events at eight weeks, suggesting there was no advantage to adding acetaminophen to tramadol relative to NSAIDs for patients with OA pain.[115]

An RCT by Banerjee et al. (2016) compared the COX-2 inhibitor etoricoxib to tapentadol and found no significant differences in pain reduction or physical function (WOMAC stiffness and function) at 12 weeks.[108] Adverse events were common in both treatment groups (49% versus 37%, p=0.048, favoring tapentadol).

Providers should note that the current VA/DoD CPG for Opioid Therapy for Chronic Pain recommends against initiating long-term opioid therapy for chronic pain.[i] Alternatives to opioid therapy (e.g., self-management strategies, other non-pharmacologic treatments) are the mainstay of management. When pharmacologic therapies are used, non-opioids are recommended over opioids.

However, patients who do not have an adequate response to several non-pharmacologic and non-opioid therapies and continue to have persistent, severe OA pain are particularly challenging to manage. In this situation, a cautious, patient-centered opioid therapy approach that prioritizes safety may be considered for carefully selected patients in which the benefits are anticipated to outweigh the risks. If opioids are prescribed for OA pain, it should be for the shortest duration and at the lowest effective dose. Furthermore, appropriate monitoring as per the VA/DoD CPG for Opioid Therapy is suggested.

As this is a *Reviewed*, *New-replaced* recommendation, the Work Group systematically reviewed evidence related to this recommendation.[104-109] The Work Group's confidence in the quality of evidence was very low. The Work Group found few active-control, comparative effectiveness, or head-to-head trials comparing the relative efficacy of opioids to other analgesics, which are more clinically relevant and informative for treatment decision-making. The evidence was limited by short-term trials (i.e., 1 – 17 weeks). Also, because of the serious risks of opioids, which include withdrawal, misuse, abuse, overdose, and opioid use disorder, and emerging evidence of endocrine dysfunction, sleep-disordered breathing, falls, fractures, and infections, the Work Group concluded that the risks associated with opioid treatment outweighed potential benefits. The evidence consistently showed the benefits of opioids include a modest reduction in pain intensity and improved function compared to placebo in patients with OA of the knee and hip, but these small benefits have not been studied over the long-term and are likely not clinically significant. However, the Work Group acknowledged that opioids may be considered for certain patients. Thus, the Work Group decided upon a "Weak against" recommendation.

Osteoarthritis is a chronic condition, yet existing studies of pharmacologic options for OA of the knee and hip are relatively short-term. Researchers should conduct longer duration studies to better assess the long-term effectiveness and safety of pharmacologic options and better reflect the chronic disease management required for OA. Also, more research is needed to assess the effectiveness and safety of the combination of pharmacologic treatments and the combination of pharmacologic, especially non-opioid, and non-pharmacologic treatments. Decision aids that assist providers in calculating the risk-benefit ratio would help with the selection of pharmacologic treatments, especially when opioids are considered.

[i] See the current VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: https://www.healthquality.va.gov/guidelines/Pain/cot/