Additional file 4: Trials of intramuscular and oral dexktoprofen in acute back pain

Reference	Methods	Details	Dosing regimen	Outcome measures	Efficacy results	Remedication, exclusions, and adverse events	Safety results	Quality score
Intramuscular								
Zippel H, Wagenitz A. A multicentre, randomised, double-blind study comparing the efficacy and tolerability of intramuscular dexketoprofen versus diclofenac in the symptomatic treatment of acute low back pain. Clin Drug Investig 2007; 27:533-543.	RCT, DB, two IM doses over 2 days, parallel groups, 6 hr analgesic washout Assessed at (1st dose) baseline, 30, 60, and 90 mins, 2, 4, and 6 hrs; (2nd dose) baseline, 1, 2, 4, 6, and 8 hrs; (3rd dose) baseline, 1, 2, 4 and 6 hrs; (4th dose) baseline and 2 hrs Acute back pain of no more than 1 wk duration and moderate to severe intensity (≥50mm VAS)	Low back pain of less than 1 week duration N= 370 21 centres in Belgium, Germany, and Poland	Dexketoprofen 50mg IM BID N= 183 Diclofenac 75mg IM BID N= 187	Pain intensity 100mm VAS Roland disability questionaire	Dexketoprofen 50mg SPID6 114.5 ± 104.66 Multiple-dose phase SPIDlast 295.6 ± 206.7 Time to peak 3.6 ± 2.1 No remedicating 72 Diclofenac 75mg SPID6 112.7 ± 105.71 Multiple-dose phase SPIDlast 284.2 ± 20 Time to peak 3.7 ± 2.0 No remedicating 62 There were no significant differences in short or longer term	Remedication permitted All randomised patients included in the ITT analysis; 20 patients withdrawn (10 per group) A total of 108 patients reported 236 adverse events, there were no significant differences between groups, and the majority of events were mild or moderate in severity	Dexketoprofen 50mg No with >1 AE 50 All cause withdrawals 10 AE withdrawals 4 Diclofenac 75mg No with >1 AE 58 All cause withdrawals 10 AE withdrawals 2	R 2 DB 2 WD 1 Total = 5 OPVS = 13/16
Oral								
Kubler U. Comparative clinical trial of the efficacy and tolerability of 25 mg dexketoprofen tid versus 50 mg tramadol tid in patients with acute lumbago of at least moderate severity. Clinical trial report 1999. Also published as: Metscher et al. [Dexketoprofen-trometamol and tramadol in acute lumbago]. Fortschr Med Orig 2001, 118(4):147-151.	RCT, DB, 3 daily doses over 7 days, parallel group, Assessed at baseline, day 4, and day 8 Medication administered to patients with untreated back pain of at least moderate intensity (50mm) of no more than 48 hrs duration	Acute lumbago of less than 2 days duration N= 193 25 centres in Germany	Dexketoprofen 25mg TID N= 97 Tramadol 50mg TID N= 95	Pain on movement 100mm VAS Pain at rest 100mm VAS Nocturnal pain 100mm VAS Schroberg's test of function for lumbar spine Global improvement - patient 7-pt VRS (very much improved, much improved, only slightly improved, unchanged, slightly worse, very much worse) Global improvement - physician 7-pt VRS (very much improved, much improved, only slightly improved, unchanged, slightly worse, very much worse) Global evaluation of efficacy - patient 4-pt VRS (very good, good, moderate, no effect) Global evaluation of efficacy - physician 4-pt VRS (very good, good, moderate, no effect)	Dexketoprofen 25mg TID Median onset 60mins Median duration of effect 155mins Pain on movement 78.9 to 17.6mm Pain at rest 73.7 to 15.9mm Nocturnal pain 44.7 to 2.5mm Restriction of movement AM 77.5 to 17mm Global improvement (patient) improved/very much improved 82 Global efficacy (patient) good/very good 81 Global improvement (physician) improved/very much improved 84 Global efficacy (physician) good/very good 85 Tramadol 50mgTID Median onset 65mins Median duration of effect 165mins Pain on movement 79.2 to 24.1mm Pain at rest 72.7 to 19.9mm