North East Essex
Clinical Commissioning Group

Guidelines for the management of

Non-cancer pain and Neuropathic pain

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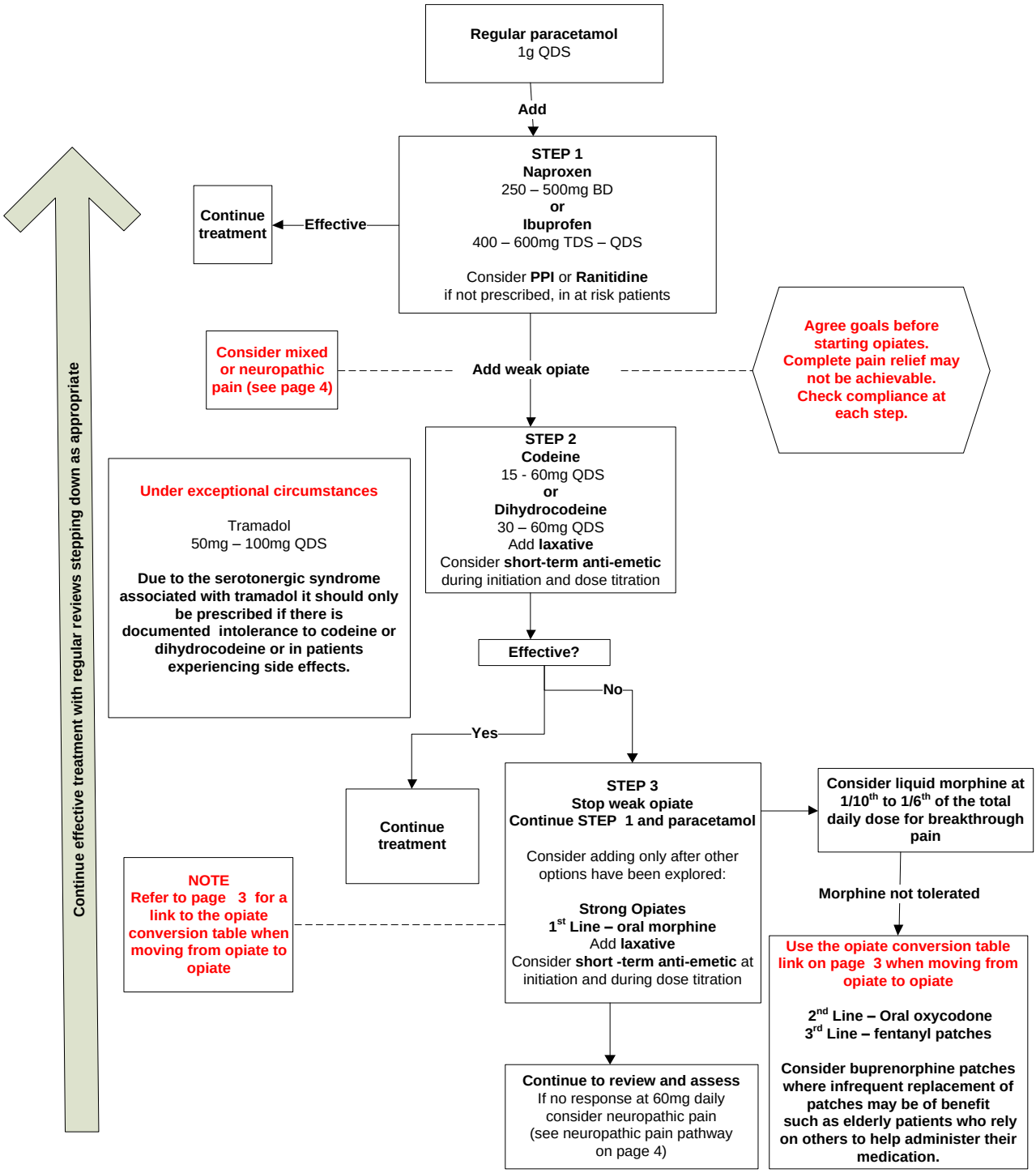
Pain management Ladder for Non - cancer pain and Non-neuropathic pain

Non-pharmacological treatment (TENS, acupuncture and relaxation) should be incorporated and psychological problems addressed at all steps of treatment. Consider referral to IAPT.
Refer to "pain management in renal impairment guidelines" for patients with chronic renal impairment.
Refer to "pain management in opioid dependent patients " for patients with opioid dependence.



