr>
<th>Oral analgesic</th>
<th>NNT for acute pain</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>400 mg = 2.5</td>
<td>tablets &amp; oral suspension</td>
</tr>
<tr>
<td></td>
<td>600-800 mg =1.7</td>
<td></td>
</tr>
<tr>
<td>Naproxen</td>
<td>500 mg = 2.7</td>
<td>NSAID with lowest risk of cardiovascular events</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>200 mg = 3.5</td>
<td>↑ risk cardiovascular events, particularly with high dose; ↓ risk gastrointestinal adverse effects (modest and not applicable if patient on a PPI for gastroprotection)</td>
</tr>
<tr>
<td></td>
<td>400 mg = 2.1</td>
<td></td>
</tr>
<tr>
<td>Ketorolac</td>
<td>10 mg = 2.6</td>
<td>↑ risk of gastrointestinal adverse effects</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>500 mg = 3.5</td>
<td>Tablets &amp; oral syrup</td>
</tr>
<tr>
<td></td>
<td>1000 mg = 3.8*</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen + ibuprofen</td>
<td>500 + 200 mg = 1.6</td>
<td>As effective than acetaminophen + opioid combinations</td>
</tr>
<tr>
<td></td>
<td>1000 + 400 mg = 1.5</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen + codeine</td>
<td>300/325 + 30 mg = 5.7</td>
<td>↑ adverse effects due to codeine content</td>
</tr>
<tr>
<td></td>
<td>600/650 + 60 mg = 4.2</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen + tramadol</td>
<td>650 + 75 mg = 2.6</td>
<td>Not covered by SPEP; relatively expensive</td>
</tr>
</tbody>
</table>

*although NNT for 1000mg is slightly higher than that for the 500mg, a wide confidence interval for the 500mg NNT suggests significant potential for inaccuracy.
2. Rectal / Parenteral Options; if patient is NPO

<table>
<thead>
<tr>
<th></th>
<th>NNT for acute pain</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal suppositories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diclofenac*</td>
<td>50 mg = 2.7 (Oral)</td>
<td>50, 100 mg ↑ CV &amp; hepatic risks</td>
</tr>
<tr>
<td>Naproxen**</td>
<td>500 mg = 2.7 (Oral)</td>
<td>500 mg</td>
</tr>
<tr>
<td>Parenterals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibuprofen injectable IV infusion ***</td>
<td>400 mg = 2.5 (Oral)</td>
<td>400 – 800 mg by IV infusion over 30 min</td>
</tr>
<tr>
<td>Morphine SC, IM, IV</td>
<td>10 mg IM = 2.9</td>
<td>IM injection painful</td>
</tr>
</tbody>
</table>

* Diclofenac rectal suppositories compared with oral formulations have more rapid onset, but slower rate of absorption → lower Cmax but similar AUC.

** Naproxen rectal suppositories are absorbed at same rate as oral formulations. Cmax occurs in 2 to 3 hours.

** NNT based on oral administration studies. Oral ibuprofen has a high availability, rapid onset; therefore IV ibuprofen effect on pain should be similar to that achieved with oral administration.

Prepared by Karen Jensen MSc, BSP; Reviewed by Loren Regier BSP’ Carmen Bell and Terry Damm BSP, medSask. November 2013

References:

2. Personal communication PPC Canada 1-800-663-9099.