



The Pharmacological Management of Adults with Chronic Non-Cancer Pain

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VERSION CONTROL. Please access via the LMMG website to ensure that the correct version is in use.

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1.0	14/5/15	First version approved
1.1	14/7/15	Updated to include information about renal safety of fentanyl and Fentanyl: oral morphine equivalence changed to 60-90mg

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1. INTRODUCTION

Chronic pain is defined as pain that has been present for more than twelve weeks¹. It occurs when pain continues after the healing process has occurred, or when pain is associated with a disease process in which healing does not take place. It is a complex bio – psycho – social phenomenon, affecting ~ 18% of the population to some extent¹. As well as causing a great deal of personal suffering, chronic pain has major economic implications for health service expenditure and for society as a whole^{1,2}.

Chronic pain presents a major clinical challenge and it is important to deal with early, if possible¹. Most people with chronic pain do not feel that their pain is adequately controlled even though there are many pain relief interventions available². This may be for a variety of reasons. Pain has a number of aetiologies, symptoms and underlying mechanisms, which can make it difficult to formulate an effective analgesic strategy¹. Some patients suffer from pain that does not respond to standard therapies & may require a more in-depth assessment by a specialist pain service¹. In addition, the patient’s expectations of pain management may not be

realistic; unfortunately achieving pain free status is not always possible, despite referral to the pain clinic.

Some patients have difficulty communicating and may be reliant on third parties to detect that they are in pain. This will require the use of non-verbal pain rating scales. In the cognitively impaired inadequately treated pain can lead to behavioural problems, anxiety and depression. Therefore before prescribing medications to manage behaviour it is important that clinicians and carers consider the possibility that a person may be experiencing pain³. See [Appendix 1](#) for more information and examples of pain assessment tools.

It should be emphasised that medicines play only one part in managing pain. Maintaining fitness, pacing activities and a generally healthy lifestyle are also important¹.

2. PURPOSE AND SUMMARY

To provide guidance on the pharmacological management of non-cancer pain in adults.

3. SCOPE

This guideline provides recommendations on the medical management of adults with chronic non-cancer pain.

It does not cover:

- Management of neuropathic pain (See [NICE CG96](#))
- Specialist medicines or medication regimens which will continue to be supplied from secondary care.
- The management of pain in palliative care. (See [the Lancashire and South Cumbria Palliative Care Prescribing Guidelines 2014](#)).
- Prescribing of analgesics within secure prison services. See the Royal College of GP: [Safer Prescribing in Prisons](#).

4. GUIDANCE

Prescribers should use this guidance in conjunction with the medication's summary of product characteristics ([SPC](#)) and the British National Formulary ([BNF](#)).

A locally adapted treatment algorithm summarising the management of chronic pain is presented in [Section 4.1](#)

Background information and prescribing information relevant to the medications presented within the algorithm, is provided in sections 4.2-4.7.

4.1 Summary of Chronic Non- Cancer Pain Management. ^{1,4,5,8,18}

To be read in conjunction with section 4.2; [Supporting Principles of Care](#) and 4.3 [General Principles of Analgesic Use](#).

Step 1: Mild Pain (Pain score 1 – 3)

Regular [Paracetamol](#)
1g four times a day

+/- When required NSAID⁷
i.e. Ibuprofen 200-400mg TDS 1st line
or Naproxen 250-500mg BD 2nd line



Step 2: Moderate Pain (Pain score 4 – 6)

Continue Regular Paracetamol

+

Start regular treatment with:

An oral [NSAID](#) (Ibuprofen or Naproxen)
and/or [weak opioid](#)
i.e. Codeine 30-60mg QDS 1st line
or Dihydrocodeine 30mg QDS 2nd line

+/- When required NSAID or weak opioid

If not effective/not tolerated, STOP & try an alternative NSAID or weak opioid

Nb. In view of side-effects, potential for interactions and controlled drug status, tramadol should be reserved for 3rd line use (after a trial of codeine and dihydrocodeine).

If sufficient pain relief has not been achieved, consider the possibility of neuropathic pain or a mixed pain presentation before moving to step 3.

Refer to [NICE CG 173](#) for more information



Step 3: Severe Pain (Pain score 7-10)

Regular Paracetamol
(Stop weak opioid)

+

Start regular treatment with:
A [strong opioid](#) (Morphine 1st line)
+/- NSAID

See [BNF](#) for morphine dosing information

If not effective/not tolerated, STOP & try an alternative strong opioid

Nb. Routine use of 'when required' opioids is not recommended in the treatment of non-cancer pain.

If Osteoarthritis⁶

Consider a **topical NSAID** instead of, or in addition to, regular paracetamol (& before the use of oral NSAIDs or opioids).

Topical capsaicin 0.025% should be used as an adjunct to core treatments in hand or knee osteoarthritis. Nb. It may need to be used for 1-2 weeks before pain relief is achieved.

See also [NICE CG177](#)

NSAIDs⁷

Consider gastro protection for patients at high risk of GI side effects when starting NSAIDs (see [section 4.4](#) & [NICE KTT13](#) for more details)

Opioids

Opioid Trial^{1,8} Some patients have pain that is not responsive to opioids. Treatment should be initiated on a trial basis, with doses increased gradually. If treatment does not improve function or doses escalate due to poor effect opioids should be reduced & stopped. See [Appendix 2](#) for details.

Consider laxatives for all patients on opioids & encourage fluid intake.

Antiemetics may be required when opioids are initiated but tolerance to nausea & vomiting usually develops

Driving⁹: Patients should be advised that opioids are likely to affect their ability to drive & that they should not drive until they know how the medicine affects them.

