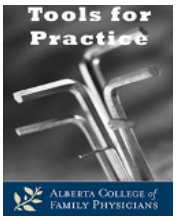
July 13, 2020




## Osteoarthritis pain getting you down? Duloxetine

## Clinical Question: Do Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), specifically duloxetine, improve pain in patients with osteoarthritis?

**Bottom Line: Duloxetine can meaningfully reduce osteoarthritis pain scores (by at least 30%) for ~60% of patients compared to ~40% on placebo. An average pain of ~6 (scale 0-10) will be reduced by ~2.5 points, compared to 1.7 on placebo. Duloxetine adverse effects lead to withdrawal in 12% of patients versus 6% on placebo.**

**Evidence:**

- Six systematic reviews with 2-7 randomized controlled trials (RCTs) and 487-2102 patients.[1-6] Duloxetine 60-120mg daily versus placebo, results statistically significant unless indicated.
    - Proportion of patients attaining a meaningful pain reduction (generally ≥30% reduction in pain score):
        - Systematic review (6 RCTs, 2060 patients)[1] of hip or knee osteoarthritis, over 10-18 weeks: 64% taking duloxetine versus 43% taking placebo, number needed to treat (NNT)=5.
        - Other systematic reviews found similar:[3,5-6] NNT=6-9.
        - One RCT (231 patients) randomized patients to 60mg or 120mg and found no difference.[7]
    - Improvement in baseline pain scores (0-10 point scale, lower scores indicate less pain):
        - Systematic review (5 RCTs, 2059 patients),[5] patients started with an average score of 5.8: duloxetine improved pain 0.8 more than placebo, achieving a mean pain score of 3.3 versus 4.1 for placebo which is likely clinically meaningful.
        - Another systematic review found similar.[3]
    - Adverse events:
        - Overall adverse events:[4] 55% versus 37% (placebo), number needed to harm (NNH)=6.
            - Most common adverse events:[4] gastrointestinal 36% versus 8% (placebo), (NNH=4).
                - Specifically[6] nausea (NNH 16), fatigue (NNH 17), constipation (NNH 19), erectile dysfunction (NNH 20), abdominal pain (NNH 34).
        - Withdrawal due to adverse events:[4] 12% versus 6% (placebo), NNH=17.
        - Other systematic reviews found similar.[1-6]

- Limitations: all industry-funded studies.

**Context:**

- No RCTs looked at venlafaxine to treat osteoarthritis pain.
- Duloxetine is "conditionally recommended" by the Osteoarthritis Research Society International guidelines and by the American College of Rheumatology, however, tolerability needs to be considered.[8-9]
- A PEER Simplified Decision Aid on osteoarthritis can assist with patient informed decision making and is available online.[10]

**Authors:**

Betsy Thomas BSc Pharm, Joey Ton PharmD, Mike Allan MD CCFP

**Disclosures:**

Authors do not have any conflicts of interest to declare.

**References:**

1. Ton J, Perry D, Thomas B, *et al.* Can Fam Physician. 2020 Mar; 66(3):e89-e98.
2. Moore RA, Cai N, Skljarevski V, Tölle TR. Eur J Pain. 2014 Jan; 18(1):67-75.
3. Wang ZY, Shi SY, Li SJ, *et al*. Pain Med. 2015 Jul; 16(7):1373-85.
4. Osani MC, Bannuru RR. Korean J Intern Med. 2019 Sep; 34(5):966-973.
5. Gao SH, Huo JB, Pan QM, *et al*. Medicine (Baltimore). 2019 Nov; 98(44):e17541.
6. Citrome L, Weiss-Citrome A. Postgrad Med. 2012 Jan; 124(1):83-93.
7. Chappell A, Ossanna M, Liu-Seifert H, *et al*. Pain. 2009 Dec; 146(3):253-60.
8. Bannuru RR, Osani MC, Vaysbrot EE, *et al*. Osteoarthritis Cartilage. 2019 Nov; 27(11):1578-1589.
9. Kolasinski S, Neogi T, Hochberg MC, *et al*. Arthritis Rheumatol. 2020 Feb; 72(2):220-233.
10. Lindblad AJ, McCormack J, Korownyk CS, *et al*. Can Fam Physician. 2020 Mar; 66(3):191-193. Available at: https://www.cfp.ca/content/66/3/191 Accessed 08-APR-2020.