Berkshire West Area Prescribing Committee Guidance

Guideline Name	Guidelines for the Management of Chronic Non-Malignant Pain (CNMP) in primary care (not including neuropathic pain)
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Berkshire West Area Prescribing Guidelines serve as a reference for clinicians. This does not overrule the clinical or budgetary responsibility of clinicians when considering treatment for individual patients.
These guidelines have been produced in consultation with Royal Berkshire Foundation Trust Hospital Foundation, Berkshire Healthcare Foundation Trust and Berkshire West CCGs.

Adapted from North West Surrey CCG guidelines with kind permission of the author (M. Allingham)

Guidelines for the Management of Chronic Non-Malignant Pain (CNMP) in Primary Care (not including neuropathic pain (NeP).

Step 1 Paracetamol +/- topical NSAIDs	***Simple analgesia*** **Regular Paracetamol: 1g QDS** • Paracetamol and / or topical NSAIDs should be considered ahead of oral NSAIDs or opioids. • **Ensure patient has been taking regularly before moving to next step** Consider offering topical **NSAIDs** for pain relief in addition to core treatment for people with knee or hand osteoarthritis.
Step 2 Regular paracetamol + oral NSAID, weak opioid or both	***Oral NSAIDs -Ibuprofen (max dose 1200mg/24 hours) or Naproxen(max dose 500mg BD). If initial NSAID not effective try switching to alternative NSAID*** • Where paracetamol or topical NSAIDs provide insufficient pain relief then consider the addition of an oral NSAID to regular paracetamol. All oral NSAIDs have analgesic effects of a similar magnitude. • Consider the patient's renal function and monitor. • No greater benefit with modified release preparations so prescribing a standard release preparation is recommended. • Prescribe a PPI (omeprazole 20mg or lansoprazole 15mg daily) in appropriate patients (NICE CG88 recommends in people over 45). *NSAIDs should be used at the lowest effective dose for the shortest possible period of time* Diclofenac is not encouraged due to the evidence about the possibility of increased cardiovascular risk associated with this drug. ***Weak Opioids*** **1st line**: Add **Codeine Phosphate (**at a max 240mg daily in divided doses) **2nd line**: Switch to **dihydrocodeine** (at a max dose of 30mg 4-6 hourly) if patients have intolerable poor or no response to codeine or intolerable side effects (doses for brands may vary so consult individual SPCs) **Buprenorphine (BuTrans®) patch up to 20mcg/hr -** The patches may be useful only for people that have not responded to maximum dose oral weak opioid analgesia and that require continuous release pain control . Also consider in patients who are nil by mouth or with mild to moderate renal impairment. Consider use of prophylactic anti-emetic for first 7-10 days of therapy. Initiate on 5mcg/hr patch and adjust dose at minimum 3 day interval (see SPC). During initiation and titration with **BuTrans®**, patients should use the usual recommended doses of short-acting supplemental analgesics as needed until analgesic efficacy with **BuTrans ®** is attained. See SPC for more information. For dose equivalencies of codeine and BuTrans see conversion table below
Step 3 **Before initiating a strong opioid consider if the patient has Neuropathic element to their pain (see NeP guidelines)** **STOP ALL WEAK OPIOIDS.**	***Strong opioids –*** **DISCUSS THE FOLLOWING WITH PATIENT BEFORE INITIATING-** • **Treatment with opioids will not achieve 100% pain relief-best case 30-50% pain reduction-goals of therapy should be laid out before a trail of opioids is initiated.** • **No evidence to support long term use of opioids but side effects with long term use include reduced immune function and, hormone imbalance leading to impotence** • **Patients need to be given advice regarding ability to drive. For further information see https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/325275/healthcare-profs-drug-driving.pdf** **1st line: Morphine sulphate MR** with oral morphine sulphate solution for breakthrough pain. • Initiate morphine sulphate MR 10mg bd with morphine sulphate solution at 1/6th of total daily dose for breakthrough pain. (4 hourly, requirement of more than 2 to 3 doses in 24 hours indicates that morphine sulphate MR needs to be increased). Titrate according to response so that use of morphine solution is hardly required. • British Pain Society recommends that if patients do not achieve useful relief of pain when titrated to doses between 120-180mg morphine equivalent per 24 hours they should be referred to a specialist in pain medicines. • Consider offering for short-term use in people with severe pain. • Patients should be reviewed monthly, consider referring people requiring prolonged use. • Prescribe laxatives (see 'Guidelines for the management of chronic constipation in adults') **2nd line:** Switch to **oxycodone MR** where patient has intolerable side effect or has poor response to morphine. • Note: morphine sulphate MR 10mg is dose equivalent to oxycodone MR 5mg. **Doses may need to be reduced in patients with renal impairment.**

Notes

1. **Co prescribing of tramadol and amitriptyline is to done with caution and on the advice of the pain clinic.**
2. **Tapentadol should not routinely be used unless advised by the pain clinic**.

