Opioids Aware Website

Introduction to the resource

This guide is aimed to provide general guidance on the use of opioid medications, it specifically excludes their use in sickle cell disease[4,5, 6], palliative and end-of-life situations. The management of pain associated with sickle cell disease may involve a different choice of medications to those in this guideline. It is intended to help clinicians on best use; it is a guide to good practice, and not a protocol.

Evidence for the use and effectiveness of opioid medications for long-term treatment is sparse, and, sadly often of poor quality, with recent analyses focusing on population risk considerations [1] e.g., individuals with an active substance use disorder or psychiatric disorder.

Pain medicine is aimed at supporting the individual, and prescribing any medication for them, potentially long-term must be underpinned by applying best professional practice, understanding the condition, the patient, and their context.

Prescribing and managing of medications should recognise the importance of patient-prescriber communication; have clear aims about the benefits and risks, and the means and opportunities to assess these; recognising proper use, prescribing practice, and inappropriate and risky use.

This resource, developed by UK healthcare professionals and policymakers, provides the information to support a safe and effective prescribing decision.

Key Messages

[1] Chronic (long-term persistent) pain is a complex condition. Patients who have refractory and disabling symptoms, and a detailed assessment of the pain experience and the effect of any treatments, medication or other, should be carefully completed and recorded. Early specialist advice should be considered.

[2] Opioids are good analgesics for acute pain and for pain at the end of life but there is a poor research base regarding their long-term use.

[3] A small proportion of people may obtain good pain relief with opioids in the long-term if the dose can be kept low and especially if their use is intermittent (however it is difficult to identify these people at the point of opioid initiation).

[4] The risk of harm increases as doses rise. Various ‘cut offs’ have been suggested for maximum opioid dose, with prescriber caution being advised above 50mg Morphine Milligram Equivalent (MME), and specialist advice suggested if a dose above 90mg MME is considered.[2, 3] Patients established on higher than recommended dose should be assessed for efficacy and side effects, and a careful plan for either continuation or reduction with monitoring should be planned. Do not discontinue abruptly.

[5] If a patient has pain that remains severe despite opioid treatment, it likely means they are not working and plans to reduce and stop them should be considered. Patient and prescriber support may be needed, and a careful reduction/optimisation plan will be needed.

Contributors

This resource is continually updated and collated by healthcare professionals with the support of stakeholder policy groups. Contributors to the resource have included representatives from:

- British Pain Society
- Care Quality Commission
- Faculty of Addictions, Royal College of Psychiatrists
- Faculty of Pain Medicine, Royal College of Anaesthetists
- NHS England
- NICE
- NHS Business Services Authority
- Public Health England
- Royal College of General Practitioners
- Royal Pharmaceutical Society

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3. The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain (magicapp.org)
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6. American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain

A. Best professional practice

Good Practice in Prescribing

Key Points

- All healthcare professionals must to be up to date with relevant law, best clinical practice, and requirements and recommendations by relevant professional bodies.[1]
- It is essential to recognise the limits of your competence and work within them.
- You should have adequate knowledge of the patient's health before prescribing and should be satisfied that the treatment is in the best interests of the patient.
- Patients do not always take medicines as intended. If this becomes apparent, further support and information should be provided.
- Ensure suitable arrangements are in place for monitoring, follow-up and review, taking account of the patient's needs and any risks arising from the medicines.
- When prescribing at the recommendation of another doctor, nurse or other healthcare professional, you must satisfy yourself that the prescription is needed, appropriate for the patient and that prescribing the medicine is within the limits of your competence. Ensure good communication with the patient's primary prescriber.
- Prescribing and administration errors by doctors are relatively common. Patients should be protected from harm and any decision or action that you consider might be unsafe should be questioned.[2]
- When a patient presents with complex needs, consider the consultation and involvement of other relevant specialities (e.g., palliative care, mental health, substance misuse).

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Further Reading

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- National Institute for Health and Care Excellence. **Guideline NG5: Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes**. 2015. Last update October 2021. Available at: https://www.nice.org.uk/guidance/ng5. Accessed 23/10/2023

- National Institute for Health and Care Excellence. **Guideine NG46: Safe use and management of controlled drugs.** 2016. Available at: https://www.nice.org.uk/guidance/ng46. Accessed 23/10/2023
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Controlled drugs and the law

The Legislation

The management of Controlled Drugs, including opioids and gabapentinoids, is governed by two key sets of legislation, the Misuse of Drugs Act 1971 and supporting regulations (Home Office legislation) and The Controlled Drugs (Supervision of Management and Use) Regulations 2013 (Department of Health legislation). There are regular updates to these legislations. The main purpose of the Misuse of Drugs Act is to prevent the misuse of Controlled Drugs by imposing restrictions on their possession, supply, manufacture, import and export. The Department of Health regulations set out strengthened governance arrangements for Controlled Drugs used as medicines.

