SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER14: MUSCULOSKELETAL CONDITIONS
NEMLC RECOMMENDATIONS FOR MEDICINE MANAGEMENT (2016 – 2018)

Medicine amendment recommendations, with supporting evidence and rationale are listed below. Kindly review the medicine amendments in the context of the musculoskeletal conditions chapter.

SECTION	MEDICINE	ADDED/DELETED/AMENDED
14.1 Arthralgia	Methyl salicylate ointment	Amended
14.2 Arthritis, rheumatoid	NSAIDs, oral	Added
	Prednisone, oral	Added and amended
	Proton pump inhibitor	Added
14.4.1 Gout, acute	Ibuprofen	Dose amended
	Prednisone, oral	Amended (indication updated)
14.5 Osteoarthrosis (osteoarthritis)	Ibuprofen, oral	Amended (prescriber level)
	Proton pump inhibitor	Added
	Amitriptyline, oral	Deleted
	Methyl salicylate ointment	Amended

14.1 ARTHRALGIA

Methyl salicylate ointment*: amended*

NEMLC amended the following text for correctness and clarity:

- Methyl salicylate ointment, topical, ~~applied to affected areas may be considered in selected patients.~~

14.2 ARTHRITIS, RHEUMATOID

NSAIDS, oral: *added*

Recommended for control of acute symptoms whilst awaiting referral (as doctor initiated) and for control of acute symptoms during disease flares and in severe extra-articular manifestations e.g. scleritis (as doctor prescribed), aligned with the Adult Hospital level STG and EML, 2015.

Level of Evidence: III Guidelines

Prednisone, oral: *added and amended*

Where NSAIDs are contra-indicated, prednisone, oral, 7.5 mg daily recommended for 2 weeks in patients (with a confirmed diagnosis of RA) with acute symptoms during disease flares, prior to referral for further management by a specialist.

An observational study[1] suggested that corticosteroids in RA are associated with a dose-dependent increase in mortality rates above the threshold of 8 mg per day.

EULAR Guidelines recommend that short-term corticosteroids should be considered when initiating or changing DMARDs, but should be tapered as rapidly as clinically feasible.

[1] del Rincón I, Battafarano DF, Restrepo JF, Erikson JM, Escalante A. Glucocorticoid dose thresholds associated with all-cause and cardiovascular mortality in rheumatoid arthritis. Arthritis Rheumatol. 2014 Feb;66(2):264-72. https://www.ncbi.nlm.nih.gov/pubmed/24504798

Rationale: Aligned with EULAR 2016 Guidelines[2] and evidence of safety recommending a daily threshold dose of corticosteroids as 8 mg.
Level of Evidence: III Observational study, Guidelines

NEMLC raised a concern was regarding prolonged use of corticosteroids (> 2 weeks) at primary level of care prior to referral and NEMLC recommended that the following note be added to the text of the STG:

Note: Patients should not remain on corticosteroids long-term in the absence of confirmed diagnosis of rheumatoid arthritis.

Proton pump inhibitor, oral: *added*
For high-risk patients: > 65 years of age; history of peptic ulcer disease; on concomitant warfarin, aspirin, or corticosteroids, lansoprazole 30 mg recommended as an example of the proton pump inhibitor class, for patients requiring NSAIDs. Aligned with the Adult Hospital Level STGs and EML, 2015.
Level of Evidence: III Guidelines

Referral
Referral criteria were amended to ensure that appropriate management of rheumatoid arthritis takes place at the appropriate level of care:

Urgent (to a specialist) Severe extra-articular manifestations. **Non-urgent** » Refer all patients early for confirmation of diagnosis and management. » Acute disease flares.

14.4.1 GOUT, ACUTE

Ibuprofen, oral: *dose amended*
The oral ibuprofen dose was aligned with the Adult Hospital Level STGs (Rationale being that available evidence[3] suggests that the ceiling dose for analgesia effect for ibuprofen, oral, is 400 mg 8 hourly). Text amended as follows:

If no response and inflammation is present: **ADD** ~~• NSAIDs, e.g.:~~ ~~• Ibuprofen, oral, 800 mg 8 hourly with or after a meal for 24–48 hours.~~ ~~Thereafter, if needed, reduce dose of NSAID, e.g.:~~ ~~• Ibuprofen, oral, 400 mg 8 hourly with or after a meal until pain and inflammation has subsided.~~ • Ibuprofen, oral, 400 mg, 8 hourly with or after a meal for the duration of the attack.

