Arden&GEM

NHS
Arden and
Greater East Midlands
Commissioning Support Unit

Non-Malignant Pain Formulary - Also see Chronic Pain Pathway Appendix 2

Formulary Key

1st line formulary choice	Encouraged
Alternative formulary choice	On Formulary
2nd line formulary choice	2nd Line
Shared Care (TAG Amber)	Shared Care Agreement

Faculty of Pain Medicine and Public Health England Guidance:

Opioids Aware: A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain

SIGN 136 Management of chronic pain Dec 2013

http://www.sign.ac.uk/assets/sign136.pdf

AGEM Key Message Bulletins

Bulletin 35 Management of Chronic Pain

Bulletin 14 Use of Opioids for Chronic Pain

Bulletin 15 Tapering Opioids in Chronic Pain

BNF 4.6 Pain

See Analgesic Pathway (Appendix 2) for use of simple analgesia and opioids for non-malignant chronic pain

STEP ONE: Simple, non-opioid analgesics

Drug		Formulation	Dose	Comments
PARACETAMOL		T/C 500mg S: 120mg/5ml, 250mg/5ml.	1g four times daily	Highly effective analgesic Ensure this is prescribed at maximum dose before escalating analgesia. Effervescent tablets have high Na+ 18.6mmol / tablet . Total of 8g of sodium per day when taking the maximum dose.
IBUPROFEN		T: 200, 400, 600mg L: 100mg/5ml	1.2g daily in 3-4 divided doses	In line with MHRA guidance - prescribe at the lowest possible dose for the shortest period of time. See NSAIDs Formulary for full guidance and BNF section 10.1.1 Lowest GI risk of standard NSAIDs. Doses less than 1200mg are not associated with increased thrombotic risk. Use omeprazole 20mg capsules once daily or lansoprazole 15mg capsules once daily for GI prophylaxis in all long-term users. CKS guidelines for use of PPIs in Gastroprotection Can also be used for migraine and dysmenorrhoea. Where possible, co-prescribing with full dose paracetamol is advised before proceeding to step two of the pain ladder.
NAPROXEN		T:250, 500mg	0.5-1g daily in 1-2 divided doses	Doses of less than 1g daily are not associated with increased thrombotic risk. Longer duration of action than Ibuprofen. For use in mild to moderate pain - Can also be used in dysmenorrhoea. Use omeprazole 20mg capsules once daily or lansoprazole 15mg capsules once daily for GI prophylaxis in all long-term users. CKS guidelines for use of PPIs in Gastroprotection Where possible co-prescribing with full dose paracetamol is advised before proceeding to step two of the pain ladder. See NSAIDs Formulary for full advice and BNF section 10.1.1. MHRA NSAID guidance

STEP TWO: Weak opioids

Use in addition to simple, non opioid analgesics as above

During titration/adjustment to the most effective dose to relieve pain it is useful to prescribe the chosen oral weak opioid separately to paracetamol - conversion to a combination product with paracetamol may encourage adherence once an effective dose is established. The most cost effective option though remains with prescribing oral weak opioids separately to paracetamol.

First Choice

DIHYDROCODEINE (DHC)		T: 30mg	**Adult:** 30mg every four to six hours when necessary.	Limit maximum dose to 120mg to 180mg daily. Higher doses offer some additional pain relief but may cause more nausea and vomiting. 120mg to 180mg daily is equivalent to 12mg to 18mg oral morphine daily. If paracetamol and dihydrocodeine combinations are needed use 10/500mg as the cost effective option. CKS - Mild to Moderate Pain