Misuse of Drugs Act 1971 and Misuse of Drugs Regulations 2001

Drugs controlled under the Misuse of Drugs Act 1971 are those that have the potential to be misused and they are classified according to their assessed harmfulness: **Misuse of Drugs Act 1971**.

Many Controlled Drugs are also essential to modern clinical care and their legitimate, clinical use is governed by the Misuse of Drugs Regulations 2001, which categorises them into five schedules based on their therapeutic usefulness and potential harms when misused:

Misuse of Drugs Regulations 2001 amendment for nurse and pharmacist independent prescribers

The Misuse of Drugs Regulations 2001 were amended in 2012 to allow nurse and pharmacist independent prescribers to prescribe any controlled drug listed in schedules 2 to 5 for any medical condition within their competence, except for diamorphine, cocaine and dipipanone for the treatment of addiction. The changes came into effect on 23 April 2012. - Authority for Nurse Independent Prescribers and Pharmacist Independent Prescribers to prescribe

Physiotherapist, podiatrist (since 2015) and therapeutic radiographers and paramedics (Since Dec 2023) can prescribe certain controlled drugs in specific routes of administration.

The Controlled Drugs (Supervision of Management and Use) Regulations 2013

The Shipman Inquiry was an independent public inquiry set up in 2000 to examine the issues arising from the case of Harold Shipman. The inquiry's fourth report "The Regulation of Controlled Drugs in the Community" was published in July 2004 and focused on the methods Shipman used to divert large quantities of Controlled Drugs for his own purposes, and considered how he was able to do it for so long without being detected. It concluded that there were serious shortcomings in the systems for regulating the governance of Controlled Drugs. In response, the Controlled Drugs (Supervision of Management and Use) Regulations 2006 were introduced and came into force in England on 1 January 2007. These have now been superseded by the new regulations, the Controlled Drugs (Supervision of Management and Use) Regulations 2013, which came into force on 1 April 2013 to reflect the changes in the NHS; the regulations and associated amendments can be found here: **The Controlled Drugs (Supervision of Management and Use) Regulations 2013**.

Prescriptions for Schedules 2 and 3 CDs can now be sent electronically via the Electronic Prescription Service (EPS) and signed with an Advanced Electronic Signature (AES) as well as handwritten. This follows changes to home Office legislation on 1 June 2015 and to NHS and Human Medicines Regulations on 1 July 2015.

- The National Health Service (Amendments to Primary Care Terms of Service relating to the Electronic Prescription Service) Regulations 2015

The Department of Health has also published information about the regulations to support the changes made in legislation: Controlled Drugs (Supervision of Management and Use) Regulations 2013 - Information about the regulations.

The Role of the Controlled Drugs Accountable Officer

The 2013 regulations require healthcare organisations such as NHS trusts and independent hospitals to appoint a Controlled Drugs Accountable Officer (CDAO) who has responsibility for all aspects of Controlled Drugs management within their organisation. They must ensure that every aspect of Controlled Drugs management is set out in appropriate and up–to–date standard operating procedures and that these are followed in practice. This does not only include procurement and storage arrangements but also

monitoring and oversight to ensure safe practices are in place for prescribing and administration; that Controlled Drugs are used appropriately; that relevant individuals are trained and that there are effective routes for reporting controlled drug related concerns.

Each area team of NHS England is also required to appoint a lead CDAO with responsibility for controlled drug concerns across their geographical area. As part of this responsibility, all the CDAOs within their geographical area are required to submit to them a quarterly occurrence report of controlled drug incidents from within their organisation so that the Area Team CDAO can identify trends of concern.

For the purpose of sharing controlled drug concerns and good practice initiatives, the area team CDAOs are required to set up Controlled Drugs local intelligence networks (CD LINs) for their area. Whilst they can determine the specific membership, it is largely comprised of the CDAOs across the area, Clinical Commissioning Group representatives and the relevant regulators and agencies as set out in the regulations.