It is an offence to drive while under the influence of morphine, but they would not be committing an offence if the medicine has been prescribed to treat a medical problem and it has been taken according to the instructions given by the prescriber **and it was NOT AFFECTING THEIR ABILITY TO DRIVE safely.**

Patient information is available [here](#)

Review treatment 4-6 weeks after initiation or dose adjustment. Withdraw unhelpful treatments.

Referral to specialist services. Some patients may require a more in depth assessment; prescribers should consider referral at any stage including initiation, as clinically indicated and with consideration of locally agreed pathways where they exist. Referral is recommended for those patients with complex pain, psychosocial problems, failed back syndrome, complex regional pain syndrome, if there are concerns about escalating opiate doses or if patients do not obtain useful pain relief with oral morphine 120-180 mg per 24 hours (or equivalent) It is also recommended that doses greater than morphine 180 mg daily (or equivalent) are only prescribed in consultation with a specialist.

4.2 Supporting Principles of Care ¹

During the Initial Patient Assessment

Consider:

- The type of pain
- Its aetiology and severity
- Analgesic history
- Impact on lifestyle & daily activities/ participation
- Common psycho-social problems. The patients' perceptions of the pain and its cause; coping strategies, mood changes, quality of sleep, and anxiety can all impact on perceived pain. Addressing these might reduce the need for analgesics.

Pain assessment tools may help with this process, particularly if patients have difficulty communicating e.g. patients with cognitive impairment or whose first language is not English. See [Appendix 1](#).

Some patients may be reluctant to report pain or may have difficulty interpreting and verbalising that they are in pain e.g. those with cognitive impairment or dementia. Clinicians and carers should consider the possibility that a person is experiencing pain and be aware that this may sometimes manifest as behavioural changes³.

Produce a Treatment Plan

When possible treatment plans should be agreed with the patient, taking into account their concerns and expectations. If initiating a strong opioid see [Appendix 2](#)

Consider:

- The cause of the pain and whether this condition has deteriorated
- Renal, hepatic function and age of the patient.
- The patient's previous experience of pain, analgesics used and any adverse effects or preferences.

Discuss with the patient:

- The reason why the treatment is being offered, along with the benefits and potential adverse effects.
- The importance of dosage titration and the titration process.
- Coping strategies for pain and for possible adverse effects of treatment. Individualised information and advice should be provided if appropriate.
- Set realistic expectations of treatment. Achieving a pain free status may not be possible.
Nb. Clinical trials consider medications to be useful interventions if they reduce the pain score by 50%. However the impact of the intervention on physical functioning and quality of life should also be considered when assessing benefit.

Review Treatment

4-6 weeks after starting or changing treatments and periodically (as appropriate to the patients pain underlying health condition and prescribed medications)

Each review should assess:

- pain control
- medication concordance
- impact on lifestyle, daily activities (including sleep disturbance) and participation
- physical and psychological wellbeing
- adverse effects
- continued need for treatment
- the need for specialist pain services input

Consider Referral to Specialist Services

Most patients pain can be managed effectively in primary care. Some e.g. with complex pain, psychosocial problems, failed back syndrome or complex regional pain syndrome may need a more in-depth assessment, which may require the involvement of multidisciplinary specialist pain/condition specific services.

Clinicians should consider referral to a specialist service at any stage with consideration of locally agreed pathways where they exist. It is important to deal with pain early, and refer if necessary.

Referral is recommended if patients do not obtain useful pain relief with doses of oral morphine 120- 180 mg per 24 hours (or equivalent) or if there are concerns about escalating opiate doses' It is also recommended that doses greater than morphine 180 mg daily (or equivalent) are only prescribed in consultation with a specialist.^{1,8,18}

4.3 General Principles of Analgesic Use ^{1,4}

- Analgesia for continuous pain should be prescribed on a regular basis.
- Opiate-based breakthrough analgesia should NOT be prescribed on a routine basis for non-cancer pain¹.
- The oral route should be used when possible, other routes should be reserved for instances when they offer specific advantages e.g. swallowing difficulties or to facilitate patient compliance.
- Treatment should be started at the step of the analgesic ladder (see [figure 4.1](#)) appropriate for the severity of the pain. Analgesia should then be adjusted as the pain severity alters i.e. moving both up and down the ladder.
- Non-opioid and/or adjuvant analgesics should be considered at each step of the pain ladder.
- A multimodal approach to pain management should be employed. Using analgesics with different modes of action can produce a synergistic effect, resulting in better pain relief at lower doses.
- **Multiple analgesics from the same class must not be prescribed concurrently.** (Unless directed by a pain specialist).
- All treatments should be titrated and given for an adequate duration prior to moving to the next option or stage of the treatment algorithm. If there has been no response to treatment 4-6 weeks after titration to a therapeutic dose patients are unlikely to develop a response thereafter.

4.4 Non-Opioid Analgesics ^{1,4,6,7}

Paracetamol

Place in therapy: Paracetamol is recommended as the **starting point of any analgesic regimen**; often undervalued it is an effective analgesic. It offers the advantages of low cost, high bioavailability, quick onset of action and extremely good safety profile. **It works in SYNERGY WITH OTHER ANALGESICS**, and consequently **should be CONTINUED at all stages of the analgesic ladder**.

Safety: Paracetamol has a **good safety profile when taken in therapeutic doses**, but overdose has the potential to cause liver damage and death. Prescribers should ensure patients know they must not exceed the prescribed dose, or take with other paracetamol containing products.