All ineffective medicines MUST be stopped, diagnosis reviewed and alternative treatment sought via referral to specialist team.

Opioid conversion:

An Opioid Conversion table is available on the North East Essex CCG website under the following link:

http://www.neessexccg.nhs.uk/library_uploads/files/opioid_conversion_chart_v2.pdf

- When converting between opioids, re-titration of the new opioid may be necessary (considerable inter-patient variation will occur). Always reassess the patient carefully and anticipate the need to titrate the dose either upwards or downwards.

- Fentanyl should not be started in opioid naive patients. Where fentanyl patches are considered appropriate the patient should be titrated with low dose immediate release morphine before transferring to patches.

Breakthrough pain:

- To manage breakthrough pain a "rescue dose" of immediate release morphine should be calculated. This is usually one-tenth to one-sixth of the regular 24-hour dose given. It can be repeated every 2–4 hours as required (up to hourly may be needed if pain is severe or in the last days of life). A review of pain management is needed if rescue analgesia is required frequently (twice daily or more).

Guideline for the Management of Neuropathic Pain in Primary Care

Please refer to the individual products SPC for full prescribing details and doses in renal/hepatic impairment: https://www.medicines.org.uk/emc

Presentation suggestive of neuropathic pain
Assess using a recognised tool such as the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)-see page 5

Start TCA – amitriptyline (off-label)
Start with 10mg a day (taken at night) and gradually titrate up to an effective dose or the person's maximum tolerated dose (no higher than 75mg a day)

Trial for 6-8 weeks with at least 2 weeks at maximum tolerated dose before deciding it is not effective

When choosing a treatment consider-
- Contra-indications and potential adverse effects.
- Interactions with concurrent medication.
- Exceptionally some patients may present initially with moderate to severe neuropathic pain. In this situation it would be acceptable to start duloxetine or pregabalin first line.
- Co-morbidities that may benefit from a specific treatment i.e. depression which may benefit from using an anti-depressant.
- Patient preference.

If ineffective - discontinue amitriptyline gradually over 4 weeks

Start gabapentin
Various dose titration regimens will be required depending on the patient and how well it is tolerated. See SPC for more information.

Trial for 3-8 weeks with at least 2 weeks at maximum tolerated dose before deciding it is not effective. It may take several weeks to reach an effective dose so an adequate trial may be 2 months or longer

Not tolerated stop gabapentin gradually over 1 week

Start pregabalin
Start at 75mg twice daily. If necessary increase after 3-7 days to 150mg twice daily and if necessary after a further 7 days to a maximum dose of 300mg twice daily. See SPC for more information.

Trial for 4 weeks before deciding it is not effective.

If ineffective - discontinue gabapentin gradually over at least 1 week

Start duloxetine
Start treatment at 60mg once daily.
If necessary, increase the dose up to a maximum of 60mg twice daily.

Trial for 8 weeks before deciding it is not effective. Additional response after 8 weeks is unlikely

