PrescQIPP Community Interest Company

Management of non-neuropathic pain

Current spend on analgesia across England and Wales is over £136.5 million (ePACT April to June 2016). This breaks down to over £18.7 million on simple analgesics, £32.9 million on weak opioids, £86.8 million on strong opioids and £15.9 million on NSAIDs.

Medicines optimisation projects in this area are aimed at reviewing pain pathways and facilitating the appropriate primary care management of pain, in all patients aged 18 years and over suffering from chronic pain. This document does not cover the specific management of pain associated with cancer. This project should be used in conjunction with other PrescQIPP projects:

Oxycodone MR https://www.prescqipp.info/oxycodone-mr/category/61-oxycodone-mr

NSAIDs https://www.prescqipp.info/nsaids/category/175-nsaids

Opioid patches https://www.prescqipp.info/opioid-patches/category/120-opioid-patches

Oxycodone/Naloxone prolonged release tablets https://www.prescqipp.info/-oxycodone/naloxone-prolonged-release-tablets/category/105-oxycodone-naloxone-prolonged-release-targinact-tablets

Tramacet® https://www.prescqipp.info/-tramacet/category/59-tramacet

Further resources available with this bulletin: Briefing, pain pathway, patient agreement, patient information of adverse effects with inappropriate use, community pharmacist support letter, audit, slide set.

Recommendations

- Use medication for pain only as part of a wider management plan aimed at reducing disability and improving quality of life. Patients should be informed that analgesia will only offer a 30-50% reduction in pain relief.[1,2]
- Consider non opioid interventions (paracetamol +/-NSAIDs and non-pharmacological interventions) before opioid therapy.[1-3] See attachment 1: Treatment pathway for non cancer pain in adults.
- Refer patients with a history of addiction (to opioids or other drugs) to specialist services with expertise in pain medicine and addiction management.[3]
- People with conditions associated with sodium retention should avoid regular use of effervescent or soluble analgesics.[4]

Opioids

- When initiating prescribing, always consider a one to two week opioid trial (or long enough to observe the effect of opioids on two or three episodes of increased pain) to establish if the patient achieves a reduction in pain intensity and ability to achieve specific functional improvements (including sleep).[3]
- Prescribe initially on acute medication records until efficacy established.[3]
- Use with caution in older people (particularly those with medical co-morbidity).[5]
- There is little evidence that opioids are helpful long term. During long term treatment, review at least monthly in the first six months after stable dosing has been achieved, then at least annually.[2,3]
- If ineffective, the opioid should be slowly tapered down and discontinued.[3]

- There is little evidence that one opioid is more effective and associated with fewer side effects than another.[2,3]
- If opioids have been started in secondary care, there should be an agreement between the hospital and the patient's GP regarding where and by whom the patient will be assessed and who should provide the repeat prescriptions.[2,3]
- Following hospital discharge, the patient and GP should be informed of the duration of opioid treatment and on how to taper the dose of drug.[2,3,6]
- Oxycodone can be considered as an option in patients who are intolerant of morphine sulfate - see PrescQIPP bulletin B52, https://www.prescqipp.info/oxycodone-mr/category/61-oxycodone-mr
- Do not routinely offer transdermal patch formulations as first-line maintenance treatment to patients in whom oral opioids are suitable.[7] See PrescQIPP bulletin B80, https://www.prescqipp.info/opioid-patches/category/120-opioid-patches
- Do not offer ergots or opioids for the acute treatment of migraine.[8]
- Do not offer paracetamol, NSAIDS, opioids, ergots or oral triptans for the acute treatment of cluster headache.[8]
- For short term use, tramadol immediate release products are more appropriate. If prescribing for longer term persistent pain, it is more appropriate to prescribe a modified release tramadol preparation.[2]
- If prescribing tramadol modified release generically, prescribe as capsules which are listed in the Drug Tariff.[9] Do not prescribe modified release tramadol generically as tablets as these are not currently listed in part VIII of the Drug Tariff. For organisations wishing to prescribe branded generics as a cost effective option, consider Marol® SR tablets, Tramulief ®SR tablets (as twice daily prescriptions) or Tradorec® XL tablets (as daily prescriptions).[10]
- There is limited and doubtful evidence on the efficacy of nefopam. Review existing patients on nefopam. If ineffective and patients cannot tolerate side effects, reduce dosage slowly and discontinue use.

Self care

- Over the counter (OTC) therapy for migraine, e.g. Migraleve®, Nurofen Max Strength® should be purchased as part of self care.
- Paracetamol may be considered as part of a self care treatment option. Patients should purchase this for short term use, e.g. headaches, colds, fever, toothache, sore throat.

Background

The British Pain Society (BPS) defines chronic pain as persistent pain beyond the time that tissue healing would normally be expected, taken as beyond three months.[1] Chronic pain is a common complex sensory, emotional, cognitive and behavioural long term health condition which occurs when pain cannot be resolved by available medical or other treatments. Patients with chronic pain commonly experience depression, sleep disturbance, fatigue, and decreased overall physical and mental functioning.[1] Unlike acute pain and cancer pain at the end of life, persistent pain not associated with cancer has an unpredictable course and may continue for many years.[3] This type of pain causes much suffering and disability and is frequently mistreated or undertreated. Patients who present for evaluation for chronic pain should undergo a careful assessment before therapy. They often require an interdisciplinary model of care, to allow care givers to address the multiple components of the patient's pain experience. After a careful evaluation, therapy may include medication, nerve blocks, active physical therapy, behavioural interventions, and assistance with vocational evaluation and training.[1]

The Annual Report of the Chief Medical Officer of 2009 in the UK highlights the scale of the problem: 7.8 million people live with chronic pain, £584 million is spent on prescriptions for pain, 1.6 million adults per year suffer with chronic back pain, 25% of people with chronic pain lose their jobs and 16% feel their chronic pain is so bad that they sometimes want to die.[1]

The principal aims of pain management are to enable people with chronic pain to achieve as normal a life as possible by reducing physical disability and emotional distress.[1]

What is the approach to management?