Second Choice				
CODEINE		T: 15mg, 30mg L: 25mg/5ml	**Adult:** 30 - 60mg every four hours when necessary to a max of 240mg daily.	**Variation in metabolism: The capacity to metabolise codeine can vary considerably leading to either reduced therapeutic effect or marked increase in effect and side effects.** **Causes constipation** **Acute moderate pain in children - ONLY for use in children OLDER than 12 years and ONLY if it cannot be relieved by Paracetamol or Ibuprofen alone. MHRA June 2013.** MHRA Codeine restrictions
COMPOUND ANALGESICS				
Combination analgesics should be avoided as first-line treatment. Prescribing single constituent analgesics allows independent titration of each drug. (CKS)				
Use cost effective preparations where possible - 15/500 Co-codamol and all strength effervescent preparations are not cost effective choices.				
Co-codamol tablets 8/500		T: 8mg codeine, 500mg paracetamol	**Adult:** One or two tablets to be taken up to four times daily as required.	**All opioid** combination products will cause constipation.
Co-codamol tablets 30/500		T: 30mg codeine, 500mg paracetamol		
Co-dydramol tablets 10/500		T: 10mg dihydrocodeine, 500mg paracetamol		
STEP THREE: Strong opioids				
The Faculty of Pain Medicine (supported by Public Health England) advise that: 1. Opioids are good for acute pain and pain at end of life but little evidence they are helpful for long term pain. 2. A small proportion of of people may obtain pain relief with opioids in the longterm if the dose can be kept low and if use is intermittent. 3. Risk of harm increases substantially at doses >120mg oral morphine equivalent / day, but there is no increased benefit. 4. If a patient is using opioids and still in pain, opioids are not effective and should be discontinued even if no other treatment available. 5. Chronic pain is complex and an assessment of the many emotional influences on an individual's pain is essential.				
Opioids Aware : A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain provides advice and guidance on reviewing the place of opioids in both acute and long term pain, trialling opioids, tapering and stopping. A section on information for patients is also available. **https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware**				
A Structured Approach to Opioid Prescribing				
Opioids - Information for Patients				
NOTE: Good Practice in MOST circumstances is to prescribe the most cost effective brand. **PALLIATIVE CARE PRESCRIBING - prescribe generically to allow pharmacy to supply a stocked brand to prevent delays in providing analgesia to the patient.**				
CONTROLLED DRUG PRESCRIBING - Department of Health Guidance 2006 - in general prescriptions for Controlled Drugs in Schedule 2, 3 and 4 to be limited to a supply of up to 30 days' treatment, exceptionally, to cover a justifiable clinical need and after consideration of any risk, a prescription can be issued for a longer period, but the reasons for the decision should be recorded on the patient's notes.				
Dosage Equivalences				
See Appendix 3 equivalent doses of opioids analgesics				
Information also available at: BNF online				
Opioids Aware				
First Choice				
MORPHINE		T: (immediate release **tablets**) 10mg, 20mg & 50mg	See notes and Chronic Pain Pathway	**STOP weak opioids prior to addition of strong opioid as the effect of taking together is unlikely to be additive. Patients who have received oral 120mg to 180mg DHC OR Codeine daily can be initiated on twice daily modified release capsules - 10mg twice daily.**
		C: (**twice daily** modified release **capsules**) - 10mg, 30mg, 60mg, 100mg & 200mg ***as cost effective brand***	See notes and Chronic Pain Pathwat	**Opioid naïve patients** must be started on low dose oral liquid 2.5mg up to six times daily to allow titration of dose required before being converted to the capsules. **Maintain paracetamol / NSAIDs at maximum dose as per pain ladder guidance.** **Titration must be slow with regular review**
		Oral liquid 10mg / 5 ml	See notes and Chronic Pain Pathway	For persistent non-malignant pain a total daily dose of 60mg of morphine with **NO** response suggests pain is unlikely to be opioid responsive. For persistent non-malignant pain it is recommended **NOT to exceed** 120 - 180mg oral morphine daily without referral to Specialist service - **See Chronic Pain - Guidance.** **The patient should be closely monitored for pain relief as well as for side effects especially respiratory depression and constipation.**

Alternative to First Choice Opioid				
Tramadol is now a Schedule 3 Controlled drug but is exempt from Safe Custody requirements. Please adhere to the Controlled Drug Prescription writing requirements: *The prescriptions must:* *• Be indelible* *• Be signed by the prescriber* *• Be dated* *• Specify the prescriber's address* *• State the name and address of patient* *• In the case of a preparation, state the form (e.g. tablet) and where appropriate, the strength* *• State either the total quantity (in both words and figures) of the preparation, or the number (in both words and figures) of dosage units to be supplied, e.g. 20 (twenty) tablets* *• State the dose* *• Note "as directed" is not legally considered to be a dose. The dose must be stated. Best practice is to avoid using "One as directed" and to give clear directions, e.g. "One to be taken twice a day"*				
TRAMADOL		C: 50 mg	**Adults**: 50–100 mg not more often than every 4 hours - Maximum 400 mg in 24 hours	**For ACUTE prescribing only - NICE NOVEMBER 2013.** 200mg daily dose of tramadol is approximately equivalent to 20mg of oral morphine. **ONCE DAILY** sustained release tramadol preparations are not a cost effective option as not listed in the Drug tariff - will be charged as a "special" **Ensure Paracetamol is titrated to maximum dose before Tramadol is considered for additional pain relief.** **Combination products are not recommended - Please prescribe paracetamol and tramadol separately to allow flexible dosing. Tramacet ® contains a low dose of paracetamol .** **For persistent non-malignant pain it is recommend NOT to exceed 400mg oral tramadol daily (equivalent to 40mg oral morphine) without referral to Specialist service.**
Second Choice				
CQC Newsletter - Safer use of controlled drugs - Preventing harm from oral Oxycodone.				
OXYCODONE		C: immediate release - 5 mg, 10 mg, 20 mg. T: twice daily modified release - 5 mg, 10 mg 20 mg, 40 mg & 80 mg ***as cost effective brand***	initially 5 mg every 4–6 hours initially, 5-10 mg every 12 hours	Oxycodone is approximately **twice as potent as oral morphine**. Oxycodone is two to four times more expensive than oral morphine. **Prescribe most cost effective brand.** **ONLY prescribe for patients who have developed tolerance to morphine.** For persistent non-malignant pain it is recommended to NOT exceed 80mg oral oxycodone daily without referral to Specialist service. Equivalent to 160mg oral morphine daily - **see guideline Appendix One** **Targinact (TAG Double Red) - contains oxycodone and naloxone.**
Third Choice - Shared Care for severe chronic pain in adults with intolerance to m-r morphine, which can be adequately managed only with opioid analgesics				
TAPENTADOL MR (Palexia® SR)		T: Modified Release 50mg. 100mg, 150mg, 200mg, 250mg	Initially 50 mg every 12 hours, adjusted according to response, maximum 500mg per day.	**Immediate release is TAG Double Red** Consultant responsible for first script See Shared Care Agreement
Reducing dosing errors with opioid medicines. National Patient Safety Agency (2008)				
National Patient Safety Agency 2008 guide				
OPIOID PATCH PRESCRIBING				
BUPRENORPHINE 7 day patch: Moderate Opioid effect in low dose (Step Two)				
Buprenorphine patches are an alternative to oral opioids for chronic pain management **ONLY when no oral route or severe renal impairment/ dialysis**. **Never** titrate using patches.				
TAG Green (Consultant should recommend, but GP can take responsibility for all scripts) for use in: Patients with renal impairment (eGFR 15-30, CKD 4) who have an accumulation of opiates and a resulting potential for toxicity (A licensed indication).				
After the application of any patch there is a delay of 24-96 hours before therapeutic levels of a drug are reached. Also, after removal of a patch, there is a delay of 24-96 hours before circulating levels of a drug drop to a subtherapeutic level, i.e. there is a **SLOW ONSET and SLOW OFFSET** of analgesia and of side effects.				
Transdermal patches are considerably more expensive than oral therapy.				

