These annexes accompany the ACE Clinical Guideline "Management of knee osteoarthritis – a joint effort with patients"

Table of Contents

Annex A: Comparison of validated assessment tools for knee OA

This table summarises the features and ease of administration of some available assessment tools for knee osteoarthritis (OA). The information is not exhaustive. Most of these tools have been validated for use across multiple clinical settings beyond their original development environments. Clinicians have the flexibility to select assessment tools which are most appropriate for their patients and feasible for their practice.

Tools	Pain	Function	Quality of life	Psychosocial factors	Ease of administration
Numeric Rating Score (NRS)[a]	✔				⏱
Visual Analogue Scale (VAS)[b]	✔				⏱
Functional Activity Scoring Tool (FAST)[1 c] (locally validated)		✔			⏱
30-second chair-stand test (CST)[c]		✔			⏱
Timed Up and Go (TUG)[d]		✔			⏱
Brief Fear of Movement Scale[c]				✔ (kinesiophobia)	⏱
Patient Health Questionnaire-4 (PHQ-4)[c]				✔ (depression and anxiety)	⏱
Keele STarT MSK Tool[2 c]		✔	✔	✔	⏱⏱
EQ-5D-5L[e]			✔		⏱⏱
Oxford Knee Score (OKS)[f]	✔	✔			⏱⏱
Knee Injury and Osteoarthritis Outcome Score (KOOS)[f]	✔	✔	✔		⏱⏱⏱
Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[e]	✔	✔			⏱⏱⏱

⏱ Can be completed under 1 min ⏱⏱ Can be completed in 2-5 min ⏱⏱⏱ Can be completed in 10 min

[a] Developed for, and validated in multiple clinical settings, including primary care, hospital and specialist pain clinics as a simple universal pain assessment tool.
[b] Developed as a psychometric tool for research settings to measure subjective experiences not limited to pain.
[c] Developed for and validated in primary care settings.
[d] Developed for and validated in geriatric care settings.
[e] Developed for and validated in research settings.
[f] Developed for and validated in orthopaedic specialist settings for patients undergoing knee replacement surgery.

Annex B. Managing knee OA flares

Flares are transient episodes of worsening pain, swelling and stiffness that typically last for several days. Flares can resolve spontaneously or necessitate adjustment to therapy.[3] Although evidence for OA flare management remains limited, several general principles can guide treatment and patient education.[4,5] Give the following advice to patients:

Exercise and movement

- Avoid prolonged periods of inactivity and keep calm as symptoms will usually resolve.
- Continue exercising to keep the knee joint flexible but adapt the routine (see Figure 4 in the ACG) and avoid sudden increases in exercise intensity.
- Warm up before exercising to loosen the knee joint and muscles. If the knee remains comfortable after warming up, it should be safe to exercise.
- Consider gentle stretching to relieve stiffness.

Medications

Use NSAIDs for a short time and only when needed to manage symptoms, if NSAIDs are suitable (see Recommendation 3 in the ACG).

Assistive devices

Consider using a knee guard or walking aid to relieve pain and reduce the load on the knee.

Medical advice

Consult a healthcare professional if symptoms do not resolve after one week. Seek medical attention earlier if there is fever, joint warmth, severe swelling, inability to weight-bear or after significant trauma (see 'Red flags and atypical symptoms' on page 3 of the ACG).

Ice

Consider applying an ice pack to the knee intermittently for a few days to reduce swelling.

Annex C. Key considerations for selecting an NSAID for knee OA

Information is sourced from international literature and local medication information resources (including package inserts). The information is not exhaustive. Refer to package inserts and medication information resources for further details.

To minimise the risk of adverse effects, both topical and oral NSAIDs should be used **only when needed** for the **shortest possible duration** and at the **lowest effective dose.**

Topical NSAIDs

Medication	Dosing frequency (PRN basis)[g]	Efficacy on pain[6-8]	Efficacy on function[6,8]	Risk of GI adverse effects[6,8,9 h]	Risk of CV adverse effects[6,8,10 i]	Risk of renal adverse effects[8,11,12 j]
Diclofenac gel	TDS or QDS	+ + +	+ +	Similar to placebo	Similar to placebo	Similar to placebo
Diclofenac SR gel[k]	BD	+ + +	+ +			
Diclofenac patch[k]	OD	+ + +	+ +			
Flurbiprofen patch	BD	+ +	Similar to placebo			
Ketoprofen gel or patch	BD	+	+ +			
Piroxicam gel	TDS or QDS	+ +	+ + +			

⚠ Contraindications

- 3rd trimester of pregnancy

⚠ Precautions

- May cause mild, local skin irritation
- Avoid using other topical medications on the same area of skin
- Avoid using airtight bandage or dressing over the area of application

BD, (up to) two times daily; CV, cardiovascular; GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory drugs; OD, once daily; PRN, as required; QDS, (up to) four times daily; SR, sustained-release; TDS, (up to) three times daily

Further information on relative efficacy for pain and function in knee OA

+ + + (≈ Probability of MCID >70%)	+ + (≈ Probability of MCID 30-70%)	+ (≈ Probability of MCID <30%)

Assessment of relative efficacy considered both the probabilities of achieving minimum clinically important difference with placebo (MCID; effect size ≤0.37)[7] and relative efficacies based on published surface under the cumulative ranking curve (SUCRA) rankings.[6,8]

Medications **bolded** denote availability on government subsidy list at the time of publication.