As detailed in the [BNF](#) caution is required if prescribing for patients with severe hepatic or renal impairment.

Dose adjustment is required if prescribing the intravenous infusion for patients with, alcohol dependence, hepatocellular insufficiency, chronic alcoholism, chronic malnutrition, dehydration and in patients who are under 50kgs.

Formulations: Paracetamol is available in a variety of formulations i.e. Oral suspension, suppositories, soluble tablets and IV infusion. **EFFERVESCENT/SOLUBLE tablets contain SIGNIFICANT AMOUNTS OF SALT** and should be avoided in patients with CV disease, renal disease and HTN. Soluble tablets offer **NO ADVANTAGE in patients who are able to swallow tablets** and should therefore be avoided unless there are specific indications.

Paracetamol capsules/caplets may be option for patients who struggle to swallow the conventional tablets.

Use of paracetamol in fixed dose combination analgesics: Fixed dose compound analgesic preparations, (usually containing opioids) **should not be used routinely**. Patients should be given the individual components where possible to allow titration of dose. However, if a patient is on a large number of tablets and a stable dose of analgesics then a combination preparation may be useful.

Non-Steroidal Anti-inflammatory Drugs (NSAIDs).⁷

1st line NSAID: Ibuprofen up to 1200mg per day

2nd line NSAID: Naproxen up to 1000mg per day

Place in Therapy: Oral NSAIDs are particularly **effective at relieving pain associated with inflammation**. They should be considered after an adequate trial of regular paracetamol or topical NSAID/capsaicin. A weak opioid may be more appropriate for some patients e.g. those at high risk of NSAID side effects.

Safety: There are long-standing and well-recognised **GI and RENAL SAFETY CONCERNS with all NSAIDs**. Evidence suggests that there are differences in the risk of upper GI side effects, with Ibuprofen being associated with the lowest risk and naproxen having an intermediate GI risk. (Nb. High doses of Ibuprofen may also pose an intermediate GI risk). See [BNF](#) for more details.

There is an **increased risk of Cardiovascular and Thrombotic events associated with COX-2 inhibitors and some traditional NSAIDs** e.g. Diclofenac. This increased risk does not appear to be shared by ibuprofen at 1200 mg per day or less, or naproxen at 1000 mg per day.

Good Practice in NSAID Prescribing:

- Prescribe the **LOWEST EFFECTIVE DOSE** of NSAID for the **SHORTEST TIME NECESSARY** for control of symptoms.
- Carefully assess the balance **RISKS vs BENEFITS**; think about CV, GI and renal issues.
- **Use a safer drug.** Ibuprofen (≤ 1200 mg per day) is an appropriate 1st choice, in view of its low risk of GI and CV side effects. Low-dose ibuprofen or naproxen 1000mg would appear more appropriate than other NSAIDs for patients in whom cardiovascular risk is a significant consideration.
- Only prescribe **ONE oral NSAID at a time**.
- Consider the potential for **INTERACTIONS** when prescribing NSAIDs, e.g. co-prescribing with **ACE inhibitors** may pose particular risks to renal function; the combination of NSAIDs with low dose **Aspirin** can increase the risk of GI side effects and should be used only if absolutely necessary.
- **CONSIDER GASTRO-PROTECTION** with a PPI for patients at high risk of GI bleeding or ulceration.

Gastro-Protection.

High GI risk patients include those: >65yrs, with a history of peptic ulcer disease or serious GI complication, those taking other medicines that increase the risk of GI side effects or those with serious co-morbidities (e.g. CV disease, diabetes, renal or hepatic impairment).

- [NICE KTT13](#) recommends that a PPI is co-prescribed for patients with Osteoarthritis, RA or low back pain (if >45yrs).
- A H2 Receptor antagonist (e.g. ranitidine) or misoprostol are alternatives for those patients who cannot have PPIs.

See [CKS: NSAID prescribing issues](#) for more details

4.5 Opioid Analgesics ^{1,6,8}

Place in therapy: Opioids have a well-established role in the management of acute pain and pain associated with cancer, but their role in non-cancer pain is less well defined. The safety and efficacy of opioids in the long term is uncertain as is their propensity to cause problems of tolerance, dependence, addiction and intolerable side effects. The benefits of opioid treatment for the patient must therefore be balanced against the risks **of long term use**⁸. See [Appendix 2](#) for a pathway for using strong opioids in patients with chronic pain.

Classification. There are a number of different classifications used for opioid analgesics. For the purposes of this guideline, the terminology used in the BNF has been adopted and they are classed as 'weak' or 'strong'.

General Considerations When Prescribing Opioids

- Clinical experience suggests that immediate release preparations are more associated with tolerance and problem drug use^{1,8}.

- **THERE ARE TWO OPTIONS FOR STARTING STRONG OPIOIDS** (See [Appendix 2](#)):

Start with **LOW DOSE OF LONG-ACTING** preparation. e.g. Zomorph or MST

OR

While establishing dose, use an **IMMEDIATE RELEASE preparation** e.g. Oramorph 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.

- **BREAKTHROUGH opioid analgesia should NOT BE PRESCRIBED ROUTINELY** in the management of non-cancer pain, but should be available if patients have an acute flare of pain. Use should be monitored to ensure that doses do not escalate inappropriately¹

- Some patients have **PAIN THAT IS NOT RESPONSIVE TO OPIOIDS**. If treatment does not improve function or doses escalate due to poor effect opioids should be reduced & stopped.