Nocturnal pain 41.4 to 7.1mm Restriction of movement AM 73.2 to 22.1mm Global improvement (patient) improved/very much improved 73 Global efficacy (patient) good/very good 70 Global improvement (physician) improved/very much improved 66 Global efficacy (physician) good/very good 62 No major differences between the two treatments, though some outcomes and adverse events better for dexketoprofen	Remedication permitted. Data for patient who withdrew before day 4 was excluded, LOCF used for patients withdrawing after day 4 1 patient was lost to follow up and excluded from analyses, 5 patients withdrew before day 4 A total of 41 patients reported 56 adverse events, significantly more adverse events occurred in the tramadol treatment group (15 v 26, p=0.04). No serious adverse events were reported, 6 patients withdrew as a result of adverse events.	Dexketoprofen trometamol 25mg TID No with >1 AE 15 All cause withdrawals 16 AE withdrawals 2 Tramadol 50mg TID No with >1 AE 26 All cause withdrawals 13 AE withdrawals 4	R 2 DB 2 WD 1 Total = 5 OPVS = 13/16

Granados et al. Clinical trial to assess the efficacy and safety of LM-1158.tris (25 mg tid) versus diclofenac (50 mg) in the symptomatic treatment of patients with acute lumbar pain. Clinical trial report 1999	RCT, DB, three daily doses over 2 wks, parallel groups, 6 hr NSAID washout Pain intensity assessed daily during the 1st wk, all other assessments at the end of wk 1 and wk 2 Medication administered to patients with back pain of at least moderate intensity (30mm) and history of previous episode within 6 months	Acute lumbar pain with no previous episodes within 6 months N= 63 4/6 centres in Spain	Dexketoprofen trometamol 25mg TID N=32 Diclofenac 50mg TID N=31	Pain intensity 100mm VAS Pain intensity 4-pt VRS (0 - no pain, 1 - mild, 2 - moderate, 3 - severe pain) Schroberg's of function for lumbar spine Global evolution of lumbar pain - patient 5-pt VRS (0 - much worse to 4 - much better OR 1 - much worse to 5 - much better) Global evolution of lumbar pain - physician 5-pt VRS (0 - much worse to 4 - much better OR 1 - much worse to 5 - much better)	Dexketoprofen trometamol 25mg TID Pain intensity (VAS) wk1 66.3, wk2 25.8, wk3 14mm Global evolution of lumbar pain (patient) little better/much better 88.9 Global evolution of lumbar pain (physician) little better/much better 96.3% Diclofenac 50mg TID Pain intensity (VAS) wk1 54.1, wk2 25.9, wk3 14.7mm Global evolution of lumbar pain (patient) little better/much better 96.4% Global evolution of lumbar pain (physician) little better/much better 100% No significant difference between the two treatments	Remedication permitted 8 patients were excluded from analyses as lost to follow up within the 1st wk In total 10 patients reported 12 adverse events, there were no significant differences between groups and all events were mild to moderate in intensity. No serious adverse events were reported	Dexketoprofen trometamol 25mg TID No with >1 AE 3 All cause withdrawals 11 AE withdrawals 1 Diclofenac 50mg TID No with >1 AE 7 All cause withdrawals 10 AE withdrawals 2	R 2 DB 2 WD 1 Total = 5 OPVS = 12/16