Level of Evidence: III Guidelines

Prednisone, oral: *amended (indication updated)*
Evidence[4] suggests that NSAIDs are associated with a risk of heart failure. Thus, indication for prednisone (alternative to NSAIDs for management of acute gout) updated to include *"existing or high*

[2] Smolen JS, Landewé R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M, et al.. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977. https://www.ncbi.nlm.nih.gov/pubmed/28264816

[3] Laska EM, Sunshine A, Marrero I, Olson N, Siegel C, McCormick N. The correlation between blood levels of ibuprofen and clinical analgesic response. ClinPharmacolTher. 1986 Jul;40(1):1-7..http://www.ncbi.nlm.nih.gov/pubmed/3522030

[4] Arfè A, Scotti L, Varas-Lorenzo C, Nicotra F, Zambon A, Kollhorst B, Schink T, Garbe E, Herings R, Straatman H, Schade R, Villa M, Lucchi S, Valkhoff V, Romio S, Thiessard F, Schuemie M, Pariente A, Sturkenboom M, Corrao G; Safety of Non-steroidal Anti-inflammatory Drugs (SOS) Project Consortium.. Non-steroidal anti-inflammatory drugs and risk of heart failure in four European countries: nested case-control study. BMJ. 2016 Sep 28;354:i4857.https://www.ncbi.nlm.nih.gov/pubmed/27682515

risk of heart failure".
Level of Evidence: II Nested case control study

14.5 OSTEOARTHROSIS (OSTEOARTHRITIS)

No response to paracetamol and inflammation is present:
Ibuprofen, oral: *amended*
Amended to allow nurses to prescribe ibuprofen for 7 days, with the following text added to the STG, "*As many of these patients, particularly the elderly, have concomitant medical conditions such as cardiovascular, gastrointestinal disease or renal function impairment, NSAIDs must be used with caution. Patients on aspirin for cardiovascular risk reduction should take aspirin 30 minutes before the 1st dose of ibuprofen in the morning, as taking aspirin and ibuprofen at the same time may reduce aspirin's efficacy",* aligned with the Adult Hospital Level STG and EML, 2015[5].
Level of Evidence: III Guidelines, Expert opinion

Proton pump inhibitor, oral: *added*
For high-risk patients: > 65 years of age; history of peptic ulcer disease; on concomitant warfarin, aspirin, or corticosteroids, lansoprazole30 mg recommended as an example of the proton pump inhibitor class, for patients requiring NSAIDs. Aligned with the Adult Hospital Level STGs and EML, 2015.
Level of Evidence: III Guidelines

Amitriptyline, oral: *not added*
Although the Adult Hospital Level STGs and EML, 2015 recommends amitriptyline, for pain management; NECML recommended that the PHC Committee review the evidence for efficacy of amitriptyline in osteoarthritis.

The PHC Committee conducted a search of Pubmed, and the Cochrane library, and could find no studies that assessed amitriptyline in osteoarthritis. The PHC Committee recommended that amitriptyline, oral be deleted from the PHC EML as add-on neuromodulator for osteoarthritis.
Rationale: Limited evidence for recommending combination therapy for inflammatory arthritis, and some evidence of benefit in fibromyalgia, but no evidence of benefit of amitriptyline in osteoarthritis.
Level of Evidence: II Systematic review of low quality studies[6]

Methyl salicylate ointment*: amended*
NEMLC amended the following text for correctness and clarity:

- Methyl salicylate ointment, topical, ~~applied to affected areas may be considered in selected patients.~~

[5] Adult Hospital Level STG, 2015:
- Ibuprofen-aspirin interaction: Gladding PA, Webster MW, Farrell HB, Zeng IS, Park R, Ruijne N. The antiplatelet effect of six non-steroidal anti-inflammatory drugs and their pharmacodynamic interaction with aspirin in healthy volunteers. Am J Cardiol. 2008 Apr 1;101(7).http://www.ncbi.nlm.nih.gov/pubmed/18359332
- Ibuprofen-aspirin interaction: Meek IL, Vonkeman HE, Kasemier J, Movig KL, van de Laar MA. Interference of NSAIDs with the thrombocyte inhibitory effect of aspirin: a placebo-controlled, ex vivo, serial placebo-controlled serial crossover study. Eur J Clin Pharmacol. 2013 Mar;69(3):365-71. http://www.ncbi.nlm.nih.gov/pubmed/22890587

[6] Ramiro S, Radner H, van der Heijde D, van Tubergen A, Buchbinder R, Aletaha D, Landewé RB. Combination therapy for pain management in inflammatory arthritis (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, other spondyloarthritis). Cochrane Database Syst Rev. 2011 Oct 5;(10):CD008886. https://www.ncbi.nlm.nih.gov/pubmed/21975788