If ineffective -discontinue pregabalin over at least 1 week

If ineffective – discontinue duloxetine gradually over 1-2 weeks

Reassess diagnosis or refer to Specialist pain team

Additional information-
- Agree goals before starting treatment. Complete pain relief may not be achievable. Check compliance at each step.
- When using gabapentin and pregabalin prescribers must be aware of the possibility of abuse/diversion of these drugs.
- For a person with very localised neuropathic pain who wishes to avoid, or cannot tolerate oral treatments, consider prescribing capsaicin 0.075% cream (Axsain®).
- For people awaiting referral after treatments have failed, consider prescribing a **short** course of tramadol **only** if acute rescue therapy is needed. **Do not** add to repeat. Tramadol is a Schedule 3 CD, prescribe cautiously bearing in mind the potential for misuse. The combination of tramadol with amitriptyline or duloxetine is associated with a low risk of serotonin syndrome.
- NICE does not specify which drug to use first line, therefore where drugs are of similar efficacy the lowest acquisition cost is preferred.
- **Do not use -** Carbamazepine (except for trigeminal neuralgia), cannabis sativa extract, capsaicin patch, imipramine, lacosamide, lamotrigine, levetiracetam, lidocaine (topical), morphine, nortriptyline, oxcarbazepine, topiramate, tramadol (long term), venlafaxine.

This guideline recommends the use of certain drugs for indications for which there is no UK marketing authorisation. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented.

The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale

Explain: This pain scale can help to determine whether the nerves that are carrying your pain signals are working normally or not. It is important to find this out in case different treatments are needed to control your pain.

A. PAIN QUESTIONNAIRE
Think about how your pain has felt over the last week. Please say whether any of the descriptions match your pain exactly.

1. Does your pain feel like strange, unpleasant sensations in your skin? Words like pricking, tingling, pins and needles might describe these sensations.
a) NO – My pain doesn't really feel like this..... (0)
b) YES – I get these sensations quite often.....(5)

2. Does your pain make the skin in the painful area look different from normal? Words like mottled or looking more red or pink might describe the appearance.
a) NO – My pain doesn't affect the colour of my skin..... (0)
b) YES – The pain does make my skin look different from normal ..... (5)

3. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity.
a) NO – My pain doesn't make my skin abnormally sensitive in that area (0)
b) YES – My skin seems abnormally sensitive to touch in that area.....(3)

4. Does your pain come on suddenly and in bursts for no apparent reason when you're still? Words like electric shocks, jumping and bursting describe these sensations.
a) NO – My pain doesn't really feel like this..... (0)
b) YES – I get these sensations quite often ..... (2)

5. Does your pain feel as if the skin temperature in the painful area has changed abnormally? Words like hot and burning describe these sensations.
a) NO – I don't really get these sensations..... (0)
b) YES – I get these sensations quite often..... (1)

Appendix 4B. SENSORY TESTING
Skin sensitivity can be examined by comparing the painful area with a contralateral or adjacent non-painful area for the presence of allodynia and an altered pinprick threshold (PPT).

1. Allodynia
Examine the response to lightly stroking cotton wool across the non-painful area and then the painful area. If normal sensations are experienced in the non-painful site, but pain or unpleasant sensations (tingling, nausea) are experienced in the painful area when stroking, allodynia is present.
a) NO – Normal sensations in both areas ..... (0)
b) YES – Allodynia in painful area only ..... (5)

2. Altered pinprick threshold
Determine the pinprick threshold by comparing the response to a 23-gauge (blue) needle mounted inside a 2ml syringe barrel placed gently onto the skin in non-painful and then painful areas. If a sharp pinprick is felt in the non-painful area, but a different sensation is experienced in the painful area, eg. none/ blunt only (raised PPT) or a very painful sensation (lowered PPT), an altered PPT is present. If a pinprick is not felt in either area, mount the syringe onto the needle to increase the weight and repeat.
a) NO – Equal sensation in both areas ..... (0)
b) YES – Altered PPT in painful area..... (3)

SCORING:
Add values in parentheses for sensory description and examination findings to obtain overall score.
TOTAL SCORE: _____ (maximum 24)
If score < 12, neuropathic mechanisms are unlikely to be contributing to the patient's pain.
If score ≥ 12, neuropathic mechanisms are likely to be contributing to the patient's pain.
Source: Bennett M, The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and sign. Pain 2001;92: 147-157

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Step 1: Paracetamol

Medication	Indications	Preparations	Dose
Paracetamol:	Mild moderate pain: usually worth continuing in conjunction with strong opioids for synergistic effect, pyrexia	• Tablets, soluble tablets: 500mg • Oral suspension: 250mg/5ml • Suppositories: 500mg	1g qds maximum 4hrly, maximum dose 4g/24hrs

Non-steroidal anti-inflammatory drugs (NSAIDs):

Remember: COX-2 inhibitors including diclofenac are contraindicated in those with: ischaemic heart disease, peripheral arterial disease, cerebrovascular disease or established congestive heart failure (New York Heart Association [NYHA] classification II–IV). They should no longer be routinely used in primary care.

