University Health System

GUIDELINES FOR THE MANAGEMENT OF OSTEOARTHRITIS (DEGENERATIVE JOINT DISEASE) (1)

Adapted from the American College of Rheumatology Guidelines

Evaluation of the adult patient with acute musculo-skeletal symptoms resulting in definitive diagnosis of osteoarthritis (2)

Individualize treatment plan, considering co-existing medical problems such as **diabetes, hypertension, heart disease, peptic ulcer disease, kidney disease, or liver disease.**

Non-pharmacologic therapy (3)

Pharmacologic therapy — pain relief is primary goal:

For chronic pain relief:

Acetaminophen up to 1000 mg qid (4)

Topical analgesics:

Methylsalicylate or Capsaicin cream may be helpful as adjunctive or monotherapy (5)

For acute flare-ups:

Opioid analgesics:

Combinations of Acetaminophen with codeine or hydrocodone (6)
(Warn patients not to exceed 4000 mg per day of acetaminophen including the combination product)

If effusion present, consider aspiration, fluid analysis and **intra-articular steroids** (7)

If response is inadequate to acetaminophen & topical analgesics for chronic pain relief:

■ Intermittent concomitant use of NSAIDs with acetaminophen Note: long-term concomitant use increases chance of toxicity.

OR

■ Regular use of one NSAID alone (8) Note: except for low-dose aspirin (cardio-protection), do not give two NSAIDs concomitantly.

If patient complains of dyspepsia, suggest taking NSAID with food or milk or with OTC antacids or H_2-blockers.

	If patient has risk factors for upper GI bleed (9): Consider switching to COX-1 sparing drug (11) **OR** Adding one of the following to NSAID: (12) misoprostol **OR** proton pump inhibitor **(NOTE: If patient is on one of these agents for NSAID-induced risk of GI- bleed, consider discontinuing this agent if initiating COX-1 sparing agent.)**		If patient has risk factors for renal disease (10): Use of NSAIDs requires strict monitoring. Consider alternative therapy.

	If response to NSAIDs or COX-1 sparing agent is inadequate, or if these agents are contraindicated, consider sodium hyaluronate / Hylan G-F20 (Synvisc) (for OA of knee only) (13) Use of this device for Carelink patients requires prior authorization.	

If response is inadequate, and surgery is contraindicated, consider referral for joint lavage &/or arthroscopic debridement (OA of the knee)		If response is inadequate, and surgery is not contraindicated, consider referral for joint surgery.

(1) Goals of management are to control pain and other symptoms, minimize disability, and educate patients and their families about the disease and its treatments.

(2) The reader is referred to *The American College of Rheumatology Clinical Guidelines for the Initial Evaluation of the Adult Patient With Acute Musculoskeletal Symptoms*. (Available on the internet at www.rheumatology.org). These guidelines are designed to provide guidance to primary care physicians by presenting a logical approach to the diagnostic work-up and treatment plan.

(3) Non-pharmacologic therapy includes (but is not limited to):

1. Patient education (videos, pamphlets, newsletters, etc. available from Arthritis Foundation) (http://www.arthritis.org)
2. Health professional social support
3. Weight loss (if overweight)
4. Physical therapy
5. Range of motion exercises
6. Strengthening exercises
7. Assistive devices for ambulation
8. Occupational therapy
9. Aerobic exercises

(4) Several short-term and long-term studies have shown **acetaminophen** (in doses up to 4 gm /day) is superior to placebo & comparable in efficacy to both ibuprofen and naproxen for symptomatic treatment of OA of the knee. Toxicity from acetaminophen at recommended doses is rare but caution patients who consume excessive alcohol. Renal toxicity has occurred when combined with NSAIDs.

(5) Various **topical products (analgesic balms and capsaicin)** are available -- all are over-the-counter, (OTC) thus are not available from University Health System pharmacies

(6) Recommended **opioid analgesics**:

DRUG	APPROXIMATE ACQUISITION COST (each)
Acetaminophen 300mg with codeine 30mg (Tylenol #3 equivalent)	$0.05
Acetaminophen 500 mg with hydrocodone 5mg (Vicodin equivalent)	$0.03

Note: Tramadol (Ultram) is not recommended and is NOT SUBSIDIZED (Cost is $0.44 per tablet)

(7) Repeated **intra-articular injections of steroids** are associated with cartilage damage, and thus should not be a part of routine management. It is usually recommended not to exceed more than 3 injections per year. This technically difficult procedure is usually performed by a rheumatologist, orthopedist, or radiologist under fluoroscopic guidance.