In 1986 the World Health Organization (WHO) proposed a step-wise approach to the use of medication in cancer related pain. The underlying principle was that medications should be used in an incremental fashion according to the patient's reported pain intensity i.e.:

Step 1 (mild pain): non-opioid analgesic such as paracetamol and/or nonsteroidal anti-inflammatory drug.

Step 2 (mild-to-moderate pain): weak opioid such as codeine, dihydrocodeine or tramadol (controlled drug), with or without a non-opioid analgesic.

Step 3 (severe pain): strong opioid such as morphine, oxycodone, fentanyl, buprenorphine, tramadol with or without a non-opioid analgesic.

The 'ladder' approach encourages use of adjunctive medicines (e.g. antidepressants, anti-epileptics) at each rung of the ladder and use of strong opioids only at the top of the ladder. Different classes are used alone or in combination according to the type of pain and response to treatment; it will usually be appropriate to continue effective or partially effective interventions in parallel with opioid therapy.[3,11]

The Faculty of Pain Medicine states that the analgesic ladder is unhelpful in persistent pain as it has an unpredictable course and may continue for many years. Substantial reduction in pain intensity is rarely an achievable goal.[3] The Scottish Intercollegiate Guidelines Network (SIGN) also states that there is little good quality evidence for use of the ladder in chronic pain, but it does provide an analgesic strategy for non-specialists. Careful assessment and diagnosis is key to initiating appropriate pharmacotherapy. Continuing success requires regular, scheduled re-assessment of pain relief and side effects.[12] Consider using the pain assessment tools in appendix 1.

A report by the UCL school of pharmacy and UKCPA notes that although valuable, the WHO ladder has been subject to growing criticism in recent years. There have been several proposals for modifications, including removing the second ('weak' opioid) step and adapting the scale to address more effectively other types of pain, such as acute and persistent non-cancer pain. Some commentators have also argued that the step-by-step process lacks urgency and is inefficient in the context of controlling intense pain.[13]

It should be emphasised that medicines play only a minor part in managing persistent pain. Maintaining fitness, weight loss, pacing activities, normal activities and a generally healthy lifestyle are important. Non pharmacological methods of pain relief such as transcutaneous electrical nerve stimulation (TENS), acupuncture and physical methods for the reduction of muscle spasm are equally important. All patients should be screened for common mental health problems that may result from experiencing difficult to control pain. An explanation is needed that pain may be resistant to medication and complete relief of symptoms is not a goal of therapy; 30-50% pain relief may only be obtained. Treatment success is demonstrated by the patient becoming able to perform tasks (including normal household activities) that the pain currently prevents. Improved sleep would also be a reasonable outcome. Regardless of pain intensity, it is rational to start with non-opioid drugs, where these have some demonstrated efficacy for the condition being treated.[3]

Specific guidance for osteoarthritis from National Institute of Health and Care Excellence (NICE) (CG177) recommends offering regular paracetamol for pain relief (in addition to core treatments) and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) ahead of oral NSAIDs, cyclo-oxygenase 2 (COX-2) inhibitors or opioids[14] – see PrescQIPP bulletin (NSAIDs) B96, https://www.prescqipp.info/nsaids/category/175-nsaids. In the 2014 update, the guideline development group (GDG) identified reduced effectiveness of paracetamol in the management of osteoarthritis compared with what was previously thought. The GDG believes that this information should be taken into account in routine prescribing

practice until the planned full review of evidence on the pharmacological management of osteoarthritis is published.[14]

NICE guidance on chronic low back pain and sciatica (NICE NG 59, November 2016) does not recommend paracetamol alone for managing low back pain. It recommends NSAIDs as first line treatment (after considerations of risk have been taken into account) or a weak opioid (with or without paracetamol) if NSAIDs are contraindicated. This guideline also states "do not offer opioids for managing low back pain".[15,16]

An algorithm for the pharmacological management of persistent pain is in attachment 1, treatment pathway for non-cancer pain in adults.

Opioid efficacy

Data demonstrating sustained analgesic efficacy in the long term are lacking. Clinical trials of opioid efficacy suggest that the drugs can provide useful analgesia in the short and medium term.

Complete relief of pain is rarely achieved with opioids.[2,3] Data demonstrating improvement in physical, social, vocational and emotional wellbeing with opioid therapy are lacking, although improvement in sleep has been demonstrated in those for whom opioids provide useful pain relief, Opioids should not be used as primary hypnotics, anxiolytics, sedatives or antidepressants. A mental health needs assessment should be made before starting strong opioids.[3]

If the prescriber and patient agree that opioid therapy may play a role in further management of the patient's pain, a trial of opioid therapy should be planned. However short term response to opioid therapy does not predict long term therapy which may be limited by adverse effects or declining efficacy. A written agreement should be considered.[2,3] See attachment 2. The Pain Assessment and Documentation Tool (PADT) in appendix 1 is an example of a tool that can be used to record baseline levels of pain score and functional ability. The PADT tool can then be used for ongoing assessment. For patients with dementia use the Pain Assessment In Advanced Dementia (PAINAD) tool.