- **All NSAIDs are contra-indicated in patients with severe heart failure.**
- The lowest effective dose for the shortest possible duration should be used to control symptoms - the renal function of such patients should be carefully monitored during NSAID treatment. Re-evaluate the patient's need for symptomatic relief and response to treatment periodically.
- Use a gastro-protective agent such as a PPI for patients at high risk patients of GI toxicity.
- Always consider that patients may be purchasing NSAID's over the counter.

Gastrointestinal Risk

All NSAIDs are associated with GI toxicity. The lowest GI risk is seen with ibuprofen (≤1200mg/day). This risk is seen as soon as the treatment is started and this increases with treatment duration and dose.

GI Risk Factors;
Age > 65, Previous GI history, serious comorbidity, concomitant antiplatelets, SSRIs, oral steroids or anticoagulants, long term use e.g. OA, RA or age > 45yrs with low back pain

Cardiovascular Risk

ALL NSAIDS including COX-2 inhibitors cause a small increase in thrombo-embolic events e.g. MI, death, even with short term use. Naproxen (1000mg/day) or low dose Ibuprofen (≤1200mg/day) are associated with a lower thrombotic risk.

CV Risk factors;
Established CVD, hypertension, heart failure, diabetes, age > 65 (especially if male)
N.B. Ibuprofen or Naproxen taken with low dose Aspirin can interfere with the anti-platelet effect of aspirin through competitive inhibition

Renal Risk

All NSAIDs increase the risk of renal events. Particular concern should be exercised in elderly patients, patients on ACE inhibitors or "sartans" or long term usage.
NSAIDs should be avoided if possible in patients with pre-existing renal impairment.

Other cautions for NSAID use;
Asthma, hepatic failure/impairment, smokers, heavy alcohol use, previous hypersensitivity, women attempting to conceive. **COX-2 inhibitors may be an alternative** if asthma is a concern and in conjunction with a PPI where there is suspected small bowel blood loss

Medication	Indications	Preparations	Dose
Naproxen	Pain associated with inflammation. Choice of NSAID is often dictated by benefit/adverse effect profile but naproxen or ibuprofen should be considered for first line treatment.	• Tablets 250mg or 500mg	250-500mg bd
Ibuprofen		• Tablets 200mg, 400mg, 600mg • Liquid 100mg/5ml	400-600mg tds-qds, max 2400mg/24 hrs. •Only consider 2400mg/day of Ibuprofen if no increase in cardiovascular risk is seen with doses up to 1200 mg per day.

Step 2: Weak opioids

Opioid analgesics

Opioids should not usually be used as first line therapy for pain. Patients with a history of addiction to opioids or other drugs need referral to services with expertise in pain medicine and addiction management.

Goals of therapy should be agreed before a trial of opioids; complete pain relief is unlikely, and treatment success is demonstrated by the patient becoming able to do things that the pain currently prevents. Treatment should be reviewed at least monthly, more often if there are any concerns.

Weak opioids:

- **Use weak opioids if the patient is unable to take NSAIDS**
- **Elderly people are more susceptible to the adverse effects of opioids.**
- Tramadol is **NOT** recommended for routine use in primary care and should **NOT** be considered as an alternative to codeine/or stepping up to stronger opioids. It has been reclassified as a Schedule 3 controlled drug due to misuse.
- There is no benefit from switching from one weak opioid to another if it is deemed to be ineffective. Instead move up to step three on the analgesic ladder. **1 in 10 Caucasians do not metabolise codeine therefore it is ineffective.**