(8) **NSAID formulary and subsidized choices**, the usual dose range, and costs are listed below:

DRUG & Subsidy Information	DOSE RANGE	APPROXIMATE ACQUISITION COST
Aspirin OTC, thus not available in UHS pharmacies	2.4 - 6 gm / day in divided doses of four to six times per day	Not applicable
Salsalate (Disalcid equivalent) Both strengths subsidized	3000 mg / day in divided doses of two or three times per day. (500 mg x 2 tid or 750 mg x 2 bid)	2 x 500 mg tid: $50 / year 2 x 750 mg bid:$46 / year
Ibuprofen (Motrin equivalent) Only 800 mg is subsidized	For OTC, may start at 400 mg tid - qid; For UHS Rx: 1.6 gm - 3.2 gm / day in divided doses of two to four times a day. (800 mg bid to qid)	800 mg qid:$3 / year
Naproxen (Naprosyn equivalent) Only 500 mg is subsidized	500 mg - 1000 mg / day in divided doses For OTC, 250 mg bid	500 mg bid: $40 / year

	For UHS Rx: 500 mg qd to 500 mg bid. Dose may be increased to 1500 mg per day for limited periods.	
Indomethacin (Indocin equivalent) Only the 25mg & 50 mg strengths are subsidized.	25 mg bid or tid; if well tolerated, ↓ daily dose by 25 mg or 50 mg at weekly intervals (if required by continuing symptoms) until a satisfactory response is obtained or until the total daily dose of 150 mg to 200 mg is reached. In patients who have persistent night pain or morning stiffness, give up to 100 mg of total daily dose at bedtime.	25 mg bid: $8 / year 50 mg tid: $18 / year 75 mg (SR) bid: $156 / year

Although NSAIDs are considered to have equal efficacy, individual patient response may vary. Salsalate has been shown to have less renal toxicity and antiplatelet effects. Ibuprofen in doses ↓ 1600mg/day may have less GI toxicity. Because the intensity of pain varies from day to day as well as within a day, it may be preferable to use a short half-life NSAID on a PRN basis. Except for the concomitant use of low dose aspirin (81-325 mg/day for its cardio-protective effects), **combinations of two or more NSAIDS should not be used because of the greater risk of adverse reactions without corresponding improvement in efficacy.**

(9) It has been estimated that 20%-30% of all hospitalizations & deaths due to peptic ulcer disease (PUD) are attributable to NSAID therapy. Therefore risk factors must be carefully evaluated and considered.

Risk factors for NSAID-induced upper GI bleed include:

Age ↓ 65 years
History of PUD or UGI bleeding
Concomitant oral glucocorticoids
Concomitant anticoagulants
Smoking
Alcohol consumption

One recommended assessment tool to evaluate risk factors is outlined below. It was developed by Gurkirpal Singh, MD, director of the Arthritis Rheumatism and Aging Medical Information System Post-marketing Surveillance (ARAMIS PMR) at Stanford University. ARAMIS is a project of the National Institute of Health. This tool can be used by the patient and/or the MD to determine risk of NSAID-induced bleed. A revised version of this tool must accompany each request for CareLink subsidy. Click here for the updated form: GI assessment tool.

Ask the patient the following six questions and assign points for the answers	POINTS
1. How old are you? Age Points <20 0 21-25 1 26-30 3 31-35 4 36-40 5 41-45 6 46-50 8 51-55 9 56-60 10 61-65 12 66-70 13 71-75 14 76-80 16 81-85 17 >85 18	
• **How do you rate your current health status on the following Scale?** Health Status Points Very Well 0 Well 1 Fair 2 Poor 3 Very Poor 4	
• **Has a physician ever told you that you have rheumatoid arthritis (not osteoarthritis)?** Yes 8 points No 0 points	
• **If you are taking prednisone or other corticosteroids, for how many months have you taken them in the past year?** Months Points Months Points 0 0 7-10 4 1-3 1 11-12 5 4-6 3	
• **Have you ever been hospitalized for a stomach or intestinal problem such as bleeding or an ulcer?** Yes 8 points No 0 points	
• **Have you ever had gastrointestinal side effects (heartburn, stomach pain, nausea, vomiting) while taking NSAID pain-relievers?**	

Yes 2 points No 0 points	
Total points	

Evaluation of patient's risk for an NSAID-induced bleed:

Level 1 (0-10 points) No risk. May use NSAID

Level 2 (11-15 points) Moderate risk. May use NSAID

Level 3 (16-20 points) Significant risk. If NSAID therapy expected to be < 30 days, use standard NSAID. If > 30 days of chronic therapy, Initiate COX-1 sparing therapy.

Level 4 (>20 points) Substantial risk Recommended to initiate COX-1 sparing therapy

More information about this tool may be found at Stanford University's website.

(10) **Risk factors for NSAID-induced renal disease** include:

Age ≥ 65 years
Hypertension
Congestive heart failure
Cirrhosis
Concomitant diuretics
Concomitant ACE-inhibitors

(11) The potential advantage of using a **COX-1 sparing agent** is decreasing the production of the inflammatory prostaglandins produced by COX-2 without decreasing the production of the prostaglandins, produced by COX-1, which are important in other body functions. This type of enzyme selectivity would allow this agent to control pain and inflammation without causing some of the toxicities associated with NSAID therapy.

Celecoxib (Celebrex) is the first agent in this class to be marketed.