Castiaux. Comparative, multicentre, randomised, double-blind, parallel-group trial on the efficacy and tolerability of dexketoprofen trometamol 25 mg tid, versus tramadol 50 mg tid in a 7-day treatment of acute low back pain. Clinical trial report 1999	RCT, DB, 3 daily doses over 7 days, parallel group, 6 hr analgesic washout Pain intensity assessed at 15 and 30 mins after morning dose and at baseline and day 7, all other assessments made at baseline and day 7 Medication administered to patients with untreated back pain of at least moderate intensity (50mm) of no more than 4 days duration	Low back pain within last 4 days N= 310 42 centres in Belgium and Germany	Dexketoprofen trometamol 25mg TID N= 155 Tramadol 50mg TID N= 152	Pain intensity 100mm VAS Pain at rest - physician 4-pt VRS (0 to 3) Pain on palpitation - physician 4-pt VRS (0 to 3) Pain on movement - physician 4-pt VRS (0 to 3) Schubert index Doodads functional index Night pain Mobility 4-pt VRS (0 to 3) Spinal contracture 4-pt VRS (0 to 3) Global efficacy - patient 4-pt VRS (0 to 3) Global efficacy - physician 4-pt VRS (0 to 3)	Dexketoprofen trometamol 25mg TID Pain after treatment - patient 75.8 to 21.7mm Change in pain at rest (physician) none/mild 146 Change in pain on palpitation (physician) none/mild 136 Change in pain on movement (physician) none/mild 124 Global efficacy (patient) good/very good 112 Global efficacy (physician) good/very good 112 Tramadol 50mg TID Pain after treatment - patient 75.7 to 26.6mm Change in pain at rest (physician) none/mild 134 Change in pain on palpitation (physician) none/mild 120 Change in pain on movement (physician) none/mild 117 Global efficacy (patient) good/very good 97 Global efficacy (physician) good/very good 100 No significant difference between the two treatments	3 patients were excluded from the ITT analyses, 2 were lost to follow-up and no information for post-treatment evaluation was available for 1 patient In total 95 patients reported 179 adverse events, there were significantly fewer adverse events with dexketoprofen (23%) than tramadol (39%)	Dexketoprofen 25mg TID No with >1 AE 36 All cause withdrawals 23 AE withdrawals 2 Tramadol 50mg TID No with >1 AE 59 All cause withdrawals 42 AE withdrawals 20	R 2 DB 2 WD 1 Total = 5 OPVS = 13/16

Bourgeois P. Multicentre, comparative, double blind study of dexketoprofen trometamol 25 mg versus Di-antalvic in the treatment of acute low back pain. Clinical trial report 1999	RCT, DB, 3 daily doses over 3 days, parallel groups, Patient assessed pain intensity at baseline, 1, and 4 hrs after administration, at night on day 1, and prior to medication in the morning and evening of day 2 and 3. Other assessment done on day 1 and day 4. Medication administered to patients with back pain less than or equal to 50mm and of no more than 5 days duration	Low back pain within last 5 days N=336 67 centres in France	Dexketoprofen trometamol 25mg TID N= 168 Dextropropoxyphene 30mg + paracetamol 400mg BID N= 167	Pain intensity 100mm VAS Lumbar pain - physician 4-pt VRS (0 - absent, 1 - mild, 2 - moderate, 3 - severe) Global efficacy - patient 4-pt VRS (1 - excellent, 2 - good, 3 - moderate, 4 - poor) Global efficacy - physician 4-pt VRS (1 - excellent, 2 - good, 3 - moderate, 4 - poor) Eiffel function index Lumbar contracture - physician 4-pt VRS (0 - absent, 1 - mild, 2 - moderate, 3 - severe)	Dexketoprofen trometamol 25mg TID Global efficacy (patient) good/excellent 78% Global efficacy (physician) good/excellent 82% Dextropropoxyphene 30mg ± paracetamol 400mg BID Global efficacy (patient) good/excellent 63% Global efficacy (physician) good/excellent No significant difference in pain between the two treatments	1 patient was excluded from the ITT analyses for failing to attend post-treatment follow-up	Dexketoprofen trometamol 25mg TID No with >1 AE 21 All cause withdrawals AE withdrawals 6 Dextropropoxyphene 30mg ± paracetamol 400mg BID No with >1 AE 18 All cause withdrawals AE withdrawals 2	R 2 DB 2 WD 1 Total = 5 OPVS = 13/16

Abbreviations: RCT = randomised controlled trial; R = randomised; DB = double blund; wD = withdrawal or dropout; OPVS = Oxfoprd 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