- The patient and prescriber should agree goals of treatment i.e. improved function, mood, sleep.
- Discuss side effects/potential problems. Patients should be advised about side effects and the likelihood of their occurrence before starting opioid therapy. The most common adverse effects are constipation, nausea, somnolence, itching, dizziness, vomiting. Adverse effects should be managed actively with laxatives, antiemetics, and antihistamines as appropriate.
- Consideration also needs to be given to communicating concerns such as addiction, tolerance, side effects and providing written and verbal information. See attachment 3. Patients with a history of addiction to opioids or other drugs need referral to services with expertise in pain medicine and addiction management. See the opioid risk tool (appendix 1).
- Set a timescale for the trial and frequency of review or guidance to stop - patients who do not achieve useful pain relief from opioids within two to four weeks are unlikely to gain benefit in the long term. Patients who may benefit from opioids in the long term will demonstrate a favourable response within two to four weeks.
- All drugs prescribed for pain should be subject to regular review to evaluate continued efficacy, and periodic dose tapering is necessary to evaluate on-going need for treatment.
- Regular review of long term therapy should be at least annually and more frequently if problems arise.[2,3]

Choice of strong opioid

There is little evidence that one opioid is more effective and associated with fewer side effects than another. Non-morphine opioids, such as fentanyl, buprenorphine and oxycodone are significantly more expensive than oral morphine. There is no consistent evidence to suggest that non-morphine opioids are any more effective, or show improved tolerability when compared with oral morphine.[2,3]

Oral morphine should be the drug of first choice. However, there is a theoretical rationale for trying an alternative opioid if the first drug tried is helpful but causes intolerable side effects.[2,3]

NICE CG 140 states not to routinely offer transdermal patch formulations as first line maintenance treatments to patients in whom oral opioids are suitable. It also recommends not to offer fast acting fentanyl as first line rescue medication.[7] PrescQIPP bulletin B52 recommends oxycodone as an option only in patients who are intolerant of morphine sulfate, i.e. develop unacceptable side effects when taking morphine even when adjunct treatment is added to reduce these side effects. The BPS and the Faculty of Pain Medicine also states NEVER prescribe opioid injections, or pethidine in any form, for the management of persistent non-cancer pain (unless on the advice of a specialist pain management team).[2,3] Use of opioid formulations with a rapid onset, such as fentanyl for transmucosal or sublingual administration are inappropriate for the management of persistent pain.[3]

The Oxford League of Analgesics put together the best available data from systematic reviews of analgesic efficacy in acute pain as a league table of Numbers Needed to Treat (NNT) in 2007. Table 1 (below) extracts data for five analgesics from this league table. Analgesic efficacy is expressed as the NNT which is the number of patients who need to receive the active drug for one to achieve at least 50% relief of pain compared with placebo over a four to six hour treatment period. The most effective drugs have a low NNT of just over 2. This means that for every two patients who receive the drug one patient will get at least 50% relief because of the treatment.[17] Equivalent doses of opioid analgesics are stated in table 2.

Table 1: Analgesic efficacy in acute pain[17]

Analgesic and dose	Number of patients in comparison	Percent with at least 50% pain relief	NNT
Codeine 60mg	1305	15	16.7
Paracetamol 1000mg + codeine 60mg	197	57	2.2
Tramadol 50mg	770	19	8.3
Tramadol 100mg	882	30	4.8
Tramadol 75mg	563	32	5.3

Table 2: Approximate equivalence of oral opioids with morphine daily dose[3,11,12]

Drug	Dose		
	Faculty of Pain Medicine[3]	BNF [11]	SIGN[12]
Morphine equivalent	10mg	10mg	10mg
Oral codeine	100mg	100mg	100mg
Oral dihydrocodeine	100mg	100mg	Not stated
Oral tramadol	67mg	100mg	50mg
Oral tapentadol	25mg	Not stated	Not stated
Oral oxycodone	5mg	6.6mg*	Not stated

*SPC for oxycodone states ratio of 1:2 to morphine.[18]

The SIGN guidelines recommend that there are two potential options for starting strong opioids:

- Start with a low dose of a long-acting preparation. If the patient is already on co-codamol or dihydrocodeine, then they are not opioid naive, particularly if they are on the maximum dose or more than one of these agents.

or

- While establishing a dose, use an immediate release preparation for short term use, only to

determine approximate dose range, then convert to equivalent long-acting preparation as soon as possible. This may be more appropriate if the patient has multiple comorbidities.

The aim is to establish the patient on a long acting opioid with no immediate release opioid if the chronic pain is stable. For patients with mild 'breakthrough pain' recommendations are to consider non-opioids (e.g. paracetamol, NSAIDs) or weak opioids.[12]

The Faculty of Pain Medicine recommends that use of immediate release preparations can provide effective symptomatic relief and use of such regimens may be justified when:

- The pain is intermittent and short-lived;
- Pain intensity varies significantly - use of regimens including immediate release preparations allows flexibility to reduce dose on days when pain is or is expected to be less severe; or
- Background pain is well controlled with modified release preparations but the patient has infrequent, short-lived episodes of increased pain.

Modified release opioids administered at regular intervals may be more appropriate for patients with persistent pain.[3]

There is no advice from NICE on the use of strong opioids for long term pain that is outside of palliative care. The guidance does state however that when starting treatment with strong opioids, offer patients with advanced and progressive disease regular oral sustained-release or oral immediate-release morphine (depending on patient preference), with rescue doses of oral immediate-release morphine for breakthrough pain. This statement is based on the evidence review where NICE identified 21 randomised controlled trials that compared the effectiveness of immediate-release morphine with sustained-released morphine, and immediate release oxycodone with sustained release oxycodone. NICE found evidence that immediate release opioids and sustained released opioids had equivalent efficacy in both the titration and maintenance phase, in terms of pain relief, adverse effects, and health related quality of life. The NICE GDG were unable to recommend one formulation over another and agreed that offering the person a choice between immediate release and sustained release formulation would be likely to improve adherence. Laxatives/and or antiemetic treatment should be prescribed and optimised before considering changing oral opioid therapy. For patients experiencing drowsiness from therapy, NICE recommends in its guidance for palliative care (CG140), either reducing the treatment dose if pain is controlled or switching the opioid if pain is not controlled.[7]

In hepatic impairment avoid use or reduce dose of strong opioids; they may precipitate coma in patients with hepatic impairment. In renal impairment, avoid use or reduce dose; opioid effects are increased and prolonged and increased cerebral sensitivity occurs.