- As per BPS and SIGN guidance **it is recommended that doses greater than morphine 90mg twice daily (or equivalent) are only prescribed in consultation with a specialist**. However, prescribers should use their clinical judgement and may refer earlier if appropriate. Referral is strongly recommended if patients do not obtain useful pain relief with oral morphine 120- 180 mg per 24 hours (or equivalent) or if there are concerns about escalating opiate doses^{1,8,18}.

- If opioids are used long term patients should be regularly reviewed & doses reduced to the lowest effective dose as soon as possible.

See [Appendix 3](#) for opioid dose conversion chart

Side Effects.

Predictable side effects of opioids should be anticipated and managed:

Nausea and vomiting is a common opioid side effect, which is usually temporary and typically subsides after three to five days of treatment.

Constipation is a long term side effect and the majority of patients will need regular laxatives for prophylaxis. The need for laxatives generally increases with the strength of opioid.

Other side effects: Drowsiness occurs at initiation and with dose increments. Long term use of opioids can cause a complex range of side-effects including hyperalgesia (where increased doses worsen pain), sexual dysfunction, and lowered immunity and fertility. Patients need to be counselled about these effects before deciding to embark on chronic treatment.

Driving⁹. It is now an offence, to drive with a specific amount of controlled drug in the body above the accepted limit for that drug.

The new offence has a statutory "medical defence" to protect those who may test positive for certain specified drugs including morphine when taken in accordance with the advice of a healthcare professional. However, it remains the responsibility of all drivers, including patients, to consider whether they believe their driving is, or might be, impaired on any given occasion, e.g. if they feel sleepy; and it remains an offence to drive whilst driving is impaired by drugs. **IF IN DOUBT, DRIVERS SHOULD NOT DRIVE.**

Side effects are most likely to occur when medications are changed. Prescribers should remind patients of their obligation to ensure they do not drive if impaired by medication when there is a change of treatment. e.g. a dose increase or conversion to a different opiate,

Patient information is available [here](#)

Dose Increases¹⁰. Where a dose increase is intended, prescribers must ensure the calculated dose is safe for the patient. e.g. for oral morphine or oxycodone in adult patients, **the dose should NOT NORMALLY BE INCREASED BY MORE THAN 50% of the previous dose**. See the NPSA alert on [Reducing Dosing Errors with Opioid](#)

4.6 Weak Opioids ^{1,6,9}

1st line weak opioid- Codeine: Is a pro-drug and must be metabolised to morphine before it can provide its analgesic effect. The **capacity to metabolise codeine can vary considerably** and lead to either reduced therapeutic effect or a marked increase in side effects.

~7% of the Caucasian population (cannot metabolise codeine and therefore will not respond to treatment with it. If patients do not respond to codeine, dihydrocodeine should be tried before considering tramadol or a strong opioid.

2nd Line weak opioid- Dihydrocodeine:

Has an analgesic efficacy similar to codeine. It is thought to be less constipating than codeine but is associated with a **greater incidence of nausea and vomiting.**

3rd line weak opioid- Tramadol: Produces analgesia by two mechanisms

- An opioid effect
- An enhancement of serotonergic and adrenergic pathways.

It has fewer typical opioid side-effects, but it **LOWERS THE SEIZURE THRESHOLD**, is associated with **PSYCHIATRIC REACTIONS** and has the potential to produce **serotonin syndrome** when **co-prescribed with tricyclic antidepressants or selective serotonin reuptake inhibitors (SSRIs).**

In **renal and/or hepatic insufficiency** the elimination of tramadol is delayed. In these patients prolongation of the dosage interval should be carefully considered and the use of **modified release preparations should be avoided.**

Place in therapy: Because of its safety/side effect profile and potential for interactions, tramadol should be **reserved for use after** a trial with codeine & dihydrocodeine but may be considered before morphine.

Controlled drug status: As a consequence of increasing reports of misuse and harms, tramadol has been reclassified as a schedule 3 controlled drug. All tramadol prescriptions need to comply with controlled drug prescription writing requirements¹¹.

4.7 Strong Opioids ^{1,6,8,9}

See [Appendix 2](#) for a pathway for using strong opioids in patients with chronic pain

1st line strong opioid- Morphine: is the **STRONG OPIOID OF CHOICE** it is the standard against which other opioids are compared and offers the advantage of familiarity, availability and low cost.

When **Modified Release** morphine tablets or capsules are used they should be **prescribed by brand name** due to **variations in release profiles.**

The **elimination** of morphine is **delayed in patients with renal and/or hepatic insufficiency.** In these patients prolongation of the dosage intervals should be carefully considered according to the patient's requirements and the use of modified release preparations should be avoided.

2nd line strong opioid- Oxycodone has an efficacy and side effect profile similar to morphine and there are **NO ADVANTAGES in using oxycodone first-line.** Prescribers should note that it is several times more expensive than the equivalent dose of both standard and slow release morphine preparations.

Oxycodone is known to have a higher oral bioavailability than morphine and a 50% dose will give the same analgesic effect.

Oxycodone is less likely to accumulate in renal impairment compared to morphine, but it is still contraindicated in severe renal impairment. Nb. Morphine can be used with caution in renal impairment (but a dosage reduction and longer dosing intervals are recommended).

Oxycodone should be **prescribed by brand name** due to the potential for **variation in release profile** between different prolonged release branded generics and to minimise the risk of **confusion between immediate and prolonged release preparations.**

Transdermal patch preparations lack the flexibility required when treating patients with fluctuating pain or uncontrolled pain. Use should be reserved for patients with stable pain who are unable to take or tolerate oral medications (including soluble tablets and liquids).