Details of all CDAOs in England are held in the Controlled Drugs Accountable Officer register, which is published on the Care Quality Commission website.

Not all healthcare organisations are required to appoint a CDAO, however, those organisations that fall outside of the 2013 regulations must still comply with the Misuse of Drugs Regulations and must have arrangements in place to ensure the safe and secure management of Controlled Drugs and the reporting of controlled drug concerns. To achieve this, they should consider nominating a lead person to ensure controlled drug governance arrangements are in place within their organisation.

Useful documents

- Misuse of Drugs Act 1971
- The Misuse of Drugs Regulations 2001
- The Controlled Drugs (Supervision of Management and Use) Regulations 2013
- Guidance for healthcare professionals on drug driving (2015)

Opioids and driving (this is the leaflet extract- can be formatted later)

Who decides if it is safe for me to drive?
If you have a medical condition listed by the Driver and Vehicle Licensing Agency (DVLA) or are having treatment that could affect your being able to drive safely, you should discuss this with your doctor. You must tell the DVLA, who decides if a person is medically safe to drive. While you are waiting for the decision from the DVLA, your doctor can discuss with you if it is safe to continue driving and you must decide if you are fit to drive. It is your decision, but if you ignore medical advice to stop driving it may affect your motor insurance cover, and you may be prosecuted if you are involved in an accident.

Am I able to drive while taking pain medicines?
Yes, but only if your ability to drive safely is not affected (the DVLA refer to this as being 'impaired'). Many medicines prescribed to help manage pain may cause side-effects such or sleepiness. This may make you less able to drive safely. You must not drive if you think your medicines are affecting how you drive.

What symptoms may mean I cannot drive safely?
Do not drive if you have symptoms that reduce your ability to drive safely. The DVLA and Police describe this as being 'impaired'. Drugs can affect your driving in many ways:

- being able to judge speed and distance
- reaction and coordination skills
- blurry or reduced vision
- sleepiness
- aggression
- changeable behaviour
- panic attacks
- visions (hallucinations)
- feeling sick
- dizziness
- shaking (tremors)

These symptoms can occur as side effects of medicines. Pain itself can also affect sleep, concentration and how your body works.

When might I be at risk of not driving safely?
There are certain times when your ability to drive safely is most at risk. Be very careful:

- When you start a new pain medicine
- When increasing or reducing the dose of a pain medicine
- If you start taking another medicine that could mean you are not safe to drive
- If you take an over-the-counter medicine that could also affect your driving
- If you drink alcohol with some pain medicines you are much more likely to have an accident.

Do I need to tell the DVLA when I start a new medicine?
You do not generally need to inform the DVLA when you start medicines for pain. However, there may be other information about your condition(s) that the DVLA needs to know. Your doctor or the DVLA can discuss this with you. As mentioned above, you must inform the DVLA if you are diagnosed with a listed condition.

Do I need to inform my motor vehicle insurance company?
We strongly advise you to inform your motor vehicle insurance company about your health and what medicine(s) you are taking to make sure your motor insurance is valid.
The 'Drug Driving' law If you have been prescribed one of the following medicines, you may be affected by this law:

- morphine or related drugs (such as codeine, tramadol, fentanyl or methadone)
- diazepam or related drugs (such as clonazepam, diazepam, oxazepam, temazepam,
- lorazepam, or flunitrazepam)
- ketamine, amphetamine (e.g., dexamphetamine or selegiline)
- cannabinoids (e.g., Sativex, cannabis).

In England, Scotland and Wales it is a criminal offence to drive above a set limit for these types of medicines (like the current rules on alcohol and driving). You may test above the legal limit even if you are taking the correct prescribed dose of this type of medicine. You should carry a copy of your hospital letter or your prescription to show the police if you are ever stopped. You have a medical defence, and you should not be prosecuted under the 'drug driving law' if:

- you are taking these medicines at the level your doctor, nurse or pharmacist has prescribed and,
- your ability to drive safely is not reduced (impaired)