BUPRENORPHINE PATCHES As 7 day patch and cost		'5' - 5micrograms/hour '10' - 10micrograms/hour	Initially **one** '5 microgram patch -then dose titrated no more Use a patch of next strength or a combination of two patches (applied at the same time) **Maximum** 2 patches applied at the same time.	A **5 microgram** buprenorphine patch is approximately equivalent to **5-10mg of oral morphine daily or 50-100mg DHC / codeine daily.** A **10 microgram** buprenorphine patch is approximately equivalent to **10-20mg of oral morphine daily or 100-200mg DHC / codeine daily.** Use '**5'** and '**10'** patches **ONLY** - **higher dose** patches are **NOT** recommended for moderate pain relief. When starting, analgesic effect should **not** be evaluated until the system has been worn for **72 hours.** **Combination use with oral low dose opioids is illogical and expensive.** Patch to be changed every 7 days - siting of replacement patch on a different area (avoid same area for at **least 3 weeks**)
Transdermal fentanyl is VERY POTENT and needs to be used with great CAUTION - Non formulary for non-cancer pain.				
Safer Controlled Drug Use - Preventing Harms From Fentanyl and Buprenorphine Transdermal Patches				

Pain Rating Scale - British Pain Society
Pain scales are also available in different languages from
https://www.britishpainsociety.org/british-pain-society-publications/pain-scales-in-multiple-languages/

PAIN RATING SCALE

(English)

Title: ..... Date: .....
First Name: ..... Patient number: .....
Surname: ..... Clinic: .....

Please mark the scale below to show how intense your pain is.
A zero (0) means no pain, and ten (10) means extreme pain.

How **intense** is your pain **now**?

0 1 2 3 4 5 6 7 8 9 10
no pain extreme pain

How **intense** was your pain **on average last week**?

0 1 2 3 4 5 6 7 8 9 10
no pain extreme pain

Now please use the same method to describe how **distressing** your pain is.

How **distressing** is your pain **now**?

0 1 2 3 4 5 6 7 8 9 10
not at all distressing extremely distressing

How **distressing** was your pain **on average last week**?

0 1 2 3 4 5 6 7 8 9 10
not at all distressing extremely distressing

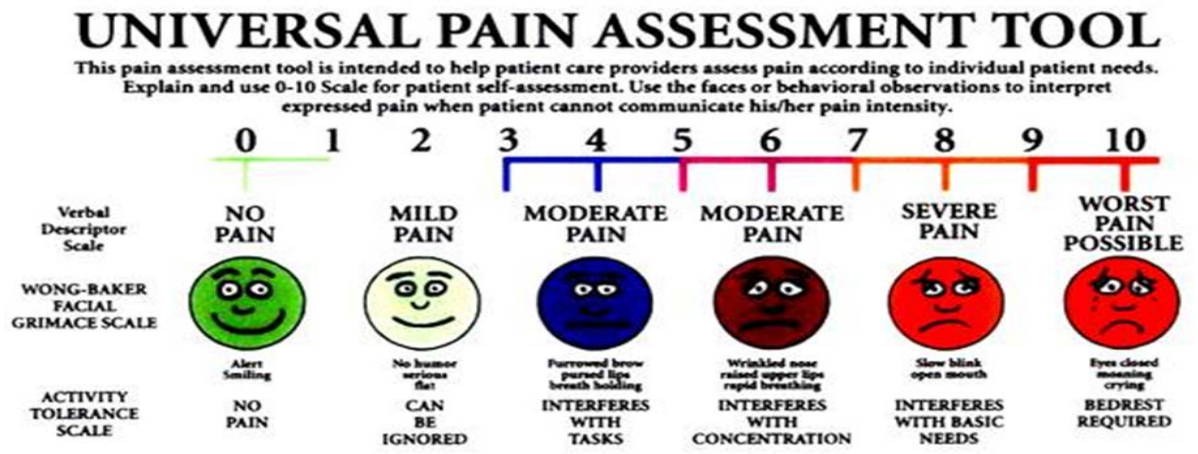
Now please use the same method to describe **how much your pain interferes** with your normal everyday activities.

0 1 2 3 4 5 6 7 8 9 10
does not interfere interferes completely

If you have had treatment for your pain, how much has this relieved (taken away) the pain?

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
no relief complete relief

Pain Score: Wong-Baker Scale. www.anes.ucla.edu/pain/FacesScale.jpg



Mild Pain – *Nagging, annoying, but doesn't really interfere with daily living activities.*

1 – Pain is very mild, barely noticeable. Most of the time you don't think about it.

2 – Minor pain. Annoying and may have occasional stronger twinges.

3 – Pain is noticeable and distracting, however, you can get used to it and adapt.

Moderate Pain – *Interferes significantly with daily living activities.*

4 – Moderate pain. If you are deeply involved in an activity, it can be ignored for a period of time, but is still distracting.