Morphine Sulphate MR is the strong opioid of choice as immediate release opioids may be associated with tolerance and problem drug use. Most patients will develop tolerance to the side effects of morphine (except constipation).If patients suffer from nausea when first starting morphine a short course of metoclopramide may be appropriate until tolerance develops. A laxative should always be prescribed with morphine (see constipation guidelines). Patients with significant renal or hepatic impairment may need a reduced dose of morphine. An immediate release preparation given at longer intervals than normal is more appropriate than using a modified release preparation in these patients. Consider referring these patients to secondary care pain clinic.
Withdrawal symptoms occur if opioids are stopped suddenly or if the dose is reduced abruptly.
If patients do not achieve useful relief of pain when titrated to doses between 120-180 mg morphine equivalent per 24 hours, referral to a specialist in pain medicine is strongly recommended.

Oxycodone has an efficacy and side-effect profile similar to that of morphine. There are no advantages in using oxycodone as first-line for moderate to severe pain, Oxycodone is an alternative for the small number of patients who develop intolerable adverse effects with oral morphine or who do not respond to morphine. **Care should be taken with dose conversion**.

In the management of Chronic Non-Malignant Pain (CNMP) in Primary Care pharmacological interventions should be increased to full therapeutic and tolerated dose before switching or adding a different agent. Pain is a biologically complex phenomenon and there is rationale for combining drugs with different mechanisms of action. Patients should be encouraged to consider non-pharmacological strategies available and where appropriate make lifestyle adjustments.
Please note: these guidelines are not intended to cover Palliative Care.

There are few trial data assessing the use of opioids for more than 12 weeks and therefore the safety and efficacy of long term opioid use is uncertain. They have long term endocrine and immunological effects. Before initiating opioids, a comprehensive assessment by the clinician is important. Patients with depression, anxiety, or other psychiatric or psychological co-morbidities will need additional support and monitoring to avoid problem drug use. Patients with a history of addiction to opioids or other drugs need referral to services with expertise in pain medicine. Goals of therapy should be agreed before a trial of opioids and treatment should be reviewed at least monthly. Requests for dose increases by the patient need to be evaluated carefully.
A good practice guide for clinicians on opioid prescribing is available. See appendix 1.
A useful booklet for patients to refer to can be found on-
https://www.britishpainsociety.org/static/uploads/resources/files/book_opioid_patient.pdf

Opioid dose conversion chart

These conversion ratios are approximate and are only intended as a guide. Patients' response to opioid varies widely and they should be monitored for response and side effects when any opioid is initiated.

Opioid Equivalence Table *(Twycross 2011, Mercadante 2011)*

These dose equivalences are **approximations** intended for use by experienced clinicians. Always seek specialist advice before prescribing unfamiliar opioids. Use particular care when converting between higher doses or where doses have recently required rapid titration. In such patients, consider a dose 25-33% lower than predicted by the ratios and ensure P.R.N.s are available

Codeine		Tramadol		Oral Morphine			Subcutaneous Morphine		Oral Oxycodone			Subcutaneous Oxycodone		Subcutaneous Diamorphine*		Fentanyl Patch**	Buprenorphine Patch*/**
Q.D.S. dose	24 hour total dose (mg)	Q.D.S. dose	24 hour total dose (mg)	4 hour / p.r.n. dose (mg)	12 hour MR b.d. dose (mg)	24 hour total dose (mg)	4 hour / p.r.n. dose (mg)	24 hour total dose (mg)	4 hour / p.r.n. dose (mg)	12 hour MR b.d. dose (mg)	24 hour total dose (mg)	4 hour / p.r.n. dose (mg)	24 hour total dose (mg)	4 hour / p.r.n. dose (mg)	24 hour total dose (mg)	Micrograms per hour	Micrograms per hour
60	240	50	200	2.5-5	10	20	2.5	10	1-2.5	5	10	1	5	1	5	½ x 12***	5
		100	400	5-10	20	40	2.5-5	20	2.5-5	10	20	2	10	2	10	12	10
				10	30	60	5	30	5	15	30	2.5	15	2.5	15	12-25	10-20
				15	45	90	7.5	45	7.5	20	40	2.5-5	20	5	30	25-37 (25+12)	**Seek specialist advice** Conversion estimates to and from buprenorphine vary considerably; higher doses preclude switching in a single step.
				20	60	120	10	60	10	30	60	5	30	7.5	40	37 (25+12)-50	
Is long term (years rather than months) opioid use anticipated? If so, seek specialist advice before titrating to the higher doses in the section below Adverse effects (particularly endocrinopathies) are common with longer term higher dose opioids; Higher doses are used for opioid-responsive pains in the *palliative prognostic context (weeks to months)* since longer term effects are not relevant Use particular care when converting between higher doses: consider a dose 25-33% lower than predicted by the ratios and ensure P.R.N.s are available																	
				30	90	180	15	90	15	45	90	7.5	45	10	60	50-75	
				40	120	240	20	120	20	60	120	10	60	10-15	80	62 (50+12)-100	
				50	150	300	25	150	25	75	150	10	75	15	100	75-125	
				60	180	360	30	180	30	90	180	15	90	20	120	100-150	
				70	210	420	35	210	35	105	210	15	105	20-25	140	125-175	
				80	240	480	40	240	40	120	240	Max**** Subcut Volume	120	25	160	125-200	
				90	270	540	45	270	45	135	270		135	30	180	150-225	