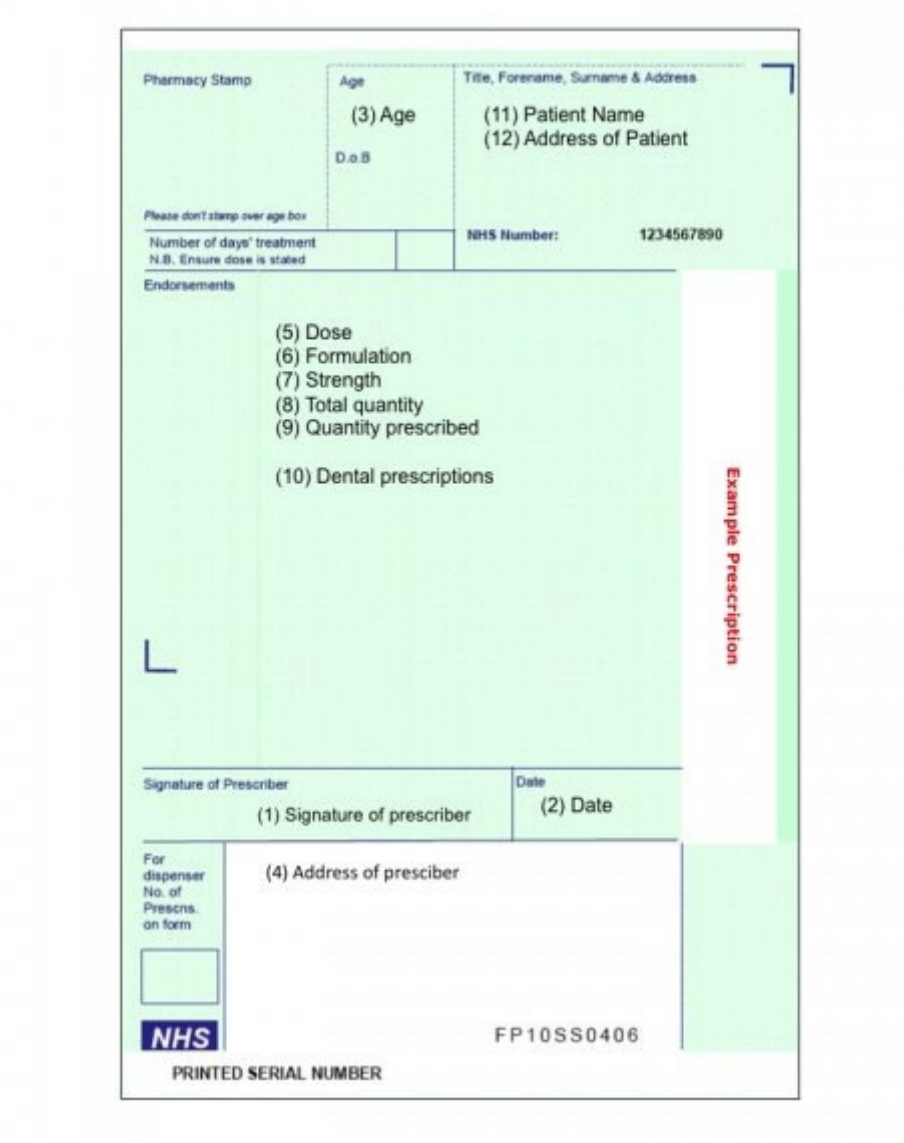
This defence cannot be used if the police think your driving ability is reduced due to medicines. They may ask you to perform tests at the roadside to check your balance and co-ordination. The following link gives guidance on what conditions/medicines you need to inform the DVLA about:
https://www.gov.uk/health-conditions-and-driving

The following websites provides further information on medicines and illegal drugs and driving law:
Drugs and driving: the law
https://www.gov.uk/drug-driving-law
Alcohol and drug driving
https://www.police.uk/advice/advice-and-information/rs/road-safety/alcohol-drug-driving/
fpm.ac.uk/patients | 3Driving and Pain

Writing Controlled drug prescriptions

The Misuse of Drugs Act 1971 (legislation.gov.uk) prohibits certain activities in relation to 'Controlled Drugs', in particular their manufacture, supply, and possession. In order to allow use of Controlled Drugs for therapeutic purposes, The Misuse of Drugs Regulations 2001 (legislation.gov.uk) (and subsequent amendments) define the classes of person who are authorised to supply and possess Controlled Drugs while acting in their professional capacities and lay down the conditions under which these activities may be carried out.