5 – Moderately strong pain. It can't be ignored for more than a few minutes, but with effort you still can manage to work or participate in some social activities.

6 – Moderately strong pain that interferes with normal daily activities. Difficulty concentrating.

Severe Pain – *Disabling; unable to perform daily living activities.*

7 – Severe pain that dominates your senses and significantly limits your ability to perform normal daily activities or maintain social relationships. Interferes with sleep.

8 – Intense pain. Physical activity is severely limited. Conversing requires great effort.

9 – Excruciating pain. Unable to converse. Crying out and/or moaning uncontrollably.

10 – Unspeakable pain. Bedridden and possibly delirious. Very few people will ever experience this level of pain.

Chronic Pain Management Pathway (see also KMB 35 and AGEM Analgesic Formulary)

Advice & Information

Exercise and activity

Weight loss

Physio-therapy

Mental Health & Wellbeing

Osteoarthritis NG177

Paracetamol + /- Topical NSAID

Ineffective

STOP Paracetamol
Start oral NSAID or COX2 inhibitor
Ibuprofen 400mg TDS **or** Naproxen 500mg BD

Insufficient

Continue Paracetamol
Add oral NSAID
Ibuprofen 400mg TDS **or** Naproxen 500mg BD

Low Back Pain NG59

Oral NSAID Ibuprofen 400mg TDS **or** Naproxen 500mg BD

Not tolerated / contraindicated

Weak Opioid
Codeine / DHC to maximum dose 120mg – 180mg daily
+ / - Paracetamol
DO NOT initiate strong opioid

Other Chronic Pain

Paracetamol + / - NSAID
Ibuprofen 400mg TDS or Naproxen 500mg **BD**

Insufficient

Not tolerated / contraindicated

ADD Weak Opioid
Codeine / DHC to maximum dose 120mg – 180mg daily **OR**
ONLY if oral route not suitable / moderate to severe renal failure:
Buprenorphine patch 5mcg or 10mcg (5mcg patch is equivalent to 5 – 10mg oral morphine daily)

Neuropathic pain likely? – see Neuropathic pain pathway and Key Message Bulletin 7

Ensure all non-pharmacologic options have been exhausted before referral to specialist or trial of strong opioid

Review Opioids (see KMB 15)

If opioid regime is **stable** and patient reports substantial relief in symptoms, **review patient every 6 months.**

If a total daily dose of 60mg oral morphine is reached without demonstrable benefit, the pain is unlikely to be opioid responsive. TAPER AND STOP.

If partial response **do not exceed 120mg daily** without specialist advice.

There is no evidence that one opioid is more effective than another.

Do not use a combination of opioids.

DO NOT initiate Fentanyl patches for non-cancer

Consider Trial of Strong Opioid (see KMB 14)

Opioid naïve patients: titrate with immediate release morphine tablets or liquid. Aim for 30-50% reduction in pain intensity.

If reduction in pain is not achieved following a single dose of immediate relief morphine 20mg, pain is unlikely to be opioid responsive. TAPER AND STOP

Patients who have received 120mg to 180mg DHC OR Codeine daily: initiate **10mg morphine BD. Use cost effective modified release capsules.** USE **immediate release** morphine up to six times daily PRN.

Review within 4 weeks: Patients who benefit from opioids long term will demonstrate a favourable response within 2-4 weeks.

Aim for 30 - 50% reduction in pain score

https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware/structured-approach-to-prescribing/dose-equivalents-and-changing-opioids

Approximate equi-analgesic potencies of opioids for oral adminstration

	Potency ratio with oral morphine	Equivalent dose to 10mg oral morphine
Codeine phosphate	0.1	100mg
Dihydrocodeine	0.1	100mg
Morphine	1	10mg
Oxycodone	2	5mg
Tapentadol	0.4	25mg
Tramadol	0.15	67mg

Transdermal Opioids

A. Buprenorphine

Transdermal buprenorphine changed at weekly intervals

	5 microgram/hr	10 microgram/hr	20 microgram/hr
Codeine phosphate (mg/day)	120mg	240mg	
Tramadol (mg/day)	100mg	200mg	400mg
Morphine sulphate (mg/day)	12mg	24mg	48mg

B. Fentanyl

Fentanyl patch strength (microgram/hr)	Oral morphine (mg/day)
12	45
25	90
50	180
75	270
100	360
300	1120

Management of Neuropathic Pain Formulary- Also see Neuropathic Pain Guide

Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings - CG173 - November 2013

CG 173

NICE BITES - Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings - CG173 - November 2013.

NICE Bites : Dec 2013

PresQIPP- Template Guidance on the management of neuropathic pain (Adults)

PrescQIPP - Downloads - Pregabalin in neuropathic pain

Formulary Key

1st line formulary choice	Encouraged
Alternative formulary choice	On Formulary
2nd line formulary choice	2nd Line
Shared Care (TAG Amber)	Shared Care Agreement

First Choice - NICE GUIDE states Offer a choice of Amitriptyline or Duloxetine or Gabapentin or Pregabalin as choices for initial treatment of Neuropathic pain (except trigeminal neuralgia)