Stopping opioid therapy

It is important to taper or stop the opioid regimen if:[2,3]

- The medication is not providing useful pain relief. The dose above which harms outweigh benefits is 120mg oral morphine equivalent/24hours. Increasing opioid load above this dose is unlikely to yield further benefits but exposes the patient to increased harm.
- The underlying painful condition resolves.
- The patient receives a definitive pain relieving intervention, e.g. joint replacement.
- The patient develops intolerable side effects.
- There is strong evidence that the patient is diverting his/her medications to others.[3]

The Faculty of Pain Medicine suggests that the dose can be tapered by 10% weekly or two weekly. The decision to taper/stop an established opioid regimen needs to be discussed carefully with the patient.[3]

Adverse effects of opioids

- 80% of patients taking opioids will experience at least one adverse effect.
- Patients should be advised about side effects and the likelihood of their occurrence before starting

opioid therapy. The most common adverse effects are constipation, nausea, somnolence, itching, dizziness and vomiting. Adverse effects should be managed actively with antiemetics, laxatives and antihistamines as appropriate.

- Tolerance to some side effects usually occurs within the first few days of initiating treatment; pruritis and constipation tend to persist. Patients using intermittent dosing schedules might not become tolerant to side effects.
- Respiratory depression is only likely to be a potential problem in persistent pain if there have been major changes in dose, formulation or route of administration. Accidental overdose is likely to be the commonest cause of respiratory depression. Particular caution is necessary for patients taking more than one class of sedative medication and in those with pre-existing disorders of respiratory control, such as obstructive sleep apnoea.
- There is little evidence that, in equi-analgesic doses, commonly used opioids differ markedly in their side effects. However, because of genetically influenced inter-individual variability in pharmacodynamics and pharmacokinetics, a patient might respond more favourably to one opioid than to another. If a patient fails to achieve useful analgesia or develops intolerable side effects with their initial opioid regimen, it may be worth trying an alternative drug.[2,3]
- Avoid codeine in breast feeding. Although the amount is usually too small to be harmful, mothers vary considerably in their capacity to metabolise codeine with the risk of morphine overdose in the infant.[11]

Long term effects of opioids

- Opioids increase the risk and incidence of falls. This is of particular importance in elderly patients. In a systematic review of observational studies, the relative risk of any fracture in patients on opioids compared to non-use was 1.38 (six studies, 95% CI 1.15 to 1.66).[19]
- Endocrine effects are probably dose related and can lead to amenorrhoea in women, reduced libido in both sexes, erectile dysfunction in men, infertility, depression and fatigue.[2]
- Both animal and human studies have demonstrated that opioids have an immunomodulating effect. These effects are mediated via opioid receptors both on immune effector cells and in the central nervous system.[3]
- Opioid induced hyperalgesia has been demonstrated in patients being treated with opioids for addiction and for pain. Clinically, the patient on long term opioid therapy presents with increased pain. This might be qualitatively distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia is more diffuse than the pre-existing pain and less defined in quality. The management of opioid induced hyperalgesia is opioid dose reduction or changing to an alternative opioid preparation; consider referral to specialist pain services.[2,11]
- Withdrawal symptoms occur if an opioid is stopped or the dose reduced abruptly, e.g. sweating, yawning, abdominal cramps, vomiting and diarrhoea. This is common with tramadol even after a short course.[2]
- Addiction is characterised by lack of control over use, craving and continued use despite harm.[2]
- Signs of excess opioid or toxicity include increasing drowsiness, vivid dreams, hallucinations, pinpoint pupils, muscle twitching/jerking myoclonus and hyperalgesia on light touch.[2]

Driving

Patients taking appropriate doses of prescribed opioids are permitted by law to drive in the UK if they are using no more than the prescribed dose and feel fit to drive. Patients should be advised to avoid driving at the start of opioid therapy and following dose changes. https://www.gov.uk/drug-driving-law

Patients should not drive for five days after starting or changing the dose, or on days where they have taken extra 'breakthrough' or 'rescue' doses, or if they feel sleepy or start taking other drugs that cause drowsiness (prescribed or purchased OTC).[2,3]

It remains the responsibility of all drivers to decide whether they consider their driving is, or might be impaired on any given occasion and they should not drive if this is the case. Drivers do not need to routinely inform the DVLA when they are taking opioids. However, it is illegal to drive if the driver is unfit to do so because they're taking legal or illegal drugs.

A checklist for prescribers is available at https://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware/structured-approach-to-prescribing/checklist-for-prescribers

Further key points on opioids other than morphine are presented below.