[g] Dosing frequency depends on the medication's strength and concentration.

[h] GI adverse effects include ulcers and bleeding.

[i] CV adverse effects include hypertension, chronic coronary syndrome, major vascular events and heart failure.

[j] Renal adverse effects include renal dysfunction, peripheral oedema and acute kidney injury.

[k] The efficacy and risk of adverse effects for diclofenac SR was assumed to be similar to diclofenac immediate release due to lack of direct evidence.

Oral NSAIDs

Medication	Dosing frequency (PRN basis)[g]	Efficacy on pain[6-8]	Efficacy on function[6,8]	Risk of GI adverse effects[6,8,9 h]	Risk of CV adverse effects[6,8,10 i]	Risk of renal adverse effects[8,11,12 j]
Non-selective NSAIDs						
Diclofenac tablet[l]	BD or TDS	+ + +	+ +	Moderate	High	Low
Diclofenac SR tablet[k,l]	OD or BD	+ + +	+ +	Moderate	High	Low
Ibuprofen tablet, capsules or **liquid**	TDS	+ +	+ +	Low	Moderate	Moderate
Indometacin tablet	BD or TDS	+ +	[m]	High	High	Moderate
Mefenamic acid tablet	QDS	[m]	[m]	[m]	[m]	[m]
Naproxen tablet or liquid	BD, TDS or QDS	+ +	+ + +	High	Low	Low
Piroxicam tablet	OD	+ +	++	Very high	High	Moderate
COX-2 inhibitors						
Celecoxib capsule	BD	+	++	Low	Moderate	Low
Etoricoxib tablet	OD	+ + +	++	Low	High	Similar to placebo

⚠ Contraindications for oral NSAIDs

- Active GI ulcer, bleeding or inflammatory GI diseases
- Severe hepatic or heart failure, or post-CABG surgery (except naproxen)
- Severe renal impairment (CrCl <30 mL/min)
- Beyond 20 weeks of pregnancy or in the 3rd trimester
- Experienced asthma, urticaria or other allergic-type reactions with aspirin or other NSAIDs
- Diclofenac only: Dose ≥150 mg/day for >4 weeks in patients with CV disease or uncontrolled hypertension
- COX-2 inhibitors only: IHD, PAD or cerebrovascular disease
- Celecoxib only: Sulfonamide allergy
- Etoricoxib only: Uncontrolled hypertension

⚠ Precautions for oral NSAIDs

- Drug interactions with diuretics, antiplatelets, OACs, anti-hypertensive medications, SSRIs
- Avoid excessive alcohol use
- Best taken with meals
- May be beneficial to add gastroprotective agent

BD, (up to) two times daily; CABG, coronary artery bypass graft; CrCl, creatinine clearance; COX-2, cyclooxygenase-2; CV, cardiovascular; GI, gastrointestinal; IHD, ischaemic heart disease; NSAIDs, non-steroidal anti-inflammatory drugs; OAC, oral anticoagulants; OD, once daily; PAD, peripheral artery disease; PRN, as required; QDS, (up to) four times daily; SR, sustained-release; SSRIs, selective serotonin reuptake inhibitors; TDS, (up to) three times daily

Further information on relative efficacy for pain and function in knee OA

+ + + (≈ Probability of MCID >70%)	+ + (≈ Probability of MCID 30-70%)	+ (≈ Probability of MCID <30%)

Assessment of relative efficacy considered both the probabilities of achieving minimum clinically important difference with placebo (MCID; effect size ≤0.37)[7] and relative efficacies based on published surface under the cumulative ranking curve (SUCRA) rankings.[6,8]

Further information on relative risk (RR) of adverse effects compared to placebo

Low risk (≈ RR 1-2)	Moderate risk (≈ RR >2-4)	High risk (≈ RR >4-6)	Very high risk (RR >6)

Medications **bolded** denote availability on government subsidy list at the time of publication; medications underlined denote availability on Healthier SG Medication List at the time of publication.

[g] Dosing frequency depends on the medication's strength and concentration.
[h] GI adverse effects include ulcers and bleeding.
[i] CV adverse effects include hypertension, chronic coronary syndrome, major vascular events and heart failure.
[j] Renal adverse effects include renal dysfunction, peripheral oedema and acute kidney injury.
[k] The efficacy and risk of adverse effects for diclofenac SR was assumed to be similar to diclofenac immediate release due to lack of direct evidence.
[l] Diclofenac has a similar COX-2 selectivity as celecoxib, but has traditionally been classified as a non-selective NSAID.[10]
[m] Limited evidence of relative efficacy and/or safety.

References

Click or scan the QR code for the reference list to this annex

ACE Clinical Guideline

Click or scan the QR code to view the ACE Clinical Guideline “Management of knee osteoarthritis – a joint effort with patients”