FIRST LINE

Tricyclics

AMITRIPTYLINE		T: 10mg, 25mg	Usual starting dose is 10mg at night. Maintenance dose to achieve 50 - 75mg at night. **Maximum dose** 75 - 150mg at night.	Use of Amitriptyline doses above 75mg daily is usually under specialist supervision. May have antidepressant effect at upper end of dose range. **Tricyclics and Duloxetine should not routinely be co-prescribed. Addition of Tramadol should be done cautiously -risk of Serotonin Syndrome.**
Try Nortriptyline **ONLY** if sedation occurs with Amitriptyline. Consider in patients who are working, driving or operating machinery where sedation with amitriptyline may cause a problem. Dose - start at 10mg for two weeks and then titrate to 20mg for two weeks. If no				

SECOND LINE- An alternative choice to Tricyclics

Anticonvulsants

See MHRA Drug safety Update: Gabapentin and risk of severe respiratory depression

GABAPENTIN		C: 300mg T: 600mg	Usual starting dose is 300mg nocte - titrate to achieve target dose of 1800 - 2700mg daily in divided doses - **Max 3600mg daily.**	**Adjust dose in renal impairment** - see BNF for full guidance. **Avoid abrupt withdrawa**l if treatment not tolerated.
PREGABALIN		C: 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg.	Usual starting dose is 150mg/day (in two divided doses) with **maximum dose** 600mg/day (in two divided doses)	A lower starting dose may be more appropriate for some people. Please dose optimise where possible and use a twice daily dosing schedule. See Key Message for full details.

Antidepressant

DULOXETINE		C: 30mg, 60mg	Usual starting dose is 30-60mg daily - **Max dose 120mg daily**	Licensed indication: diabetic neuropathy

Additional Therapy

Opioids

TRAMADOL		C: 50mg	Usual dose 50-100mg not more often than every four hours - total of more than 400mg daily not usually required.	**Consider ONLY for acute rescue therapy.** **NOT for long term use.**

Trigeminal Neuralgia				
Anticonvulsants				
CARBAMAZEPINE		T: 100mg , 200mg, 400mg.	Initially 100mg 1-2 times daily, increased gradually according to response. Usual dose 200mg 3-4 times daily	**To be offered as initial treatment for trigeminal neuralgia.** If initial treatment is not tolerated or is contraindicated seek specialist advice.
Lidocaine Plaster 5% as Monotherapy				
Lidocaine Plasters 5% may be used in patients with localised neuropathic pain where first line systemic therapies are ineffective or not tolerated. Treatment is to be used as a last resort, This is classified as Green (GP prescribable following Consultant/Specialist initiation).				
Specialist Pain Consultant option for Focal Neuropathic Pain				
LIDOCAINE 5% PLASTERS		Patch: 10 cm x 14 cm 700 mg (5% w/w) lidocaine	To be applied for 12 hours per 24 hour interval Most patients will require only **one or two plasters** at a time. For some people part of one plaster will suffice. Plasters can be **cut into smaller** segments	**All oral treatment** for neuropathic pain managent is to be stopped prior to **initiation** of Lidocaine plaster treatment. Specialist consultant only to **initiate** and **provide** the **first 4 weeks** of treatment. Effectiveness to be assessed at 2 - 4 weeks and continued ONLY if effective. i.e 30% reduction in pain scale. **GP** may continue precribing **IF** proven effectiveness, reviewing **every 3 months**. Not more than three plasters should be used at the same time. (SPC) Hairs in the affected area must be cut off with a pair of scissors (not shaved).

Neuropathic Pain Management

This document is to enable practitioners to manage neuropathic pain according to the NICE Guidelines.

NICE recommends a choice of Amitriptyline, OR Duloxetine, OR Gabapentin, OR Pregabalin

The guideline excludes Imipramine as a treatment option as there is an absence of effectiveness evidence. Nortriptyline did not have sufficient evidence to enable the guidance development group to recommend that it should **not** be used and therefore no explicit recommendation was made [1].

Neuropathic pain is very challenging to manage because of the heterogeneity of its aetiologies, symptoms and underlying mechanisms. It results from damage to or dysfunction of the peripheral or central nervous system. Peripherally it can arise as a result of trauma, surgery, post herpetic neuralgia, trigeminal neuralgia or painful diabetic neuropathy[1]. Centrally from stroke, spinal cord injury, and multiple sclerosis.

Identification of Suspected Neuropathic Pain includes description of:

- Burning, stabbing, shooting, tingling, pins and needles, electric shocks.
- Pain often worse towards the end of the day
- Pain may be spontaneous (intermittent or continuous)
- Stimulus Evoked — Allodynia - pain from noon-painful stimuli eg. Light touch , clothes contact.
- Other — Hyperalgesia - increased sensitivity to normal pain stimuli.
  Autonomic Signs - skin changes: oedema, sweating, shininess
  Motor signs - Dystonia, weakness and paralysis, fasiculations.

Screening tools can be a useful guide to diagnosis and assessment of response to treatment. The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)[2] can be a useful tool for diagnosis and the Neuropathic pain Scale (NPS) [3] may be useful for detecting change in pain after treatment.

Refer - (at any stage of treatment)	•	**Identification of Complex Regional Pain Syndrome (reflex sympathetic dystrophy) acute is treatable however in delayed treatment or chronic condition it becomes untreatable.**
	•	**patients with severe pain.**
	•	**pain significantly limiting lifestyle, daily activities and participation.**
	•	**Underlying health condition has deteriorated.**

NICE Guideline 173 - Key principles of care [1]:

In addition to Pharmacological treatment, patient's beliefs and perceptions of pain and it's cause require to be considered. This includes it's cause, mood changes, coping strategies, anxiety and disturbed sleep and should be addressed as part of the patient's management. The patient's expectations of treatment and pain reduction also requires to be discussed and to note that it is not usually possible to achieve a completely pain free status. A clinically significant 30% reduction in pain is achievable for some patients.