Oxycodone – See bulletin B52 for full guidance

Oxycodone can be considered as an option in patients who are intolerant of morphine sulfate, i.e. develop unacceptable side effects when taking morphine even when adjunct treatment is added to reduce these side effects. Prescribing is detailed in PrescQIPP bulletin 52, https://www.prescqipp.info/oxycodone-mr/category/61-oxycodone-mr

Opioid patches – fentanyl, buprenorphine see bulletin B80 for further guidance

NICE CG 140 recommends initiating transdermal patches with the lowest acquisition cost for patients in whom oral opioids are not suitable and analgesic requirements are stable, specialist advice should be sought when needed.[7] https://www.prescqipp.info/opioidpatches/category/120-opioid-patches

Tramadol

On long term use, tolerance, psychological and physical dependence may develop. Concern has risen over the increased use of tramadol. Reports of dependence and withdrawal syndromes have been reported.[20] Tramadol can be sought by drug abusers and people with addiction disorders which make it subject to criminal diversion. The UK Home Office announced in March 2014 that tramadol would become a Schedule 3 Controlled Drug, following the finding of an increased number of deaths associated with use of the drug which rose from 83 in 2008 to 175 in 2012.[21] It should only be prescribed if first line opioids are not appropriate or tolerated. Tramadol is neither more effective nor better tolerated than other weak opioid analgesics for moderate to severe pain.

If tramadol is needed long term, consider using a MR preparation. If prescribing generically, prescribe as capsules. Do not prescribe generically as tablets as these are not currently listed in part VIII of the Drug Tariff.[9] For organisations wishing to prescribe branded generics as a cost effective option, consider Marol SR tablets, Tramulief SR tablets (both as twice daily prescriptions) or Tradorec XL tablets (as daily prescriptions).[9,10] Table 3 lists cost effective branded generics of tramadol MR.

Table 3: Costs of branded generic preparations of tramadol[9,10]

Strength	Costs for 30 days (1 twice daily)[9,10] * once daily prescribing								
	Drug Tariff cost (caps only)	Maxitram SR (caps)	Marol SR (tabs)	Oldaram SR (tabs)	Tramulief SR (tabs)	Tradorec XL* (tabs)	Tramquel SR (caps)	Zamadol SR (caps)	Zydol SR (tabs)
50mg SR	£7.24	£4.55	n/a	n/a	n/a	n/a	£7.24	£7.24	£4.60
100mg SR	£14.47	£12.14	£6.94	£18.20	£6.98	£14.10	£14.47	£14.47	£18.26
150mg SR	£21.71	£18.21	£10.39	£27.30	£10.48	n/a	£21.71	£21.71	£27.39
200mg SR	£28.93	£24.28	£14.19	£36.50	£14.28	£14.98	£28.93	£28.93	£36.52
300mg SR	n/a	n/a	n/a	n/a	n/a	£22.47	n/a	n/a	n/a

Tramacet® – See PrescQIPP bulletin 62

Tramacet® contains 37.5mg tramadol hydrochloride and 325mg paracetamol. At current prices, Tramacet® is about 70% more expensive than co-codamol (30mg/500mg), an established compound analgesic. Published studies have shown Tramacet® to be no more effective than co-codamol (30mg/500mg) or ibuprofen. The BNF supports this, and says: "Compound analgesic preparations that contain a simple analgesic (such as aspirin or paracetamol) with an opioid component reduce the scope for effective titration of the individual components in the management of pain of varying intensity".[11] https://www.prescqipp.info/-tramacet/category/59-tramacet

Tapentadol

Tapentadol produces analgesia by two mechanisms. It is an opioid-receptor agonist and it also inhibits noradrenaline reuptake. The immediate release (IR) preparations are indicated for the relief of moderate to severe acute pain in adults, which can be adequately managed only with opioid analgesics.

In one study, the efficacy of immediate-release tapentadol (50 and 75mg) was similar to immediate-release oxycodone (10mg) for osteoarthritis pain due to moderate to severe joint disease (in 659 patients). Again, gastrointestinal effects were less for tapentadol than oxycodone.[22]

Tapentadol SR (prolonged release) is indicated for the management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics. It has been compared to controlled-release oxycodone for chronic low back pain and osteoarthritis in several trials. In a pooled analysis of three trials (2968 patients), tapentadol (100–250 mg twice daily) was not inferior to oxycodone (20–50 mg twice daily) for pain associated with osteoarthritis of the knee and low back pain over 12 weeks of maintenance treatment.[23] There was improved gastrointestinal tolerability compared to oxycodone.[22,23]

A comparison of adverse effects (adapted from Best Practice Advocacy Centre New Zealand (BPAC)[24]) is summarized in table 4.

Table 4: Summary of adverse effects of codeine/dihydrocodeine, tramadol, tapentadol and morphine [11,24]

	Codeine and dihydrocodeine	Tramadol	Tapentadol[25]	Morphine
Metabolised by	Codeine –CYP2D6 Dihydrocodeine – CYP2D6 and CYP3A4	CYP2D6 and CYP3A4	Glucorinidation	Glucorinidation
Main action	Mu-opioid	Mu-opioid and monoaminergic	Mu-opioid and noradrenaline reuptake	Mu-opioid
Constipation	+++	+	++	++
Nausea and vomiting	++	++++	++	++
Sedation	+++	++++	++	+++
Dizziness	++	+++	++	++
Addiction risk	++	++	++	++
Respiratory depression	++	+	+	++
Serotonin toxicity		++	+ (isolated cases)	
Seizures	+	++	+	+
Maximum daily dose	240mg/day (=morphine 24mg)	400mg/day (=morphine 60mg)	600mg	Not defined
CD schedule	-	Schedule 3 (CD No reg POM)	Schedule 2	Schedule 2

Nefopam[26]

The efficacy profile of nefopam is poorly understood as there is limited data. SIGN guidelines state that the evidence identified on the use of nefopam for chronic pain relief is not sufficient to support a recommendation.[12] It is not endorsed in the guidelines issued by NICE for palliative care or lower back pain.[7,15] A Cochrane review established that in the absence of evidence for efficacy for oral nefopam in acute postoperative pain, its use in this indication is not justified.[27]

There has been an increase in cost of nefopam 30mg over the last six months. The current cost is £55.50 for 90 tablets.[9] There is no specific guidance on stopping nefopam; when discontinuing therapy, it would seem prudent to reduce the dose slowly and ensure regular review, and monitoring of CNS effects.