Safety of Transdermal Formulations

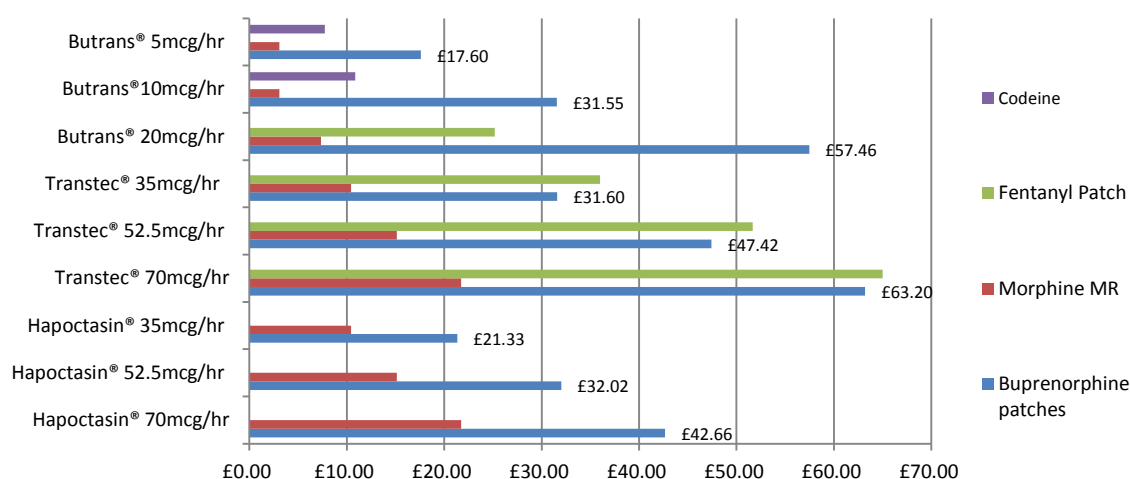
- When transdermal preparations are exposed to heat e.g. if a patient takes a hot bath or has a fever, it may cause increased drug absorption
- USED PATCHES still contain a significant amount of ACTIVE DRUG.** To avoid accidental transfer or exposure to another person, prescribers should advise patients:
 - to choose the patch application site carefully and check the adhesion of the patch once applied, especially the edges
 - to fold the used patch as soon as it is removed so that the adhesive side of the patch sticks firmly to itself and dispose of the folded patch safely
 - if a patch is transferred to another person, remove it immediately and seek medical advice, if a patch is swallowed, seek medical help immediately

For more information see the [MHRA transdermal fentanyl safety update](#). (Although this does not specifically relate to buprenorphine the same principals apply).

Cost.

Both buprenorphine and fentanyl patches are several times more expensive than equivalent doses of oral analgesics, therefore inappropriate use of transdermal preparations has cost implications for commissioners. To facilitate local review, it is recommended that the reason for using patch formulations is documented on initiation and if appropriate patients are switched back to oral formations at review.

Cost comparison of transdermal opioid preparations Vs ~ equivalent dose of oral opioid (Costs/ 28 days treatment)



MIMS March 2015 prices have been used.

Dose equivalences are based on the following assumptions:

- Oral morphine is about 10 times the potency of oral codeine
- Transdermal buprenorphine is 100 times more potent than PO morphine.
- Transdermal fentanyl is approximately 1.4 times more potent than transdermal buprenorphine
- Buprenorphine costs are compared to approximate equivalent dose of Filnarine®, The costs of the Filnarine® have been calculated using the nearest practicable dose. (N.B. MST Continus® used for 5mg bd dose):
- Costs of Transtec® calculated using 2 patches per week as suggested in SPC i.e. a total of 8 patches per 28 days.
- Costs of Hapoctasin® calculated using 1 patch every 3 days i.e. a total of 9 patches per 28 days.
- Where the buprenorphine patch is comparable to a dose range of alternative opioid, the average cost of that range has been used. This applies to the codeine dose equivalent to 5 & 10mcg buprenorphine and fentanyl dose equivalent to 52.5 & 70mcg

Fentanyl ^{5,9,13} is a **POTENT OPIOID ANALGESIC**—a 25 microgram/hr fentanyl patch equates to approximately 60-90mg of oral morphine. Patches should only be used in patients who have **previously tolerated opioids** because of a **RISK of significant RESPIRATORY DEPRESSION** in opioid-naïve patients.

Dosing. The **initial dose of fentanyl patch** should be based on a patient's **opioid history**.

Information on starting doses and dose conversion can be found in the [SPC](#)

- Caution is required when making dose adjustments
- The analgesic effect should not be assessed until the patch has been worn for at least 24hrs⁵
- It takes ~17hrs for the plasma concentration to decrease by 50% when the system is removed

Renal Safety. Fentanyl is metabolised primarily in the liver with <10% being excreted unchanged by the kidney, additionally there are no known active metabolites which are renally excreted. The SPC recommends that when used in patients with renal impairment, they should be observed for signs of fentanyl toxicity and the dose reduced if necessary.¹²

Brand prescribing: Patches are available as matrix and reservoir formulations; these should not be used interchangeably. To ensure consistency of supply to patients, it is recommended that all fentanyl patches are prescribed by brand.

RESERVOIR PATCHES (e.g. Tilofyl) **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

Safety information for patients is available from the MHRA [here](#)

Fentanyl products designed for breakthrough pain.

Such as lozenges, nasal preparations and sublingual or buccal tablets are not licensed for non-cancer pain, prescribing requires specialist knowledge and formulations are extremely expensive.