In addition to usual prescription requirements, additional information must be provided.
https://bnf.nice.org.uk/medicines-guidance/controlled-drugs-and-drug-dependence/



1. **SIGNATURE**: the prescription needs to be signed by the prescriber with their usual signature.
2. **DATE**: the prescription needs to include the date on which it was signed. Controlled Drugs prescriptions are valid generally for 28 days.
3. **PATIENT'S AGE**: if under 12 years

4. **PRESCRIBER'S ADDRESS**: the address of the prescriber must be included on the prescription and must be within the UK
5. **DOSE**: the dose does not need to be in both words and figures however it must be clearly defined
6. **FORMULATION**: the formulation must be stated; the abbreviations "tabs" and "caps" are acceptable
7. **STRENGTH**: the strength only needs to be written on the prescription if the medicine is available in more than one strength. To avoid ambiguity, where a prescription requests multiple strengths of a medicine to fulfil a particular dose, each strength should be prescribed separately (i.e., separate dose, total quantity, etc)
8. **TOTAL QUANTITY**: the total quantity must be written in both words and figures. If the medicine is in dosage units (tablets, capsules, ampoules, millilitres, etc), the Home Office advises this must be expressed as a number of dosage units (e.g., 10 tablets [of 10mg] rather than 100mg total quantity). The total quantity can be expressed as the multiplication of two numbers provided both components are clearly and unambiguously written in words and figures (e.g., "2 packs of 30; two packs of thirty"). Liquids should be expressed as millilitres.
9. **QUANTITY PRESCRIBED**: the Department of Health and the Scottish Government have issued strong recommendations that the maximum quantity of Schedule 2, 3 or 4 Controlled Drugs prescribed should NOT exceed that needed for 30 days. This is not a legal restriction, but prescribers should be able to justify the quantity requested (on a clinical basis) if more than 30 days' supply is prescribed. There may be genuine circumstances for which medicines need to be prescribed in this way in which case the prescribing decision needs to be clearly documented.
10. **DENTAL PRESCRIPTIONS**: where the Controlled Drug prescription is written by a dentist, the words "for dental treatment only" should be present
11. **NAME OF PATIENT**
12. **ADDRESS OF PATIENT**

A pharmacist is **not** allowed to dispense a Controlled Drug unless all the information required by law is given on the prescription. In the case of a prescription for a Controlled Drug in Schedule 2 or 3, a pharmacist can amend the prescription if it specifies the total quantity only in words or in figures or if it contains minor typographical errors, provided that such amendments are indelible and clearly attributable to the pharmacist. Failure to comply with the regulations concerning the writing of prescriptions will result in inconvenience to patients and delay in supplying the necessary medicine. A prescription for a Controlled Drug in Schedules 2, 3, or 4 is valid for 28 days from the date stated.

Record keeping

Basic documentation guidance is described in the GMC's Good Medical Practice 2024 Domain Three Sections 69-70

- **"Record your work clearly, accurately, and legibly**

- You must make sure that formal records of your work (including patients' records) are clear, accurate, contemporaneous, and legible.

- You should take a proportionate approach to the level of detail, but patients' records should usually include:
  - relevant clinical findings
  - drugs, investigations, or treatments proposed, provided, or prescribed
  - the information shared with patients
  - concerns or preferences expressed by the patient that might be relevant to their ongoing care, and whether these were addressed
  - information about any reasonable adjustments and communication support preferences
  - decisions made, actions agreed (including decisions to take no action) and when/whether decisions should be reviewed
  - who is creating the record and when."

These have altered from the previous iteration, and the greater emphasis on shared and agreed decision making is especially important when the potential long-term use of opioid medication is being considered.

Additional Consideration when prescribing Opioids

For prescription of opioids there should a focus on:

- The aims of treatments – this may include allied aspects such as function
- The drug and formulation(s) – e.g., modified release and immediate release
- Any guidance (oral and/or written) on use and patient choices (e.g., dose escalation/reduction, PRN options) – where provided
  - Best practice is to provide written guidance and/or address this in correspondence to the patient and GP.
- the means of assessing the aims
- the timescale of reviews
  - these should be frequent until stability of treatment and outcome are apparent
- the management of the outcomes
  - From the outset there should be clear criteria for the optimisation, reduction and/or stoppage of the medications
    - and how this may be achieved

It should be clear that this is an agreed plan of management between the patient and the prescriber.