When agreeing a treatment plan with the person, take into account their concerns and expectations and discuss [1]:

- the severity of the pain and its impact on lifestyle, daily activities (including sleep disturbance) and participation.
- the underlying cause of the pain and whether this condition has deteriorated.
- why a particular pharmacological treatment is being offered.
- the benefits and possible adverse effects of pharmacological treatments.
- coping strategies for pain and for possible adverse effects.
- non-pharmacological treatments.

Review

Patients treated for neuropathic pain require regular clinical review to ensure effective dose titration and optimal drug therapy

- At least monthly in the early stages
- Periodically thereafter

Monitoring should include:

- Pain reduction
- Tolerability and adverse effects of medication
- Ability to participate in daily activities
- Mood - especially anxiety and depression
- Overall improvement as described by the patient

References:

1. NICE clinical guideline 173, Neuropathic pain in adults - pharmacological management in non specialist setting : Available at https://www.nice.org.uk/guidance/cg173
2. Leeds Assessment of Neuropathic Symptoms and Signs (LANSS). [Accessed March2014]

Neuropathic Pain Flow Chart

Consider use of background simple analgesia

Paracetamol or NSAIDs, have minimal analgesic effect in neuropathic pain but may be effective in reducing any concomitant nociceptive pain and/or inflammation.

Assess for anxiety or depression

- Analgesia can be reduced with effective management of pain associated anxiety /depression.
- Tricyclic antidepressants (TCAs) may have antidepressant effect at the upper end of dosage range.
- Consider SSRI for treatment of depression if TCAs not tolerated or contraindicated.

Prescribing Notes:

- Doses should be started low and titrated up to and effective or highest tolerated dose (Not exceeding the max dose)
- Target doses stated are the likely effective dose. Patients may respond to lower doses.
- If the target dose is reached with NO or partial response move to the next step in the pathway.

Referral Considerations

- Suspected complex regional pa syndrome – immediate referral.
- No significant improvement in pain after adequate trial of drug treatments in algorithm.
- The patient does not want drug therapy.
- Further advice is needed or diagnosis on presenting set of clinical symptoms.

Neuropathic Component to Pain Likely

FIRST LINE: Amitriptyline *
(Usual starting dose 10mg nocte)
(Target dose 50-75mg [max. 75mg-150mg] daily

Amitriptyline contraindicated / not tolerated or ineffective

SECOND LINE: Gabapentin**
Usual starting dose 300mg nocte
Target dose 1800-2700mg
Maximum dose 3600mg daily

OR

Pregabalin Usual starting dose is 150mg/day
(in two divided doses)
Maximum dose 600mg/day (in two divided doses)

OR

Duloxetine
Usual starting dose 30-60mg daily
Maximum dose 120mg daily
Stop TCA and/or SSRI if prescribed

Caution with gabapentin: rare risk of severe respiratory depression – dose reduction may be required in respiratory or neurology disease, elderly, renal impairment, concomitant CNS depressants.

Caution with gabapentin / pregabalin if history of drug abuse – both drugs have abuse potential, are increasingly used illicitly and have a 'street value'.

Consider duloxetine if anxiety / depression †

Insufficient pain relief

Add Tramadol $
Acute prescribing only-
Must NOT be used long term

Specialist Pain Consultant option for focal neuropathic pain:
Stop the above – listed treatment options
Consider monotherapy with LIDOCAINE 5% PLASTERS

- To be applied for 12 hours per 24 hour interval.
- Consultant to prescribe the first 4 weeks' of treatment
- Effectiveness of application to be reviewed after 2 to 4 weeks, and ONLY continued if pain scores improve by a minimum of 30% on a verbal rating scale.
- GP may continue prescribing proven effective cases.
- Review every 3 months to assess whether ongoing application is required.
- Most patients will require only one or two plasters at a time. For some people part of one plaster will suffice.
- Plasters can be cut into smaller segments.
- Supported for use only as monotherapy for neuropathic pain which is localised to a small area.

REVIEW PATIENT / DIAGNOSIS/ TREATMENT AT LEAST MONTHLY

* Use of **Amitriptyline** doses above 75mg daily is usually recommended only under specialist supervision.
** **Gabapentin** (Neurontin): risk of severe respiratory depression MHRA Oct 17 https://www.gov.uk/drug-safety-update/gabapentin-neurontin-risk-of-severe-respiratory-depression#recommendations-to-minimise-risk
† **Serotonin Syndrome:** Tricyclic antidepressants, SSRIs, duloxetine and tramadol all have serotonergic actions and therefore, combination therapy increases the risk of **serotonergic syndrome. Tricyclics and duloxetine should not routinely be co-prescribed and tramadol should be used in caution in patients taking TCAs or duloxetine. Tramadol should only be prescribed as rescue treatment for short term only.**
$ **Morphine** may be used as an alternative opioid if tramadol not tolerated.