Table 5: Cost comparison for strong oral opioids for 30 days (nb. doses do not imply equivalence or an equianalgesic effect. Costs are stated as the Drug Tariff costs and the least costly brand)[9,10]

	Doses	Drug Tariff costs[9]	Most cost effective brand[10]
Tramadol SR Capsules	100-200mg twice daily	£14.47- £28.93	£6.94 - £14.19 (Marol)
Morphine SR (Zomorph)	30mg-60mg twice daily	£8.30-£16.20	£8.30 -£16.20 (Zomorph)
Oxycodone MR	20mg–40mg twice daily	£53.66-£107.35	£26.83 -£53.66 (Longtec, Reltebon)
Tapentadol prolonged release tablets	100-250mg twice daily	£49.82-£124.55	£49.82 – £124.55 (Palexia SR)

Shared decision making

Shared decision making in relation to opioid treatment should include the patient, the prescriber, the patient's GP (if not the prescriber) and other key individuals involved in the patient's care.[3] Dosing errors with opioid medicines has been part of a National Patient Safety alert. Every member of the team has a responsibility to check that the intended dose is safe for the individual patient.[6]

If care is shared between hospital and community, be clear who is responsible for prescribing. Within the GP practice, only one clinician should be signing repeat opioid prescriptions. Acute prescriptions may be safer if there are concerns.[2]

As opioids play an important role in acute pain management, many patients in hospital with physical trauma or following surgery will be expected to have some pain for a short period following discharge. It may be appropriate to offer the patient a supply of opioid medicine sufficient for a few days after which opioids are unlikely to be needed. The patient must be given clear instructions regarding how to taper the dose of drug as natural recovery takes place and the treatment plan including the estimated time of cessation of opioid therapy should be communicated to the patient's GP.[3]

Prescribing in older people

Management of pain in later life can be complex; problems with both nociceptive and neuropathic pain are common and often coexist. Management is further complicated by age related physiological changes, which lead to altered drug absorption and decreased renal excretion, sensory and cognitive impairments, polypharmacy, and multimorbidity, particularly chronic conditions such as disorders of gait and balance, and kidney, lung, and cardiovascular disease. Other barriers to management include a limited evidence base to guide decisions, concerns about the potential for treatment related harm, as well as older adults' beliefs about pain and treatments for the pain.[28-30] Guidance on the management of pain in older people from 2013 falls in line with the Faculty of Pain Medicine guidance.[31]

In a small retrospective cohort study of (n=133) older patients (mean age 82) newly started on an opioid because of pain due to chronic musculoskeletal conditions, reductions in pain were recorded in 66% of participants. However, opioids were discontinued in 48% of the participants, mostly as a result of poorly tolerated side effects, including constipation, changes to mental status, and nausea.[29] A 2010 systematic review found that the long-term safety, efficacy, and abuse potential in older persons with chronic non cancer pain remains to be determined.[30]

If an opioid trial is undertaken, it is important to closely monitor (that is, every two weeks, during the initiation and dose titration phase of treatment) whether treatment goals are being met. If not, the drug should be tapered and discontinued.[28]

Opiates have been categorised into a moderate falls risk category in older people by the SIGN polypharmacy document. The guidance states that tolerance to drowsiness and sedation is usually

seen within two weeks of continuous treatment. Drowsiness and sedation is rare with codeine unless concurrently used in combination with other drugs with CNS effects. Confusion is reported with tramadol.[5]

Effervescent/soluble formulations

Some effervescent medicines contain significant amounts of sodium. At maximum daily doses of these preparations, the amount of sodium ingested may exceed the maximum recommended daily amount (approximately 100mmol sodium for adults). People who have a condition associated with sodium retention, such as hypertension, heart failure or renal impairment, or are following a salt-restricted diet, should avoid regular use of effervescent or soluble analgesics. The amount of sodium in non-soluble analgesics is insignificant. Orodispersible preparations do not contain significant amounts of sodium.[4]

Opioids in headaches

Do not offer ergots or opioids for the acute treatment of migraine.[8]

Do not offer paracetamol, NSAIDS, opioids, ergots or oral triptans for the acute treatment of cluster headache.[8]

Self care

Organisations may wish to consider the following self-care measures. Patients should purchase:

- OTC therapy for migraine e.g. Migraleve®, Nurofen Max Strength® etc.
- Paracetamol for short term use e.g. headaches, colds, fever, toothache, sore throat.

Cost savings (ePACT data April to June 2016 used)

The annual cost of analgesics across England and Wales is over £546 million.

If reviewing prescribing and discontinuing treatment no longer needed resulted in a 20% reduction, this would lead to over £109 million worth of savings across England and Wales. This equates to £179,494 per 100,000 patients.

Use of opioid formulations with a rapid onset, such as fentanyl for transmucosal or sublingual administration are inappropriate for the management of persistent pain and need to be reviewed. The current annual cost of these formulations across England and Wales is over £10.4 million
Opioid injections, or pethidine in any form, for the management of persistent non cancer pain (unless on the advice of a specialist pain management team) should not be prescribed. The current annual cost of pethidine across England and Wales is over £1.9 million.

Review existing patients on nefopam. If ineffective and patients cannot tolerate side effects, reduce slowly and discontinue. The current annual cost of nefopam across England and Wales over £24.4 million.
If a review of prescribing led to a 50% reduction in fentanyl, nefopam or pethidine formulations then this would lead to annual savings across England and Wales of over £19.4 million. This equates to £31,887 per 100,000 patients.

