INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: *Osteoarthritis*
-May 2023-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of agents for the management of osteoarthritis. Medications listed on the IHS National Core Formulary (NCF) relevant to this condition include aspirin, diclofenac (any formulation), duloxetine, ibuprofen, indomethacin, meloxicam, naproxen, and salsalate. Following clinical review and analysis, **the NPTC made no modifications to the NCF** for the treatment of osteoarthritis.

Discussion:

Osteoarthritis is characterized by joint pain and functional impairment involving a multifactorial biopsychosocial process and is influenced by environmental and psychosocial factors[1]. Pain related to osteoarthritis can have negative impacts on mood and sleep and frequently affects participation in occupational and recreational activities[1].

Osteoarthritis is the most common form of arthritis and commonly affects the hands, hips, knees, feet, and spine[2]. There are currently 528 million people globally and 52 million Americans[2] with osteoarthritis. It's estimated that 40% of males and almost 50% of females will develop osteoarthritis in their lifetime, this chance increases with age. There is limited data on osteoarthritis for the Alaska Native and American Indian population; however, it is estimated that the prevalence is higher in Alaska Natives (26.1%) and lower in the Southwest American Indian (16.5%) populations compared to the general United States prevalence (21.5%)[3]. In the United States, the knee is the most common site of osteoarthritis (80%) followed by hand (8%) and hip (5%)[2]. The morbidity associated with osteoarthritis is the leading cause of lower extremity disability in older adults and cardiovascular death is the most common cause of mortality. Other risk factors associated with the development of osteoarthritis include age, the strongest predictor, female sex, previous joint injury, and obesity[2].

The management of osteoarthritis ranges from non-joint specific approaches such as the treatment of depression, sleeping disturbances, and social problems to joint-specific interventions including non-pharmacological, pharmacologic, and surgical options[1]. The goal of treatment and management of osteoarthritis focuses on improving pain and maintaining function[1]. Despite the many treatments for osteoarthritis, there are currently no FDA-approved treatment options that modify the course of the disease[1].

Clinical guidelines focus on a few general principles for patients to begin managing their osteoarthritis including education regarding the disease, risk factors, prognosis, and treatments; self-management and support; and appropriate goal setting[4-6]. Treatment should be patient specific based on disease, risk factors, and drug profiles and generally include a combination of nonpharmacological therapy, pharmacological therapy, and/or surgery. Non-pharmacological therapy is the mainstay and focuses on weight management, exercise, braces/orthotics/assistive devices, and education. If pharmacological therapy is needed, first-line therapy includes topical NSAIDs followed by oral NSAIDs, duloxetine, and in some cases, intra-articular glucocorticoids. Surgical interventions, such as total joint replacements, can be effective with conservative therapies have failed[4-6].

Topical diclofenac patches have been shown to improve pain (SMD −0.81, 95% CI: −1.12 to –0.52) and topical piroxicam have been shown to improve function (SMD −1.04, 95% CI: −1.60 to –0.48) in those with osteoarthritis without increasing adverse effects (OR 1.38, 95% CI: 0.99-1.92)[7]. When compared to oral NSAIDs, topical NSAIDs were shown to be equally effective in reducing pain and improving function[8]. Additionally, overall adverse reactions were similar between topical and oral NSAIDs (OR 0.63, 95% CI: 0.36-1.12; p=0.11), GI reactions were more common with oral (OR 0.30, 95% CI: 0.16-0.56; p=0.0001), and skin reactions were more common with topical agents (OR 5.22, 95% CI: 2.0-13.6; p= 0.0007)[8].

When topical agents do not provide satisfactory relief, oral NSAIDs can be used[4-6]. Acetaminophen has been shown to be more effective than placebo but less effective than other oral NSAIDs[9]. Improvements in pain and function have been shown with oral diclofenac (HR –0.57, 95% CI: -0.69 to -0.46)[9]. Oral NSAIDs such as celecoxib have been shown to have similar pain reduction and function improvement and no difference in withdrawals or serious adverse effect[10]. Compared to other oral NSAIDs, celecoxib showed no additional improvement in pain reduction, a slight improvement in function, and no major differences in withdrawals or adverse effects[10-11]. Comparatively, celecoxib does provide GI protection without increased risk in cardiovascular mortality (RR 0.75, 95% CI: 0.57-0.99) or all-cause mortality (RR 0.81, 95% CI: 0.66-0.98)[11].

Generally, the use of opioids is not recommended for the treatment of pain associated with osteoarthritis[12]. Clinical trials have shown that despite opioids providing more effective pain control (SMD -0.28, 95% CI: -0.35 to -0.20; NNT=10), and improving function (SMD -0.26, 95% CI: -0.35 to -0.17; NNT=11), opioid use in those with osteoarthritis resulted in more serious adverse events (RR 3.35, 95% CI: 0.83 to 13.56) and withdrawals (RR 2.76, 95% CI: 2.02 to 3.77)[12]. Tramadol has also been studied in osteoarthritis treatment and was shown to have no difference in pain control or function compared to acetaminophen while having increased withdrawal and serious side effects[13].

Antidepressants have been used to support the treatment of osteoarthritis and have shown improvement in function (MD −5.65 points, 95% CI: −7.08 to −4.23) and quality of life (MD 0.04, 95% CI: 0.01 to 0.07)[14]. However, antidepressant use also increased the risk of adverse events (RR 1.27, 95% CI: 1.15 to 1.41; NNH=7) and withdrawal (RR 2.15, 95% CI: 1.56 to 2.97; NNH=17). The use of duloxetine did improve pain (SMD -0.38, 95% CI: -0.48 to -0.28), function (SMD -0.35, 95% CI: -0.46 to -0.24), and quality of life (SMD 0.40, 95% CI: 0.26 to 0.53) for those with knee osteoarthritis but was also associated with a higher rate of discontinuation due to GI side effects[15].

Controversy exists around the appropriate use and patient selection for intra-articular injections for osteoarthritis treatments[4-6]. Improvements in pain control (SMD -0.40, 95% CI: -0.58 to -0.22; NNT=8) and function (SMD -0.33, 95% CI: -0.56 to -0.09; NNT=10) have been observed but are limited in duration to a just a few weeks[16]. Additionally, the use of intra-articular glucocorticoids did not improve quality of life (SMD -0.01, 95% CI: -0.30 to 0.28) or joint space narrowing (SMD -0.02, 95% CI: -0.49 to 0.46)[16].

Findings:

Osteoarthritis is the most common form of arthritis and is caused by degeneration of the joint cartilage and growth of new bone, cartilage and connective tissue. The disease is associated with major disability including increased pain, reduced function, and impaired quality of life. There are multiple risk factors have been linked to osteoarthritis including age, joints, obesity, genetics, anatomy, and sex. The mainstay of treatment includes exercise, weight management and other non-pharmacological approaches however the use of topical NSAIDs, oral NSAIDs, duloxetine, and some intra-articular injections have been shown to decrease pain and increase function.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

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