* Where possible, morphine, oxycodone and fentanyl are recommended choices to ensure familiarity with a smaller number of opioids.
** Conversions to and from transdermal patches are especially unpredictable. Prescribers unfamiliar with such products are encouraged to seek specialist advice
*** Matrix fentanyl patches can be cut diagonally in half for smaller dose increments where a smaller patch size is unavailable (unlicensed use)
**** At usually available concentrations. If higher doses required, seek specialist advice about higher concentration preparations or alternatives.

† = Off-label indication or route, # = unlicensed product

Breakthrough or rescue dose: Oral Morphine at 1/6th of the total 24 hour oral dose should be used for breakthrough pain.

For further dose conversions please see- opioid conversion calculator- **http://book.pallcare.info/index.php?op=plugin&src=opiconv-**Ensure that ALL opioids are included

Information about Drugs NOT recommended as first line choice

Transdermal Patches should be reserved for use in the limited number of patients who are unable to tolerate oral medications or if morphine or oxycodone is contra-indicated e.g. severe renal impairment.

Fentanyl patches should not be prescribed under any circumstances for opioid naïve patients. Note-they are only licensed for use in chronic intractable pain. Take care with calculation of dose equivalents. **A 25mcg patch is equivalent to 90mg morphine per day** (see conversion chart). When starting, evaluation of the analgesic effect should **not** be made before the patch system has been worn for 24 hours. Previous analgesic therapy should be phased out gradually from time of first patch application; if necessary dose should be adjusted at 48-72 hour intervals in steps of 12-25micrograms/hour. **NOTE-** *it may take up to 17 hours for the plasma concentration to decrease by 50%. In view of long duration of action, patients who have had severe side-effects should be monitored for up to 24 hours after patch removal.*

Buprenorphine patches should not be used for acute pain.

BuTrans ® patches (5mcg-20mcg/hr) should be reserved for patients who have not responded to maximum dose oral weak opioid analgesia codeine and dihydrocodeine, and that require continuous release pain control. Also consider in patients who are nil by mouth or those with mild to moderate renal impairment. Consider use of prophylactic anti-emetic for first 7-10 days of therapy. Initiate on 5mcg/hr patch and adjust dose at a minimum of 3 day intervals (see SPC for further information). During initiation and titration with **BuTrans®**, patients should use the usual recommended doses of short-acting supplemental analgesics as needed until analgesic efficacy with **BuTrans ®** is attained.

Transtec® patches (35-70mcg/hr) is licensed for moderate to severe cancer pain and severe pain which does not respond to non-opioid analgesics. The patches are equivalent to strong opioid doses and are not suitable for the treatment of acute pain. They should be reserved for patients who are nil by mouth or where there is severe renal impairment. (see SPC for further information).

See opioid conversion chart for approximate equivalencies.

Fixed dose combination products (e.g. **Co-codamol 30/500mg**) do not allow titration to the most effective analgesic dose to match the individual's requirements and so have a limited role.
Low-dose weak opioid and paracetamol preparations (e.g. **Co-codamol 8/500mg, Co-dydramol**) still lead to opioid adverse effects and there is no evidence to show that they are more effective than Paracetamol alone.

Effervescent or soluble formulations offer no advantage in patients who are able to swallow tablets, contain high concentrations of sodium and are expensive. These formulations should be avoided unless there are specific indications (e.g. swallowing difficulties).

Co-proxamol is no longer licensed in the UK.

Targinact® (Oxycodone / naloxone): prescribing of this product is not routinely recommended. This

product is considerably more expensive than oxycodone prescribed as a single component. Also opioid use may not be the only cause of constipation

Tramadol is neither more effective nor better tolerated than other weak opioid analgesics for moderate to severe pain and its safety profile is problematic. Where use of tramadol is considered necessary for control of chronic pain, the use of SR preparations of tramadol should be considered. Co-prescribing of tramadol and amitriptyline should be avoided due to the increased risk of CNS toxicity with this combination.

Tramacet® is a fixed dose combination of Tramadol 37.5mg and a sub therapeutic dose of Paracetamol 325mg. Prescribing of this product is not routinely recommended as it offers little advantage in terms of efficacy, adverse effects or convenience over standard analgesics.