Medication	Indications	Preparations	Dose
Codeine:	Moderate pain Avoid combination preparations such as co-codamol and co-dydramol. Instead prescribe regular weak opioid with regular paracetamol. Only consider combination preparations in stable chronic pain.	• Tablets 15mg & 30mg • Syrup 25mg/5ml	15-60mg qds
Co-codamol:		• Tablets 8/500 & 30/500	2 tabs qds
Dihydrocodeine:		• Tablets 30mg • Oral Solution 10mg/5ml	30-60mg qds
Co-dydramol:		• Tablets 10/500	2 tabs qds
Tramadol:	Should be initiated only under exceptional circumstances	• Capsules 50mg. • MR Tramulief tablets 100mg, 150mg, 200mg (Twice daily formulation)	Max 400mg/24 hrs
Buprenorphine Patches	Should only be initiated by specialist recommendation only	• Butec 7 day patches: 5mcg/hr, 10mcg/hr, 20mcg/hr • Transtec 4 day patches: 35mcg/hr, 52.5mcg/hr, 70mcg/hr.	See below

- **NOTE:** Tapentadol preparations are **NOT** recommended by NEE CCG.

Buprenorphine Patches

On specialist recommendation only when used in step 2

- A partial opioid agonist **not suitable for the treatment of acute pain**
- **Onset of action occurs in 12-24 hours; therefore previous analgesia should be continued for 12 hours after the first buprenorphine patch is applied.**
- Elimination plasma half-life varies but is long therefore once a patch has been removed and not replaced the buprenorphine will continue to work for at least a further 24 hours. Do not start other opioids within 24 hours or patch removal
- Patients should be advised of the risk of increased absorption and the risk of toxicity if they are exposed to increased temperature e.g. hot bath/sauna (these should be avoided) or fever.

Medication	Indication	Preparations	Additional information
Buprenorphine	Patients unable to take oral opioids or have gastrointestinal absorption problems **Patches should not be used in patients with acute, uncontrolled pain.**	• Butec 7 day patches: 5mcg/hr, 10mcg/hr, 20mcg/hr • Transtec 4 day patches: 35mcg/hr, 52.5mcg/hr, 70mcg/hr. To avoid any confusion, it is recommended that buprenorphine patches are prescribed by the brand name.	• Patches should be changed every 4 or 7 days depending on brand. • After the first application it takes 9 days to reach steady state plasma concentrations. Steady state then remains throughout patch changes. • No dosage adjustments should be made for the first 72 hours. After 72 hours if the patient continues to require two or more doses of breakthrough analgesia the next strength patch should be used.

Step 3: Strong opioids:

- **Morphine sulphate is the oral opioid of first choice for moderate to severe pain.**
- For patients with **renal failure** please seek specialist advice refer to **Guidelines for pain management in renal impairment**
- Talk to the patient; allay any fears or concerns (e.g. addiction, side effects, associated with opioids)
- Write doses of liquid in mg not mls
- 'As required' analgesia for patients on regular opiates (1/6th of total 24 hour dose available up to hourly if needed)
- Co-prescribe a stimulant laxative as per local formulary at the same time as initiation of the opioid.
- Prescribe an anti-emetic if required during initiation and dose titration (e.g. metoclopramide 10-20mg tds max duration 5 days or cyclizine 50mg tds max duration 5 days)
- When analgesic requirements are stable convert to a sustained release preparation
- When prescribing opioids brand names should be used
- When converting between opioid preparations please refer to the opioid conversion chart – link provided on page 3.

Medication	Indication	Preparations	Dose
Morphine Sulphate	Moderate to severe pain	Immediate release: • Oramorph oral solution: 10mg/5ml • Sevredol tablets: 10mg, 20mg, 50mg Sustained release over 12 hours: • Tablets: 5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg (MST) • Capsules: 10mg, 30mg, 60mg, 100mg, 200mg (Zomorph) **NOTE: Zomorph capsules can be swallowed whole or opened and the contents sprinkled on soft food**	• Start a low dose of regular morphine (2.5 - 5mg four hourly in opioid naive patients or 5-10mg four hourly in patient previously on weak opioids. 10-20mg BD 12 hourly slow release tablets can also be used) • Morphine sulphate liquid takes 20-30 minutes to work and lasts up to 4 hours. • Morphine sulphate immediate release tablets take 90 minutes to work and last up to four hours. • Assess for pain relief and side effects • If pain still present and opioid sensitive, increase dose by 30-50%