Prescribers **should NOT USE oral/nasal fentanyl products for non-cancer pain**. If acute breakthrough analgesia is required consideration should be given to the use of non-opioids or alternative opioids such as oral morphine.

Buprenorphine^{5,9} is a partial agonist with poor oral bioavailability. It has pure partial agonist activity at the mu-opioid receptor and antagonistic activity at the kappa-opioid receptor.

When **HIGH DOSES** of buprenorphine are used, in patients who are **DEPENDENT ON OTHER OPIOIDS**, it **MAY PRECIPITATE WITHDRAWAL symptoms including pain**. Other opioids e.g. morphine, can still provide effective breakthrough analgesia if used with buprenorphine in therapeutic doses. However, the routine use of opioid breakthrough analgesia is not recommended.

A range of buprenorphine formulations are available:

- Use of Buccal formulations is **not** recommended.
- Butrans® patches are licensed for use in moderate pain and are changed every 7 days.
- Transtec® and Hapoctasin® patches are licensed for use in severe pain and are changed every 4 days.

Patients not previously receiving opioids should start on 5 or 10microgram/hr (Butrans®) patches. Patch formulations must be worn for at least 3 days until maximal effect is achieved.

Use should be reserved for those patients with stable pain who are unable to take or tolerate oral medicines.

Please check local commissioning arrangements before prescribing. Buprenorphine is not approved for by some local CCGs

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Appendix 1. Pain Assessment Tools^{3,16}

A large number of pain assessment tools exist and their content varies. These examples are not exhaustive and alternative assessment methods may be used.

Pain severity has historically been assessed using a basic scale as outlined below. The patient is asked to rate their pain between 0-10, with 0 representing no pain and 10 representing the worst pain imaginable. The pain scores broadly equate to mild, moderate or severe pain and can be cross referenced with [Section 4.1](#) and used to guide analgesic choice. **However, because pain has complex mechanisms, different approaches to pain assessment including the use of more in depth multidimensional assessment tools should be considered, these provide a fuller assessment of the patients pain and treatment effectiveness.**

Figure 1. Pain Rating Scale

0	1	2	3	4	5	6	7	8	9	10
No pain	Mild pain			Moderate pain			Severe Pain			Worst pain

Multidimensional pain assessment tools, measure the intensity, nature, and location of pain, and in some cases, the impact that pain is having on a patient's activity or mood; multidimensional scales are useful in complex or chronic pain. Examples are:

- [The Pain Rating Scale](#) Produced by the British Pain Society and [Brief Pain inventory](#) which allow patients to rate the severity of their pain and the degree to which their pain interferes with common dimensions of feeling and function.
- [McGill](#) The McGill Pain Questionnaire can be used to evaluate a person experiencing significant pain. It can be used to monitor the pain over time and to determine the effectiveness of any intervention.

For patients who do not speak English as their first language: The British Pain Society has produced a series of pain scales in multiple languages. These can be downloaded and printed for free from their [website](#).

For patients with poor cognitive function: Observed non-verbal pain assessment scales may be needed. These require that the patient is observed at rest, on movement and for behavioural changes that may indicate pain. Therefore appropriate use will necessitate input from carers or family and variable amounts of training. Further guidance on the [assessment of pain in older people](#) has been produced by the British Pain Society in collaboration with the British Geriatrics Society and Royal College of Physicians. **Examples are:**

- [Checklist of non-verbal pain indicators \(CNPI\)](#)
This considers vocalization, facial expression, stimulus, friction, agitation and verbal complaints. These are marked as "present" or "absent" under two conditions: movement and at rest.
[Doloplus 2](#). This assesses the progression of the pain experience and consists of 10 items, divided into three groups, namely, somatic reaction, psychometric reaction and psychosocial reaction.

Appendix 2. Pathway for using strong opioids in patients with chronic pain¹.

Adapted from SIGN 136. Management of Chronic Pain. December 2013

Step 1: Assessing suitability for strong opioid

Assess pain

If likely to respond to opioid, consider opioid trial e.g. if nociceptive or some benefit from weak opioids,

If less likely to respond to opioids consider specialist advice before opioid trial OR avoid opioids. e.g. no analgesia at all from weak opioids. Nb. If Neuropathic pain, refer to Neuropathic pain guidance.

Risk assess the potential for medication abuse, diversion or accidental ingestion

Consider psychosocial factors. e.g. children in house or other family members with a history of substance misuse problems.

Risk of misuse or developing iatrogenic dependency. e.g. history of drug (including licensed medications) or alcohol abuse, mental health problems.

Other comorbidities.

- **Cognitive impairment:** cognitive side effects are more likely; concordance and safety may be an issue
- **Renal impairment:** There is potential for accumulation of active metabolites with some opioids
- **Gastrointestinal pathology:** Opioids have an adverse effect on bowel function.

Ensure that the benefits of treatment outweigh potential risks before initiating therapy and where possible take measures to minimise risks.

Discuss the plan with the patient before starting opioids

Provide patient information on the use of opioids in chronic pain and driving advice. (See [Appendix 4](#))

Establish goals of treatment

Primary: pain relief (define the degree that would be acceptable to the patient)

Secondary: improved function, sleep, mood.

Be aware that opioids should NOT be used as anxiolytics.

Discuss the side effects/potential problems. The patient needs to be aware of the potential side effects and they need to be acceptable to the patient, side effects include:

- GI dysfunction; nausea, vomiting, constipation
- central nervous system; memory and cognitive impairment, nightmares, hallucinations, visual disturbance
- endocrine; fertility, sexual function
- immune function
- misuse potential
- tolerance
- opioid-induced hyperalgesia

Step 2: Starting a strong opioid

Factors to consider

Route of administration; When possible oral is the preferred route.