Further reading: Good practice in prescribing and managing medicines and devices (gmc-uk.org)

Improving patient safety and minimising patient harm

Key Points

- Potent opioid analgesics are frequently involved in serious medication incidents, often because of incorrect dose calculations.
- The National Reporting and Learning System (NRLS) collects, analyses, and learns from all types of patient safety incidents.
- NHS England encourages all patient safety incidents to be reported through the NRLS.
- The acute sector reports the largest number of medication incidents with far fewer reports from primary care. [1]

Medication errors

Opioid analgesics are frequently involved in serious medication errors and are frequently implicated in serious errors to the NHS Litigation Authority, the Medical Defence Union, and the dispensing error analysis scheme. Morphine is one of the most frequently involved drugs in medication errors in other countries too, including the United States and Sweden. [3-5] In the National Patient Safety Agency (NPSA) report 'Safety in doses: medication safety incidents in the NHS' published in July 2007, opioids were highlighted as being one of the most implicated in medication incidents resulting in severe harm or patient death. [2]

Reporting adverse events

Reports of suspected Adverse Drug Reactions should be made through the Yellow Card website, hardcopy form, smartphone app or using your clinical IT system where feasible).

References:

1. National patient safety incident reports up to June 2022. NHS England. https://www.england.nhs.uk/publication/national-patient-safety-incident-reports-up-to-june-2022/ Accessed 24/10/2023.

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Further Reading

- Care Quality Commission newsletters:
  - The safer management of controlled drugs: annual update 2022
- CQC Controlled Drugs National Group.
- National Patient Safety Agency. **Patient Safety Alert 21 Safer practice with epidural injections and infusions**. 2007
- National Patient Safety Agency. **Patient Safety Alert 12 Ensuring safer practice with high dose ampoules of diamorphine and morphine.** 2006
- National Patient Safety Agency. **Rapid Response Report 05. Reducing dosing errors with opioid medicines.** 2008
- National Institute for Health and Care Excellence. **Guideline NG46: Safe use and management of controlled drugs.** 2016 NG46 Controlled drugs: safe use and management full guideline (nice.org.uk)
- NHS Improvement. National Reporting and Learning System.
- Smith J. **Building a safer NHS for patients: improving medication safety**. 2004
- Medicines and Healthcare Products Regulatory Agency**. The Yellow Card Scheme: guidance for healthcare professionals**. 2015
- https://www.sciencedirect.com/science/article/pii/S1551741118306351

Non-medical prescribing

Non-medical prescribing (NMP) refers to any prescribing provided by healthcare professionals other than doctors or dentists. A range of professionals can qualify to be a non-medical prescriber (NMP) although there may be restrictions on what they can prescribe and the terms under which a prescription can be provided.

The following professional groups can become NMPs

- Nurses / Midwives
- Pharmacists
- Physiotherapists
- Podiatrists
- Paramedics
- Optometrists
- Therapeutic radiographers
- Diagnostic radiographers
- Dietitians

Supplementary prescribing*
Supplementary prescribing is defined as “A voluntary partnership between a doctor or dentist and supplementary prescriber, to prescribe within an agreed patient-specific clinical management plan (CMP) with the patient's agreement”. Currently, nurses, midwives, optometrists, pharmacists, physiotherapists, podiatrists, radiographers, paramedics, and dietitians may become supplementary prescribers. Once qualified, they may prescribe any medicine (including Schedule 2-5 controlled drugs but excluding diamorphine, cocaine and dipipanone for treatment of substance misuse) within their clinical competence and according to the CMP.

*Royal Pharmaceutical Society. A Competency Framework for all Prescribers. Effective: September 2022. https://www.rpharms.com/resources/frameworks/prescribing-competency-framework/competency-framework (Accessed: October 2023)

Independent prescribing
A prescribing healthcare professional who is responsible and accountable for the assessment of patients with undiagnosed or diagnosed conditions and for decisions about the clinical management required, including prescribing*. Medical doctors can prescribe any controlled drug to be administered via any route. Dentists can only prescribe controlled drugs included in the Dental Prescribing Formulary on an FP10D (England), GP14 (Scotland) or WP10D (Wales) Nurse and pharmacist independent prescribers (IPs) can prescribe and administer any controlled drug from Schedule 2-5, excluding cocaine, dipipanone and diamorphine for treatment of substance misuse. Physiotherapist IPs can prescribe only diazepam, dihydrocodeine, lorazepam, morphine, oxycodone and temazepam for oral administration. They can also prescribe morphine for injectable administration and fentanyl for transdermal administration. Chiropodists and podiatrist IPs are able to prescribe diazepam, dihydrocodeine, lorazepam and temazepam for oral administration only. Paramedic IPs are able to prescribe morphine sulphate, diazepam, midazolam by oral and by injection, lorazepam by injection only and codeine phosphate oral administration. Therapeutic radiographer IPs are able to prescribe tramadol, lorazepam, diazepam, oxycodone and codeine by oral and morphine by oral or by injection. Optometrist and Community Nurse IPs are not allowed to prescribe any controlled drugs.