Vimovo® (naproxen ec 500mg/ esomeprazole IR 20mg) is not recommended for use as there is little advantage over use of NSAID + PPI as separate components.

Rubefacients/intra-articular hyaluronan injections / **chondroitin or glucosamine** are not recommended for the treatment of osteoarthritis (NICE CG 59).

Meptazinol is associated with rebound pain and an unacceptable level of side effects and is therefore not recommended to be prescribed routinely

Tapentadol: For use only on advice of the pain clinic

Once daily preparations: There is little good evidence to suggest clinical advantage of once daily dosing

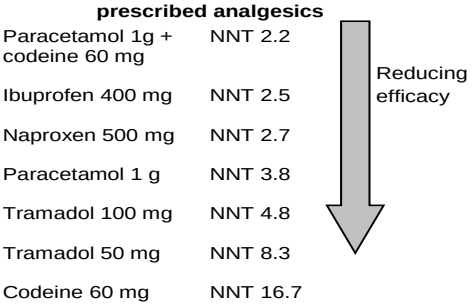
To minimise the risk of dependence-

- CSM has advised that treatment should be kept short and intermittent
- Only use for moderate to severe pain where first-line medication, such as codeine is not appropriate
- Prescribe regular paracetamol concurrently to encourage tramadol use on a 'when required' basis
- Use with great caution in patients with a history of addiction or dependence
- Use with caution in patients with depression
- Patients receiving repeat prescriptions for tramadol are reviewed on a regular basis (about every 6 months)

To minimise the risk of adverse effects

- Avoid using in patients with a history of epilepsy or those susceptible to seizures.
- Tramadol should be used with caution in patients taking medication that interacts, such as warfarin, SSRIs, TCAs and MAOIs*
- Tramadol should be used with caution in patients with renal impairment and the dose adjusted according to the GFR* (see SPC for more information)

Figure 1. NNT figures for commonly prescribed analgesics



Appendix1

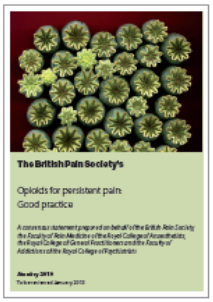
Opioids for persistent pain

June 2010

Summary of guidance on good practice from the British Pain Society

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

Full guidance for prescribers and patients available at http://www.britishpainsociety.org/book_opioid_main.pdf
and http://www.britishpainsociety.org/book_opioid_patient.pdf



This advice relates to the use of strong opioids (and weak opioids at doses higher than recommended in BNF) for persistent pain.

Cautions

- The safety and efficacy of long term opioid use is uncertain (there are few trial data for use more than 12 weeks), although use may be appropriate in some cases of persistent pain (somatic, visceral or neuropathic).
- Local and national prescribing guidance should be followed carefully.
- Medication for pain should be used only as part of a wider management plan aimed at reducing disability and improving quality of life.
- Opioids should not usually be used as first line therapy for pain.
- Opioids should not be used in children or pregnant women without specialist advice, and they should be used with caution in older people (particularly those with medical co-morbidity).
- Patients with a history of addiction to opioids or other drugs need referral to services with expertise in pain medicine and addiction management.
- Patients should not drive when starting opioids or adjusting dose or if they feel unfit to drive.

Prescribing

- **Comprehensive assessment** is important; patients with depression, anxiety, or other psychiatric or psychological co-morbidity will need additional support and monitoring to avoid problem drug use.
- **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.
- Start with a low dose and titrate up according to analgesia and side effects. Doses greater than **180 mg morphine daily (or equivalent) require specialist advice.**
- Where possible use regular dosing with **modified release preparations**; immediate release opioids may be associated with tolerance and problem drug use.
- Efficacy and adverse effects are similar for all opioids, though patients may tolerate one drug better than another.
- Requests for **dose increase** need careful evaluation.
- **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).
- 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.

Adverse effects

- 80% of patients taking opioids will experience at least one adverse effect e.g. constipation, nausea, itching, dizziness. Side effects should be managed promptly with laxatives, anti-emetics etc as appropriate.
- Opioid toxicity (sedation, slow respiration, cyanosis) is more likely with increasing age, co-morbidity, co-prescribing, and if opioids are taken with alcohol or illicit drugs.
- Opioids have long term endocrine and immunological effects.
- Withdrawal symptoms occur if opioid is stopped/dose reduced abruptly e.g. sweating, yawning, abdominal cramps. This is common with Tramadol even after a short course.
- Addiction is characterised by impaired control over use, craving and continued use despite harm.
- Opioid induced hyperalgesia may occur: pain becomes more diffuse and qualitatively different from pre-existing pain. Specialist advice is needed.

THE BRITISH PAIN SOCIETY