OTC proprietary therapy such as Panadol®, Migraleve®, Nurofen® Max Strength Migraine Pain Caplets should be purchased as part of self care rather than be prescribed. The current cost of these formulations across England and Wales is over £2.5 million. **An 80% reduction in prescribing of these items could lead to savings of over £2 million which equates to £3,303 per 100,000 patients.**

Summary

- The safety and efficacy of long term opioid use is uncertain (there are few trial data for more than 12 weeks use), although use may be appropriate in some cases of persistent pain (somatic, visceral or neuropathic).
- Medication for pain should be used only as part of a wider management plan aimed at reducing disability and improving quality of life.
- Paracetamol +/- NSAIDs (if appropriate) should usually be used as first line therapy for pain.
- If considered appropriate, a trial of opioid should be planned. If ineffective, it should be tapered-off and discontinued even if no other treatments are available.

References

1. The British Pain society. Guidelines for pain management. Programmes for adults. An evidence based review. November 2013. Accessed via https://www.britishpainsociety.org/static/uploads/resources/files/pmp2013_main_FINAL_v6.pdf
2. The British Pain Society. Opioids for persistent pain. A consensus statement prepared on behalf of the British Pain Society, Faculty of Pain Medicine of the Royal College of Anaesthetists, Royal College of General Practitioners and the Faculty of Addictions of the Royal College of Psychiatrists. January 2010. Accessed via http://www.rcoa.ac.uk/news-and-bulletin/rcoa-news-and-statements/opioids-persistent-pain-good-practice
3. Faculty of Pain Medicine. Supported by Public Health England. Opioids Aware: A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain. Accessed via http://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware 10/12/2016
4. McEntee J. What is the sodium content of medicines? UKMi Q&A 145. 6 May 2016. Accessed via https://www.sps.nhs.uk/wp-content/uploads/2014/09/NW-QA145.6-What-is-the-sodium-content-of-medicines-.pdf on 09/12/16
5. Scottish Government Model of Care Polypharmacy Working Group. Polypharmacy Guidance (2nd edition). March 2015. Accessed via http://www.sign.ac.uk/pdf/polypharmacy_guidance.pdf
6. National Patient Safety Agency. NPSA/2008/RRR05. Reducing Dosing Errors with Opioid Medicines. Accessed via http://www.npsa.nhs.uk/patientsafety/alerts-and-directives
7. National Institute for Health and Care Excellence (NICE). Clinical guideline 140. Opioids in palliative care: safe and effective prescribing of strong opioids for palliative care in adults. May 2012. http://guidance.nice.org.uk/CG140
8. National Institute for Health and Care and Excellence (NICE). Clinical guideline 150. Headache in over 12s. September 2012. http://guidance.nice.org.uk/CG150
9. Prescription Pricing Division (PPD). NHS Business Services Authority. Drug Tariff March 2016. Accessed via http://www.nhsbsa.nhs.uk/PrescriptionServices.aspx on 21/03/16
10. Haymarket Publishing, London. MIMS. March 2016. Accessed via www.mims.co.uk on 21/03/16.
11. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press; January 2016. Accessed 19/01/16.
12. Scottish Intercollegiate Guidance Networks. SIGN. Management of chronic pain. Guideline 136. Last updated August 2015. Accessed via http://sign.ac.uk/guidelines/fulltext/136/section5.html on 21/03/16.
13. Gill JA, Taylor D. Royal Pharmaceutical Society. Relieving Persistent pain, Improving Health outcomes. UCL School of pharmacy/UKCPA. January 2012. Accessed via http://www.rpharms.com/public-affairs-pdfs/relieving-persistent-pain-final-10-01-12.pdf
14. National Institute for Health and Care Excellence (NICE). Clinical guideline 177. Osteoarthritis: care and management. February 2014. Accessed via https://www.nice.org.uk/guidance/cg177/chapter/1-recommendations