Further Reading

- Royal Pharmaceutical Society. A competency framework for all prescribers. Effective September 2022. Available from: https://www.rpharms.com/resources/frameworks/prescribing-competency-framework/competency-framework (Accessed October 2023)

- Community Pharmacy England. Who can prescribe what? Updated 10th November 2022. https://cpe.org.uk/dispensing-and-supply/prescription-processing/receiving-a-prescription/who-can-prescribe-what/ Accessed October 2023
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Pharmacists and safe opioid prescribing

Key Points

- Pharmacists are medicines experts and advise patients about improving safety, efficacy and adherence in medicines use, including opioids.
- Pharmacists provide training and education in the safe, evidence-based use of opioids and other analgesics to colleagues from different healthcare professions
- Pharmacists and their teams work to safety-net prescribing undertaken by professional colleagues, which might include querying and adjusting doses, reviewing the necessity and rationale for additional medicines, and advising on potential interactions or safety concerns
- Pharmacists and pharmacy technicians carry out medicines reviews which examine the effectiveness and tolerability of opioid analgesics., They also provide the opportunity to support people to adopt self-management strategies as part of a pain management plan
- Pharmacists have an increasing role within or alongside pain management services in all sectors, and should lead on pharmacological management guideline development and safety initiatives to reduce the harm caused by opioids

Pharmacists and opioid stewardship

Pharmacists are experts in medicines and their use. They tend to have a particular focus on safe and rational prescribing, acting as a safety-net for people receiving prescriptions or medicines advice from other healthcare professionals. Pharmacists have a wide range of roles across primary care, Community services, hospitals and in industry and can develop competencies at advanced and consultant level, working alongside other healthcare practitioners to provide multi-disciplinary care. Pharmacists can qualify as independent prescribers and so have potential to develop their own caseloads, clinics or services in any healthcare setting that could include acute or chronic pain support and prescribing.

In primary care, community pharmacists are the most accessible community healthcare professional for many individuals. In addition to a core dispensing role, pharmacists and their teams can advise on managing minor conditions including many common acute musculoskeletal conditions which present with pain. Working with other healthcare organisations such as Health Boards, Primary Care Networks (PCNs) and Integrated Care Boards (ICBs), community pharmacists provide services specific to people living with pain. This may be part of a locally enhanced or nationally developed services and whilst tending to have a focus on medicines use, will also encourage discussion of self-management and

signposting to local services. Examples include the Medicines Care and Review service in Community Pharmacy Scotland. *

*https://www.cps.scot/core-2/medicines-care-and-review

General Practice (GP) Pharmacists work alongside General Practitioners and other healthcare professionals, providing medicines-focussed clinical care. Pharmacists also have roles across networks of GP practices and other community services, such as PCNs in England and Primary Care Clusters in Wales. Primary Care Pharmacists often have highly developed expertise in the management of long-term conditions and increasingly support people living with pain, particularly in relation to reducing the harm from analgesic medicines. Pharmacists are likely to be the professional group most involved in reviewing and advising on tapering analgesic medicines in Primary Care. The increasing focus on reviewing medicines associated with dependence and withdrawal is leading to larger numbers of Primary Care pharmacists and pharmacy technicians, developing skills and expertise support wider pain management, as part of a multi-disciplinary approach to supported pain management and harm reduction.

Hospital pharmacists will see people presenting or living with pain in all specialties and are likely to be asked for advice on analgesic medicines use. Pharmacists working in hospital will develop specialisms and it is not uncommon to have specialist surgical pharmacists working with acute pain teams and other anaesthetic colleagues. Similarly, to the changes in Primary Care and the focus on reducing analgesic-related harms, pharmacists are more frequently being employed as part of multi-disciplinary pain teams. In these roles, it would be expected for pharmacists to lead on medicines education, safety, and reviews in a clinical setting and for the rest of the team.