Choice of opioid Oral Morphine is the strong opioid of choice **for first line use** unless otherwise contra-indicated. (See [Section 4.7](#))

Dose; there is considerable variability in the dose needed to effectively treat pain. Careful titration to the lowest effective dose, balanced against side effects and regular review is required.

There are two potential options for starting strong opioids

Start with low dose of long-acting preparation e.g Zomorph or MST. If the patient is already on codeine 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 dose, use an immediate release preparation, e.g. Oramorph, 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.

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

Step 3: Monitoring opioid trial

Monitor adverse effects

Gastrointestinal:

- Nausea/vomiting; tolerance usually develops after 3-5 days. Consider short term use of an antiemetic at initiation of therapy. See [BNF](#) for further information on the choice of antiemetic. Avoid cyclizine if there is a risk of abuse.
- Constipation: tolerance often does not develop to this. Use stool softeners/stimulant laxatives or a combination.

Central nervous system:

If these do not resolve, then either dose reduction or rotation will be needed.

- Impaired memory, concentration
- Hallucinations, milder visual disturbance
- Sedation, confusion, cognitive impairment
- Myoclonic jerks.

Other:

- Sweating
- Reduced libido, fertility: Consider stopping, testosterone replacement, opioid rotation (may need endocrine review)
- Respiratory depression: Stop opioid until resolves; consider factors contributing to event
- Tolerance: rotate opioid or reduce and stop
- Opioid induced hyperalgesia: rotate opioid or reduce and stop; seek specialist advice.

Step 4: Continuing opioid therapy

Regular review

Ideally with one prescriber:

- At least annual, more frequently if problems arise.
- Have a clear plan for flare-up management (including availability to out of hours service).
- Monitor patients for side effects (see step 3)
- Consider a trial of dose reduction.

Appendix 3: Opioid Dose Conversion Chart for Adults.

Dose conversion ratios are approximate as there is a lack of definitive trial data to demonstrate dose-equivalence. They are intended as a guide and may be subject to individual variation. Prescribers should use with caution, particularly in the elderly, if there are significant co-morbidities or polypharmacy.

If switching opioids because of possible opioid-induced hyperalgesia, it is prudent to reduce the calculated dose of the new opioid by 25-50%¹⁷.

Morphine compared to weaker Opioids

Refer to the BNF & Summary of Product Characteristics for further information

Oral Morphine total 24hr dose	Oral Codeine total 24hr dose (dihydrocodeine is roughly equipotent to codeine)	Oral Tramadol total 24hr dose	Buprenorphine Patch Microgram/hr dose
	30 – 60 mg	≤50 mg	
5 – 10 mg	60 – 120 mg	50 – 100 mg	
10 – 20 mg	120 – 180 mg	100 – 200 mg	5 micrograms/hr (BuTrans® Change every 7 days)
20-30 mg	180 – 240 mg	200-300 mg	10 micrograms/hr (BuTrans® Change every 7 days)

Morphine compared to other Strong Opioids

(each preparation is compared to morphine and not necessarily equivalent to others in the table)

Morphine Oral Total 24 hour dose	Oxycodone Oral Total 24 hour dose	Fentanyl Patches Change every 3 days (72 hours)	Buprenorphine Patch Microgram/hr dose
30 – 60 mg	15 – 30 mg	12 micrograms/hr	20micrograms (BuTrans® Change every 7 days)
60 – 90 mg	30 – 45 mg	25 micrograms/hr	35 micrograms/hr (Transtec®/Hapoctasin® Change every 4 days/96 hours)
90 – 135 mg	45 – 70 mg	25 – 50 micrograms/hr	52.5 micrograms/hr (Transtec®/Hapoctasin® Change every 4 days/96 hours)
135 – 190 mg	70 – 100 mg	50 – 75 micrograms/hr	70 micrograms/hr (Transtec®/Hapoctasin® Change every 4 days/96 hours)
190 – 225 mg	100 – 120 mg	50 – 87 micrograms/hr	
225 – 315 mg	120 – 160 mg	75 – 100 micrograms/hr	
315 – 405 mg	160 – 200 mg	100 – 125 micrograms/hr	

Assumptions for Dose Conversion Chart for Adults¹⁷:

- Oral morphine is about 10 times the potency of oral codeine
- Oral dyhydrocodeine is equipotent to oral codeine
- Oral morphine is about 10 the potency of oral tramadol
- Transdermal buprenorphine is 100 times more potent than PO morphine.
- Transdermal fentanyl is approximately 1.4 times more potent than transdermal buprenorphine

Information for Patients – Opioids for Chronic Pain

What is chronic pain?

Chronic pain is a pain that lasts for more than three months and can last for years. Some chronic pain starts because of a specific injury but it is not always clear why some people get chronic pain.

Pain that doesn't get better can cause tiredness, irritability and distress. Your sleep may be affected and it can cause problems with daytime activities and moving around. Because of this, it can also affect relationships with friends and family.

Chronic pain can be difficult to treat and usually it is not possible to get rid of the pain completely.

Your health-care team may be able to offer help in treating symptoms and to reduce the effect the pain has on your life.

What are opioids?

Opioid medicines either come from the opium poppy or are chemically related to drugs made from opium. Opioids have been used for many years to treat pain.

Common forms include opioids such as:

- codeine
- dihydrocodeine
- tramadol

Sometimes opioids are combined with paracetamol in one tablet. These combinations include:

- codeine and paracetamol (co-codamol);
- dihydrocodeine and paracetamol (co-dydramol)
- tramadol and paracetamol (Tramacet).

