### Gynaecological

<table>
<thead>
<tr>
<th>Reference</th>
<th>Methods</th>
<th>Details</th>
<th>Dosing regimen</th>
<th>Outcomes</th>
<th>Efficacy results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ezcurdia et al. Comparison of the efficacy and tolerability of dexketoprofen and ketoprofen in the treatment of primary dysmenorrhoea. J Clin Pharmacol 1998; 38(12 Supp): 65S-73S.</td>
<td>R, DB, oral doses, crossover, 12 hr analgesic washout</td>
<td>5 centres in Spain, Exclusion of patients who remedicating within 1 hr</td>
<td>Dexketoprofen 12.5mg, Dexketoprofen 25mg, Ketoprofen (racemic) 50mg, Placebo</td>
<td>Each patient received a different treatment for each of four consecutive menstrual cycles</td>
<td>Dexketoprofen 12.5mg SPID6 (VAS) 198.6 ± 143.9, TOTPAR6 15.8 ± 7.4</td>
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<td>Dexketoprofen 25mg SPID6 199.0 ± 140.7 TOTPAR6 15.9 ± 8.9</td>
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<td>Ketoprofen 50mg SPID6 248.4 ± 135.9 TOTPAR6 17.7 ± 5.9</td>
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<td>Placebo SPID6 (VAS) 89.4 ± 175.8 TOTPAR6 8.5 ± 8.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Remedication, exclusions, and adverse events</th>
<th>Safety results</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexketoprofen 12.5mg</td>
<td>R 2</td>
<td>WD 1</td>
</tr>
<tr>
<td>No with &gt;1 AE 7</td>
<td>All cause withdrawals NR AE withdrawals 0</td>
<td></td>
</tr>
<tr>
<td>Dexketoprofen 25mg</td>
<td>R 2</td>
<td>WD 0</td>
</tr>
<tr>
<td>No with &gt;1 AE 10</td>
<td>All cause withdrawals NR AE withdrawals 0</td>
<td></td>
</tr>
<tr>
<td>Ketoprofen 50mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No with &gt;1 AE 5</td>
<td>All cause withdrawals NR AE withdrawals 0</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No with &gt;1 AE 5</td>
<td>All cause withdrawals NR AE withdrawals 0</td>
<td></td>
</tr>
</tbody>
</table>

Additional file 5: Trials of oral dexketoprofen in gynaecological and other acute painful conditions

<table>
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<tr>
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<th>Dosing regimen</th>
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<tbody>
<tr>
<td>Mercorio et al. Oral dexketoprofen for pain treatment during diagnostic hysteroscopy in postmenopausal women. Maturitas 2002; 43: 277-281.</td>
<td>R, parallel group</td>
<td>1 centre in Italy, Assessed during the procedure, at 30, 60, and 120 mins</td>
<td>Dexketoprofen 25mg (1hr before the procedure) N= 305 Intracervical injection of 5ml mepivacaine 2% N= 150</td>
<td>Significantly lower pain scores with oral dexketoprofen than intracervical mepivacaine between 30 and 120 minutes</td>
<td>No data reported</td>
</tr>
</tbody>
</table>

Patients remedicating within 1 hr were excluded, after 1 hr LOCF for pain intensity and pain relief set to 0.

Single dose phase - only patients completing at least the 1st hr post study drug administration in all 4 cycles were included (N=46). Repeated dose phase - only patients taking a minimum of 2 doses of study drug and assessments were available for all cycles (N=13).

8 patients were excluded; 3 patients were lost to follow-up, 2 patients remedicating within 1 hr, 2 patients failed to comply with the protocol, 1 patient withdrew due to inefficacy.

30 patients reported 45 adverse events, most were mild to moderate, there were no significant differences between groups, no event caused withdrawal. One serious adverse event occurred but not related to treatment.
Limb injury


RCT, DB, single oral dose, parallel groups
Assessed at baseline, 15, 30, 45, and 60 mins
Medication administered to patients with acute lower limb injury and a pain score of at least 3. Nurse judged whether patient required narcotic analgesia instead

N= 122
1 centre in UK

Dexketoprofen 25mg N= 65
Diclofenac 50mg N= 57

Pain intensity
11-pt VRS

Dexketoprofen 25mg Pain score baseline 6.35 (5.99 to 6.72) Pain score 15 mins 5.65 (5.2 to 6.09) Pain score 30 mins 4.98 (4.57 to 5.4) Pain score 45 mins 4.51 (4.07 to 4.95) Pain score 60 mins 4.46 (3.98 to 4.93)

Diclofenac 50mg Pain score baseline 6.33 (6.01 to 6.66) - p=0.5 Pain score 15 mins 6.18 (5.85 to 6.50) - p=0.026 Pain score 30 mins 5.88 (5.34 to 6.03) - p=0.009 Pain score 45 mins 5.4 (5.02 to 5.78) - p=0.002 Pain score 60 mins 5.29 (4.88 to 5.7) - p=0.008

8 patients requested further analgesia
19 patients had either missing data sheets or study drug boxes were found to be empty post randomisation
No drug-related adverse events were reported