Neuropathic Pain Flow Chart
AGEM CSU

Version 2.1
Issued: Aug 2018
Review: Aug 2020

NSAIDs Formulary - See also NSAIDs Guide.
Relevant NICE guidance and other resources relating to NSAIDs.
CKS NSAIDs - prescribing issues Last revised in July 2015
CKS NSAIDs
Management of Osteoarthritis - CKS guidelines
CKS Osteoarthritis
NICE Osteoarthritis: care and management - Clinical Guideline 177 February 2014
CG 177
The management of Rheumatoid Arthritis in adults NICE Clinical Guideline 79 - updated December 2015
NICE Clinical Guideline 79
Non-steroidal anti-inflammatory drugs - NICE advice KTT13 January 2015
NICE Advice KTT13
High-dose ibuprofen (≥2400mg/day): small increase in cardiovascular risk - MHRA June 2105. EU review confirms that the cardiovascular risk of high-dose ibuprofen (≥2400mg/day) is similar to COX 2 inhibitors and diclofenac.
MHRA June 2015

Formulary Key	
1st line formulary choice	Encouraged
Alternative formulary choice	On Formulary
2nd line formulary choice	2nd Line
Shared Care (TAG Amber)	Shared Care Agreement

10. Musculoskeletal System

4. Pain and inflammation in musculoskeletal disorders

Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

First Line

IBUPROFEN		T: 200, 400, 600mg L: 100mg/5ml S/F	1.2g daily in 3-4 divided doses	In line with MHRA guidance - prescribe at the lowest possible dose for the shortest period of time. Lowest GI risk of standard NSAIDs. Doses less than 1200mg are not associated with increased thrombotic risk. Use omeprazole 20mg capsules once daily or lansoprazole 15mg capsules once daily for **GI prophylaxis in all long-term users**. Where possible co-prescribing with full dose paracetamol is advised before proceeding to step two of the pain ladder Can also be used for migraine and dysmenorrhoea.
NAPROXEN		T:250, 500mg	0.5-1g daily in 1-2 divided doses	Doses of less than 1g daily are not associated with increased thrombotic risk. **375mg tablets are NOT cost effective** Longer duration of action than Ibuprofen. For use in mild to moderate pain - Can also be used in dysmenorrhoea. Use omeprazole 20mg capsules once daily or lansoprazole 15mg capsules once daily for **GI prophylaxis in all long-term users**. Where possible co-prescribing with full dose paracetamol is advised before proceeding to step two of the pain ladder

Topical NSAIDs				
All are licensed for short-term use only				
For acute, self-limiting conditions please advise patient to buy Over The Counter (OTC)				
Caution : To be applied with gentle massage only. Not for use with occlusive dressings.				
Please encourage self-care. If prescribing ensure appropriate quantity is provided: Topical application of large amounts can result in systemic effects: including hypersensitivity and asthma.				
IBUPROFEN		Gel 5% & 10%	Three times daily	PRESCRIBE BY MOST COST EFECTIVE BRAND **e.g. Fenbid 100g**
Rubifacients are not recommended for prescribing due to a lack of evidence of clinical effectiveness and are avilable to purchase OTC.				
See NHSE Guidance: Items which should not routinely be prescribed in primary care				
NICE Clinical Guideline 177 Osteoarthritis: care and management does NOT recommend offering rubefacients for treating osteoarthritis				

Prescribing guidelines for NSAIDs (including COX II selective inhibitors)

Oral NSAIDs

The potential for reduced pain and inflammation with NSAIDs must be weighed against the well established multiple risks of treatment. They include: hypersensitivity reactions e.g. asthma. Severe dyspepsia, GI bleeds and ulceration, precipitating and enhancing hypertension & heart failure, functional and intrinsic renal toxicity and thrombosis are all well established risks. These adverse effects lead to a wide range of absolute and relative contraindications. Side effects, in combination with a range of drug interactions; makes oral NSAIDs difficult to prescribe safely in accordance with National guidance.

Osteoarthritis is probably a reasonable model for the long-term prescription of NSAIDs in primary care (as distinct from acute strains and sprains). Recent NICE OA Guidance[1] has recognised the shifting balance of evidence between toxicity and efficacy of long-term oral NSAIDs and recommends them fourth line to non-drug interventions, high dose regular paracetamol & topical NSAIDs (for which there is now more evidence to support their use).
The Norfolk and Waveney Prescribing Reference Group suggests a cautious and conservative approach to the prescribing of oral NSAIDs – see below.

GI side effects

All NSAIDs (including COX-IIs) increase the risk of serious GI bleeds. NICE OA[1] and RA Guidance[2] advocate co-prescription (usually a PPI - to reduce risk of GI damage) in ALL patients IF an NSAID has to be prescribed. This applies to all NSAIDs including COX-II inhibitors.

Ibuprofen up to 1200mg daily carries the lowest risk of GI injury followed by diclofenac and naproxen.

COX-II NSAIDs have a marginally lower risk of GI damage **BUT evidence does not support the advantage of COX-IIs being maintained when either a COX-II or "standard NSAID" are co-prescribed with a PPI[3].**
Cox-II NSAIDs should not be prescribed with aspirin.

Cardiovascular toxicity

Thrombotic risk is slightly increased with COX-II inhibitors and diclofenac (especially at doses of 150mg daily). This small increased risk is shared with ibuprofen at doses above 1200mg daily.
Low dose ibuprofen – less than 1200mg daily and Naproxen up to 1000mg daily have a minimal risk.

Whilst the absolute increase in risk is small, the very widespread use of NSAIDs in the UK, means, for example that **high dose diclofenac alone may result in 2000 premature or additional thrombotic events annually.**

Renal toxicity

All NSAIDs can precipitate functional renal insufficiency, especially in patients with existing renal impairment; this is usually dose dependent. NSAIDs are also directly reno-toxic, causing (rarely) renal papillary necrosis and interstitial fibrosis leading to renal failure (which may be irreversible)[4].