Oxycodone

For patients with renal failure please seek specialist advice refer to the Guidelines for pain management in renal impairment

Oxycodone is approximately twice as strong as morphine

Oxycodone should only be initiated in:

- Patients with opioid sensitive pain who have side effects (e.g. hallucinations) with morphine
- Patients with moderate to severe renal failure - use cautiously. Start with small prn doses.

Medication	Indication	Preparations	Dose
Oxycodone oral	Moderate to severe pain	**Immediate release:** • Oxynorm liquid (oral solution): 5mg/5ml • Shortec Capsules: 5mg, 10mg, 20mg • **Sustained release over 12 hours:** • Longtec Tablets: 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg, 120mg	• Start a low dose of regular oxycodone (1.25 - 2.5mg four hourly in opioid naive patients or 2.5 - 5mg four hourly in patient previously on weak opioids) • Oxycodone liquid takes 20-30 minutes to work and lasts for up to four hours. • Assess for pain relief and side effects • If pain still present and opioid sensitive, increase dose by 30-50%

Fentanyl patches

- **Should not be used in patients with acute, uncontrolled pain.**
- **Onset of action occurs in 12 hours; therefore previous analgesia should be continued for 12 hours after the first fentanyl patch is applied.**
- Elimination plasma half-life is 15 - 17 hours; therefore once a patch has been removed and not replaced the fentanyl will continue to work for at least a further 12 hours.
- Patients should be advised of the risk of increased absorption and the risk of toxicity if they are exposed to increased temperature e.g. hot bath/sauna (these should be avoided) or fever.
- Patches are available as matrix and reservoir formulations. Patient familiarity with one brand is important. Reservoir patches (e.g. Tilofyl, Fentalis) must not be cut because damage to the rate-limiting membrane can lead to a rapid release of fentanyl resulting in overdose. If the prescriber intends the patch to be cut (NB: unlicensed and not recommended by the MHRA) then the prescription must specify a brand of matrix formulation patch (e.g. Fencino, Matrifen). For accuracy the matrix patch should be cut diagonally; the other half should be disposed of, in the correct manner as for a controlled drug. N.B. cutting a fentanyl matrix patch renders the use of the drug as "off label" and becomes the prescriber's responsibility.

Medication	Indication	Preparations	Additional information
Fentanyl, transdermal	Patients with opioid sensitive pain experiencing side effects with morphine Patients unable to take oral opioids or have gastrointestinal absorption problems Patients in renal failure **Patches should not be used in patients with acute, uncontrolled pain.**	• Self-adhesive matrix patch. • Patch sizes: 12, 25, 50, 75 and 100mcg/hr (e.g. Fencino or Matrifen)	• Patches should be changed every 72 hours. • After the first application it takes 36 - 48 hours to reach steady state plasma concentrations. Steady state then remains throughout patch changes.

Adjuvants use if pain is not adequately controlled with standard analgesia alone.

- If pain is of mixed origin, use standard analgesics in addition to a tricyclic antidepressant e.g. amitriptyline (off-label use) or gabapentin (or pregabalin if gabapentin is ineffective or poorly tolerated) .
    - ❖ Titrate according to clinical effect
    - ❖ Combining with opiate will result in cumulative drowsy side effect
    - ❖ Seek specialist advice or consider referral if pain persists

- **Pain that is purely neuropathic refer to the neuropathic pain pathway**

- Muscle spasm (widespread)
    - ❖ Patients with co-existing anxiety diazepam 2-5mg up to three times a day for 2-5 days
    - ❖ **Diazepam can cause addiction**
    - ❖ Baclofen is an alternative to diazepam but must be titrated slowly
- There is no clear evidence that any muscle relaxant drug is superior to any other.

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