Keller FT. Multi-center, double-blind study to evaluate the efficacy and safety of oral dexketoprofen trometamol in comparison to paracetamol-codeine in the treatment of ankle sprains. Clinical trial report 1999

RCT, DB, three oral doses daily over 4 days, parallel groups
Assessed at baseline and day 4
Medication administered to patients with acute distortion of the ankle joint (not requiring surgery or cast) presenting within 24 hrs of injury an pain intensity of (pain on motion) of at least 5cm on 10cm VAS

N= 210
21 centres in Germany and UK

Dexketoprofen trometamol 25mg TID N= 106
Paracetamol 500mg ± codeine 30mg TID N= 103

Pain on movement 4-pt VRS (1 - absent, 2 - mild, 3 - moderate, 4 - severe)
Pain at rest 4-pt VRS (1 - absent, 2 - mild, 3 - moderate, 4 - severe)
Pain on pressure 4-pt VRS (1 - absent, 2 - mild, 3 - moderate, 4 - severe)
Pain on movement 10cm VAS
Pain at rest 10cm VAS
Pain on pressure 10cm VAS
Ankle circumference

Dexketoprofen trometamol 25mg TID Pain on movement VAS 7.67 ± 1.13 to 2.74 ± 0.26cm Pain on pressure VAS 7.66 ± 0.18 to 3.02 ± 0.26cm Pain at rest VAS 4.94 ± 0.25 to 1.22 ± 0.19cm Pain on movement (mild/absent) 68 Pain at rest (mild/absent) 98 Overall efficacy (patient) good/excellent 80 Overall efficacy (physician) good/excellent 88

Paracetamol 500mg ± codeine 30mg TID Pain on movement VAS 7.91 ± 0.14 to 3.49 ± 0.26cm Pain on pressure VAS 7.83 ± 0.15 to 3.37 ± 0.27cm Pain at rest VAS 5.14 ± 0.15 to 1.38 ± 0.15cm Pain on movement (mild/absent) 60 Pain on pressure (mild/absent) 52 Pain at rest (mild/absent) 91 Overall efficacy (patient) good/excellent 81 Overall efficacy (physician) good/excellent 76

No significant difference between the treatments

1 patient was excluded prior to randomisation due to failing to meeting eligibility criteria, 7 patients withdraw for reasons other than lack of efficacy and were excluded from efficacy analyses

Dexketoprofen trometamol 25mg TID No with >1 AE 5 All cause withdrawals AE withdrawals

Paracetamol 500mg ± codeine 30mg TID No with >1 AE 7 All cause withdrawals AE withdrawals

A total of 12 patients reported 14 adverse events, there were no significant differences between groups and all adverse events were mild in intensity except one case of moderate gastric pain/heartburn. No serious adverse events were reported.
## Bone cancer pain analgesic efficacy


**Bone cancer pain**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Centres in Spain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexketoprofen trometamol</td>
<td>57</td>
<td>12</td>
</tr>
<tr>
<td>Ketorolac 10mg</td>
<td>58</td>
<td></td>
</tr>
</tbody>
</table>

### Pain Intensity

- **100mm VAS**
- **4pt-VRS (1 = slight, 2 = bothersome, 3 = severe, 4 = unbearable)**
- **PID >20mm from baseline to final visit**
- **SPID NR**
- **TOTPAR NR**
- **Global good/excellent NR**
- **Time to onset/peak NR**
- **Time to remedication NR**
- **No remedicating 71%**

### Analgesics taken

- **4-pt VRS (1 = few, 2 = few but regularly, 3 = a lot and regularly, 4 = a lot and continuously)**
- **4-pt VRS (1 = autonomous activity, 2 = occasional help, 3 = frequent help, 4 = complete [confined to bed])**

### Incapacity due to pain

- **4-pt VRS (1 = normal, 2 = wakes up, 3 = insomnia, 4 = use of hypnotics/sedatives)**

### Sleep disturbance

- **4-pt VRS (1 = normal, 2 = wake up, 3 = insomnia, 4 = use of hypnotics/sedatives)**

### Overall efficacy (patient and physician)

- **4-pt VRS (0 = ineffective, 1 = poorly effective, 2 = quite effective, 3 = very effective)**

### Remedication

- **18 patients did not complete the study; due to lack of efficacy, 6 due to adverse events, 5 due to concomitant disease. 2 patients were excluded from efficacy population due to missing efficacy assessments**
- **Most adverse events were mild or moderate intensity, 3.5% of patients reported serious adverse events in both treatment groups, 6 patients withdrew due to adverse events. There were 3 deaths, none considered related to treatment**

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**Abbreviations:** RCT = randomised controlled trial; R = randomised; DB = double blind; WD = withdrawal or dropout; OPVS = Odometer Pain Validity Score; LOCF = last observation carried forward; ITT = intention to treat; N = number; LA = local anaesthetic; VAS = visual analogue scale; VRS = verbal rating scale; AE = adverse event; SPID = summed pain intensity difference; TOTPAR = total pain relief