15. National Institute for Health and Care Excellence (NICE). NICE Guideline NG59. Low back pain and sciatica in over 16s: assessment and management. November 2016. Accessed via https://www.nice.org.uk/guidance/NG59/chapter/Recommendations#non-invasive-treatments-for-low-back-pain-and-sciatica on 09/12/2016
16. National Institute for Health and Care and Excellence (NICE) Clinical Knowledge summaries (CKS). Back pain – low (without radiculopathy). Last revised April 2015. Accessed via http://cks.nice.org.uk/back-pain-low-without-radiculopathy on 10/12/16
17. Ong CKS , Link P, Tan CH et al. An Evidence-Based Update on Nonsteroidal Anti-Inflammatory Drugs. Clinical Medicine and Research 2007; 5(1): 19-34. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1855338/ accessed 7/10/16
18. Summary of Product Characteristics. Oxycontin prolonged release tablets. Napp Ltd. Last updated 22/08/16,accessed via https://www.medicines.org.uk/emc/medicine/29384 on 09/12/16
19. Takkouche B, Montes-Martinez A, Gill SS, et al. Psychotropic medications and the risk of fracture. A meta-analysis. Drug Safety 2007; 30: 171-184.
20. Summary of Product Characteristics. Tramadol capsules. Actavis UK Ltd. Last updated 22/09/15, accessed 19/01/16. Accessed via https://www.medicines.org.uk/emc/medicine/24186 on 09/12/16
21. Office for National Statistics. Deaths Related to Drug Poisoning in England and Wales, 2012. Accessed via http://www.ons.gov.uk/ons/dcp171778_320841.pdf on 03/01/16
22. Hartrick C et al. Efficacy and Tolerability of tapentadol IR and oxycodone IR in patients awaiting surgery for end stage joint disease: A 10-day, phase III, randomised, double blind active and controlled placebo study. Clin Ther 2009; 31: 260–71.
23. Lange B, Kuperwasser B, Okatoto et al. Efficacy and safety of tapentadol prolonged release for chronic osteoarthritis pain and low back pain. Adv Ther 2010; 27:381-399.
24. Best Practice Advocacy Centre New Zealand (BPAC) WHO Analgesic Ladder: which opioid to use at step two. BPJ 2008:18. Accessed via http://www.bpac.org.nz/BPJ/2008/December/ladder2.aspx on 21/03/16
25. Summary of Product Characteristics. Palexia SR prolonged release tablets. Grunenthal Ltd. Last updated 15/10/14, accessed 22/05/16. Accessed via https://www.medicines.org.uk/emc/medicine/28375 on 09/12/16
26. Summary of Product Characteristics. Nefopam. Beechmere Pharmaceuticals Ltd. Last updated 12/11/15, accessed 22/05/16. Accessed via https://www.medicines.org.uk/emc/medicine/31146 on 09/12/16
27. Kakkar M, Derry S, Moore RA et al. Single dose oral nefopam for acute post operative pain in adults. Cochrane Database of Systematic Reviews July 2009. Accessed via http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007442.pub2/abstract;jsessionid=8F3366AC0C94CFD2654A0CAFFC409141.f04t03
28. Reid MC, Eccleston C, Pillemer K. Management of chronic pain in older adults. British Medical Journal 2015; 350 doi: http://dx.doi.org/10.1136/bmj.h532
29. Reid MC, Henderson CR Jr, Papaleontiou M, et al. Characteristics of older adults receiving opioids in primary care: treatment duration and outcomes. Pain Med 2010; 11: 1063-71.
30. Papaleontiou M, Henderson CR Jr, Turner BJ, et al. Outcomes associated with opioid use in the treatment of chronic non-cancer pain in older adults: a systematic review and meta-analysis. J Am Geriatr Soc 2010; 58: 1353-69.
31. Guidance on the management of pain in older people. Age Ageing 2013; 42 (suppl 1): i1-i57 http://www.bgs.org.uk/pdfs/pain/age_ageing_pain_supplement.pdf

Additional PrescQIPP resources

 Briefing

 Data pack

 Audits, pathways, patient letters

Available here: https://www.prescqipp.info/resources/category/349-non-neuropathic-pain

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Contact help@prescqipp.info with any queries or comments related to the content of this document.

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The use and application of this guidance does not override the individual responsibility of health and social care professionals to make decisions appropriate to local need and the circumstances of individual patients (in consultation with the patient and/or guardian or carer). Terms and conditions

Appendix 1: Useful resources to aid the decision making process

Assessment tools

British Pain Inventory – Use to quantify level of pain and provide a baseline http://www.healthcare.uiowa.edu/igec/tools/pain/briefpain.pdf

http://www.euroqol.org/fileadmin/user_upload/Documenten/PDF/Products/Sample_UK__English__EQ-5D-5L_Paper_Self_complete_v1.0__ID_24700_.pdf

Pain self efficacy questionnaire https://www.worksafe.vic.gov.au/__data/assets/pdf_file/0020/10955/pain_self_efficacy_questionnaire.pdf

STarT back screening tool (Keele University) - A brief validated tool (Hill et al 2008), designed to screen primary care patients with low back pain for prognostic indicators that are relevant to initial decision making https://www.keele.ac.uk/media/keeleuniversity/group/startback/Keele_STarT_Back9_item-7.pdf

Patient Health Questionnnaire (PHQ9) score – Use to measure severity of depression and response to treatment http://patient.info/doctor/patient-health-questionnaire-phq-9

General pain management tools www.britishpainsociety.org

Understanding and Managing Long Term Pain – Information for People with Pain (for purchase)

https:// https://www.britishpainsociety.org/static/uploads/resources/files/book_understanding_pain.pdf

Practitioner decision aid - For opioid use with patients with persistent pain. Initial and follow up assessment. https://www.northkirkleesccg.nhs.uk/wp-content/uploads/2013/07/practitioner_decision_aid_-_opioid_use_OUPA.pdf

Pain Assessment In Advance Dementia Scale (PAINAD) https://www.healthcare.uiowa.edu/igec/tools/pain/PAINAD.pdf

Pain Assessment and Documentation Tool (PADT) – Assesses pain and progress on long term opioid treatment for chronic pain, and is used throughout opioid treatment http://www.practiceadvisor.org/docs/default-source//Documents/Pain_Assessment_and_Documentation_Tool

Opioid risk tool https://www.drugabuse.gov/sites/default/files/files/OpioidRiskTool.pdf

Opioids aware - A resource for patients and healthcare professionals to support prescribing of opioid medicines for pain http://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware

For prescribers

Checklist for prescriber – What to discuss with the patient when considering opioid treatment https://www.rcoa.ac.uk/system/files/FPM-OA-checklist-for-prescribers.pdf

Pain Association Scotland - Chronic pain and the benefits of self-management booklet http://www.rpharms.com/public-affairs-pdfs/83187-pas-gp-brochure-12pp-low.PDF

For patients

www.paintoolkit.org

www.painuk.org

For community pharmacists

Talking about pain – 8 questions to ask http://www.rpharms.com/public-affairs-pdfs/talking-about-pain-patients-8-questions.pdf

Talking about pain – interpreting the answers to 8 questions http://www.rpharms.com/public-affairs-pdfs/talking-about-pain-pharmacist-info.pdf

The British Pain Society. Manging your pain effectively using OTC medicines https://www.britishpainsociety.org/static/uploads/resources/files/patient_pub_otc.pdf