DOSING for osteoarthritis: **200mg once daily or 100mg twice daily**.

CONTRAINDICATIONS: Celecoxib is contraindicated in patients with a documented allergic-type reaction to sulfonamides and in patients with a documented allergy to aspirin or other NSAID.

WARNINGS / PRECAUTIONS: Use with caution in patients with GI bleed, advanced renal disease, late-stage pregnancy, presence of infection, elevation in LFTs, fluid retention & edema.

MONITORING: Monitor renal function and LFTs.

DRUG INTERACTIONS: Celecoxib may inhibit CYP2D6. Fluconazole may increase celecoxib levels two-fold. Celecoxib may increase lithium levels. Patients on ACE-inhibitors or diuretics may be more susceptible to renal toxicity. Concomitant aspirin use may increase rate of GI complications. Antacids will decrease celecoxib absorption.

200 mg: $1.49 each $1.49 / day $544/year
100 mg: $0.88 each $1.76 / day $642/year

(12) Drugs used to prevent NSAID-induced GI bleeds:

Misoprostol (Cytotec) is the only drug FDA-approved for the prevention of NSAID-induced gastric ulcers. RESTRICTIONS are already in place for the use of misoprostol:

To have a prescription filled and subsidized, a patient with osteoarthritis must have

A. Documented previous peptic ulcer disease or upper GI bleed

OR

B. Two of the following three conditions:

1. Age > 50 years
2. Concomitant debilitating disease
3. Current smoking history > pack per day.

CONTRAINDICATIONS: Must not be used during pregnancy

DOSE: 200 mcg qid with food. If not tolerated, ↓ to 100 mcg qid. Continue for the duration of NSAID therapy.

COST: 200 mcg: $0.44 each $1.75 / day $637/yr

While not FDA-approved, proton pump inhibitors have been shown to inhibit the development of PUD. There are two formulary proton pump inhibitors (omeprazole & lansoprazole), but only lansoprazole (Prevacid) is subsidized. The usual dose should be one capsule once daily.

Lansoprazole 15 mg or 30 mg qd:

ACQUISITION COST: omeprazole 20mg qd: $2.58/day $940/year $1.78/day $649/year

NOTE: Patients taking a COX-1 sparing agent (celecoxib) should not need concomitant therapy with misoprostol or a proton pump inhibitor. The need for these agents should be reviewed when initiating therapy with celecoxib.

(13) Osteoarthritis can affect the integrity and rheology of synovial fluid. Intra-articular visco-supplementation with **sodium hyaluronate/hylan GF 20 (Synvisc)** is aimed at improving the elasticity and viscosity of synovial fluid.

DOSING: 20mg/2 ml weekly by intra-articular injection for 3 weeks for one cycle. **Safety & efficacy of repeat cycles have not been established.**

CONTRAINDICATIONS: This product (which is actually classified as a device by the FDA) is contraindicated if a patient has a hypersensitivity to hyaluronan or any of its components (it is extracted from chicken or rooster combs). It must not be given if there is evidence of infection or skin disease in the area of the injection site.

WARNINGS / PRECAUTIONS: Precipitation of the drug may occur if used concomitantly with skin disinfectants containing quaternary ammonium salts. Do not administer with other intra-articular injectables. Safety & efficacy has not been established in pregnant &/or lactating women. Effusions should be removed before administration of this drug. Inject local anesthetic prior to administration. Only physicians specially trained for intra-articular administration should give this agent.

ACQUISITION COST: $511 per treatment cycle (kit contains 3 doses)

REFERENCES:

The American College of Rheumatology Clinical Guidelines, a CME monograph published by the American College of Rheumatology, 1997. Supported by an unrestricted educational grant from Searle.

Shmerling RH, and Fuchs HA, co-chairmen of the Ad Hoc Committee on Clinical Guidelines, et al: Guidelines for the Initial Evaluation of the Adult Patient with Acute Musculoskeletal Symptoms. *Arthritis & Rheumatism* Vol 39, No.1, January, 1996, pp 1-8 (Available at the www. rheumatology.org website)

Hochberg MC, et al: Guidelines for the Medical Management of Osteoarthritis, Part I -- Osteoarthritis of the hip. *Arthritis & Rheumatism* Vol 38, No.11, November 1995, pp 1535-1540. (Available at the www. rheumatology.org website)

Hochberg MC, et al: Guidelines for the Medical Management of Osteoarthritis, Part II -- Osteoarthritis of the knee. *Arthritis & Rheumatism* Vol 38, No.11, November 1995, pp 1541-1546. (Available at the www. rheumatology.org website)

Monograph for celecoxib (Celebrex), a Pharmacy & Therapeutics Review published by *The Formulary Monograph Service.* March 1999

Monographs for misoprostol, proton pump inhibitors, NSAIDs and sodium hyaluronate in *Drug Facts and Comparisons*.

Monographs for misoprostol, proton pump inhibitors, and NSAIDs in *American Hospital Formulary Service Drug Information*.