Alternatively your health-care team may recommend that you take regular paracetamol alongside your opioid. This can enable the dose of the opioid to be adjusted, reducing the amount required and reducing the incidence of side-effects.

Stronger opioid medicines include:

- morphine
- oxycodone
- methadone
- fentanyl
- buprenorphine
- diamorphine

Opioid medicines can help manage some but not all types of chronic pain. Some types of pain might respond better to other medicines than to opioids. Some types of pain need opioids together with other types of medication. Your team will only prescribe opioids for you if they think they are the best treatment for your pain. It is unusual for opioids to get rid of pain completely.

The aim of treatment is to reduce your pain enough to help you get on with your life.

Medicines work best if you combine them with other ways of managing symptoms such as regular activity and exercise, and doing things which are satisfying or enjoyable, such as work or study, and social activities.

Setting goals to help improve your life is an important way to see if medicines are helping.

Your health-care team will adjust the dose to give you pain relief most of the time, and so you don't get too many side effects. Short-acting opioid drugs and opioids which can be injected are not very useful for managing continuous pain. You should always take the correct dose of prescribed medicines. If you feel the dose isn't enough, or if the side-effects interfere with your life, you should discuss this with your health-care team.

What are the side-effects of opioids?

When you first start taking opioids you can get some side effects, which usually stop after a few days. These include:

- feeling dizzy
- feeling sick (nausea)
- being sick (vomiting)
- feeling sleepy
- feeling confused

These side-effects can go on for longer than the first few days. Your health-care team may give you some other medicines to help, such as anti-sickness tablets.

If pain has affected your sleep, opioids may help you to recover your normal pattern of sleep, but they should not make you drowsy in the daytime.

Opioid medicines can cause some problems when you take them for long periods of time. These problems include:

- constipation
- itching
- weight gain
- lack of sex drive
- difficulty breathing at night. This is most common if you are overweight and if you snore heavily. If you have a condition called obstructive sleep apnoea it may not be safe for you to take opioids.

Constipation is a common problem. You may need to try laxatives to treat constipation. If you experience a lot of side-effects your team may suggest changing to another opioid drug.

What are the long-term effects of taking opioids?

If you take opioid medicines for many months or years it can affect your body in other ways. These problems are more common if you take high doses of drugs for long periods. These problems include:

- reduced fertility
- low sex drive
- irregular periods
- erectile dysfunction in men (the inability to keep an erection)
- reduced ability to fight infection
- increased levels of pain

If you are worried about any of these problems, please discuss this with your health-care team. Your team will be able to tell you whether you are at risk of developing these problems.

Can I drive if I am taking opioids?

A law about driving after taking certain drugs, including some opioid medicines came into force in 2015.

- This law states that it is an offence to drive with certain drugs (including morphine) above specified levels in the body, whether your driving is impaired or not
- If you are taking these medicines as directed and your driving is not impaired, then you are not breaking the law
- It may be helpful for you to keep some suitable evidence with you when driving, which shows that you are taking the opioid as a medicine prescribed by a healthcare professional and in accordance with the leaflet accompanying the medicine
- Keep taking your medicines as prescribed
- Check the leaflet that comes with your medicines for information on how your medicines may affect your driving ability
- Do not drive after taking your medicines until you know how they affect you
- Do not drive if you feel drowsy, dizzy, unable to concentrate or make decisions, or if you have blurred or double vision
- If your driving is impaired then you are guilty of breaking the law

You are responsible for making sure you are fit to drive. The only organisation that can advise you about your legal right to hold a driving licence is the Driving and Vehicle Licensing Authority (DVLA).

Will my body get used to taking opioids?

Opioids can become less effective with time (this is called tolerance). This means that your body has got used to the pain-relieving effect of the medicine. You can also become dependent on opioid medicines (dependence). This means that if you stop taking the drug suddenly, or lower the dose too quickly, you can get symptoms of withdrawal. If you run out of medicine, you can experience the same symptoms which include:

- tiredness
- sweating
- a runny nose
- stomach cramps
- diarrhoea
- aching muscles

Can I become addicted to opioids?

We do not know exactly how many people get addicted when they are taking opioids for pain relief but it is very uncommon.

People who are addicted to opioids can:

- feel out of control about how much medicine they take or how often they take it
- crave the drug
- continue to take the drug even when it has a negative effect on their physical or mental health

Addiction may be more common in people who have been addicted to opioids (including heroin) or to other drugs (or alcohol) before; and in people with severe depression or anxiety. This does not mean that if you have had an addiction problem before or you are very depressed and anxious you will become addicted. It only means that you are more likely to become addicted than someone who has not had these problems. Most people do not become addicted.

So, if you have had a problem with drug or alcohol addiction in the past this doesn't mean that you cannot take opioid medicines for your pain. However, your health-care team will need to know about your past or current drug-taking to prescribe opioids safely and to help you watch out for warning signs.

What do I do if I want more information?

Please talk to your doctor or pharmacist. They are knowledgeable and experienced with medicines and will be pleased to answer your questions.

Your Prescriber's Contact details:

Name:

Telephone:

Adapted from '*opioids for persistent pain*' with permission from the British Pain Society.

(Accessed via https://www.britishpainsociety.org/static/uploads/resources/files/book_opioid_patient.pdf)

This guidance does not override the individual responsibility of health professionals to make decisions in exercising their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer. For full prescribing information please refer to the BNF and SPC.

Leads for this guidance: Midlands and Lancashire CSU	
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