Topical NSAIDs

NICE guidance on Osteoarthritis: care and managemnt (CG177) recommends topical NSAIDs should be considered for people with hand or knee osteoarthritis ahead of oral NSAIDs or COX -2 inhibitors.

However, topical NSAIDs must be systemically absorbed to have an effect. They cause similar systemic adverse effects to oral NSAIDs but only rarely and usually when used to excess.

Hypersensitivity reactions e.g. asthma do occur with topical NSAIDs

Photosensitivity reactions can occur with all topical NSAIDs – being more common with ketoprofen - occurring in between 1-2 cases per 10,000 patients. Patients should be advised against excessive exposure to direct sunlight[5,6].
There is more evidence to support the effectiveness of topical NSAIDs for chronic pain conditions when compared to rubifacients e.g. Algesal. There are very few data to support the use of capsaicin (which is expensive) [6].
NICE CG177 does not recommend offering rubifacients for treating osteoarthritis.

Summary - Formulary Choices:

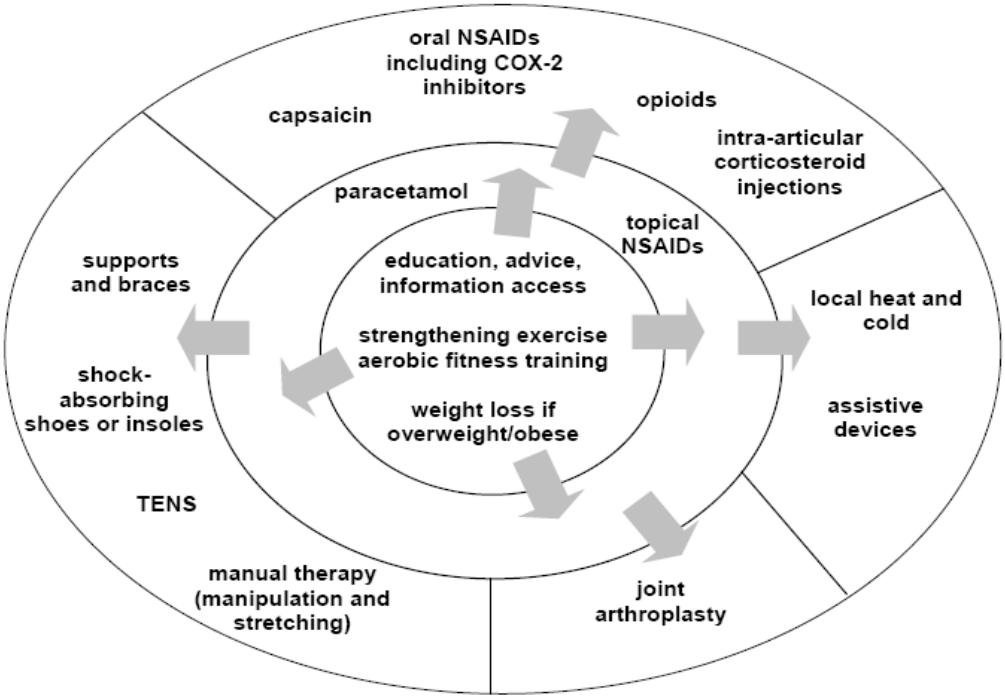
The majority of patients who MUST be prescribed an ORAL NSAID (including those where enhanced CV risk is a concern), should first be tried with ibuprofen (up to 1200mg daily). Naproxen (up to 1000mg daily) is the next logical choice.

Prescribing of a low dose PPI to reduce GI damage is required IF an NSAID is to be taken regularly.
Diclofenac and COX IIs have been removed from the formulary, due to their increased cardiovascular risk over other NSAIDs and the lack of proven advantage of COX-IIs when prescribed with a PPI to reduce GI damage.

To avoid oral NSAIDs first try non-drug interventions, then high dose regular paracetamol, then topical ketoprofen or piroxicam gel, then a rubifacient e.g. Algesal, then Capsaicin (which is expensive).

1. NICE Osteoarthritis Care and Management CG 177 - February 2014
2. NICE Rheumatoid Arthritis Clinical Guideline CG079 February 2009 - updated December 2015.
5. MHRA Drug Safety Up-date 2009;2(11):5
6. Bandolier Extra. Topical Analgesics. A Review of Reviews and a bit of Perspective. March 2005.

NICE Clinical Guideline 59: Osteoarthritis, Feb 2008



Guidelines for prescribing NSAIDs

1. Don't use them unless you have to

- The only way to avoid NSAID side effects is not to use them
- Paracetamol works for many - use regular dosing
- Employ non-drug interventions routinely - as above
- Consider topical NSAIDs ahead of oral NSAIDs for OA

2. If you have to use them, use them wisely

- The balance of benefits and risks needs to be carefully assessed; think about CV, GI and renal issues routinely
- Consider other renally excreted, renally toxic and GI irritant medications taken concomitantly
- Use a *safer* drug (Ibuprofen, then Naproxen) in the **lowest** effective dose for the **shortest** period
- NSAID users should be a high priority for medication review: are all NSAIDs still needed and effective? Consider Drug holidays? Don't issue repeat prescriptions without review

3. Consider gastroprotection in those taking regular oral NSAIDs of any type

- PPIs are the treatment of choice
- Double-dose H2RAs (less evidence) or misoprostol (effective but poorly tolerated) are alternatives

NICE CG 177 - Holisitic Assessment
Available at LINK