Medication reviews take different forms in different settings, however, as a general rule, the purpose of an analgesic review is to determine*:

- the effectiveness of current treatment in terms of reducing pain intensity and how the medicine(s) allow the person to improve or maintain a satisfactory level of function
- any adverse effects being experienced – these could be due to interactions with other medicines or conditions the person has or as a direct result of the analgesic medicine(s)
- the risks and benefits of continuing the current analgesics at the same dose, adjusting the dose, or stopping it altogether and the person’s preference for the same
- any signs the person is developing problematic use of the analgesic medicines including dependence
- who can be contacted if they have any problems or concerns about their analgesic medicines

Other interventions that pharmacists provide for patients with pain include:

- Lifestyle advice, including diet and exercise, and supported self-management of pain.
- Improving protection against potentially harmful over-use of analgesics including those available to purchase from shops and pharmacies
- Informing public understanding of different types of pain and the safe, evidence-based use of analgesic medicines

Signposting to other support which might include local pain services, third sector providers or facilitating the use of relevant online services

*

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A. Understanding Pain and Medicines for Pain

About pain

Pain is one of the most common human experiences, and mild, short-lived pains, like headaches, minor injuries and musculoskeletal aches and pains are a feature of everyday life.

The experience of pain is affected by many things including mood, past experience and concerns of the cause, and these can magnify or reduce the suffering itself.

Pain can be due to a wide variety of causes and last for a variable amount of time.

In healthcare, a number of terms are often added to help describe the pain better and direct to specific treatments. Often common words are used with specialist meaning which can cause confusion.

Common terms include:

Acute / Chronic

These two terms are used to describe how long a pain is lasting, not its severity. *Acute* describes a pain, usually lasting for less than 3 months, and *Chronic* for more than 3 months. Sometimes 6 months is used as a cut-off.

Although these terms refer to time, they may give some indication as to the treatment options.

Other terms used may refer to the underlying cause:

Nociceptive

This means there is some tissue damage, which is the most common cause of pain. e.g., broken bone, skin burn, infection, toothache, etc.

These types of pain are usually acute (short-lasting) and settle with the normal healing process. This does not always happen.

Neuropathic

This means there is direct damage to some part of the nervous system e.g., brain, spine, nerves (large and small).

These pains are often associated with ‘strange’ unpleasant sensations and are more commonly associated with chronic (long-term) pain. The damage may be a relative short-term event but healing in the nervous system is slow and unpredictable.

Examples include diabetic neuropathy, post-amputation pain, post-shingles pain, post-stroke pain and sciatica

<u>Other terms</u>

Nociplastic / Central Sensitisation

These terms are used to describe the apparent changing quality or severity of a pain, not associated with any obvious change in the underlying cause. It is assumed to be related to changes in how the nervous system responds to persistent pain.

Cancer Pain is a term often used to describe the complex mix of the above types of pain; both in terms of time, cause and how they vary over the course of the condition.

Treatments

Healthcare initially focuses on the reason for a pain; investigating its cause (e.g., X-rays, blood tests etc), applying treatments (e.g., medicines, surgery) focused on the cause. The pain is often managed as a parallel issue – anticipated to settle as the problem is cured.

But what if the pain doesn't settle or no cause is discovered?

For some pain problems when serious, sinister or progressive conditions have been ruled out as a cause, we might not find out what is causing the pain. It is in these cases where holistic pain management is helpful in managing the pain as the *disease, when* we are unable to determine the cause of the pain.

Many long-term pain problems do not respond well or at all to medications, including opioids, and other strategies may be far more helpful. These can include physiotherapy to help improve general activity and improved muscle support for painful areas (especially for spinal and joint pains), coping strategies to understand the nature of pain and develop skills such as relaxation, mindfulness, pacing, goal setting to avoid over- and under-activity cycling. Occasionally focused injections may be considered. Some people gain benefit from 'alternative' treatments such as acupuncture or a TENS machine.

Challenges of long-term pain management

The experience of pain is complex and influenced by the degree of tissue injury, current mood, previous experience of pain and understanding of the cause and significance of pain. Previous unpleasant thoughts, emotions and experiences can also contribute to the current perception of pain and, if unresolved, can act as a barrier to treatment. The assessment of chronic pain needs to be wide-ranging and comprehensive. The persistence of symptoms is particularly relevant in relation to prescribing where patients may be exposed to cumulative harms of drugs over prolonged periods.

- **If a patient continues to have pain despite taking a number of medications, drugs should be sequentially tapered or stopped to determine continued effectiveness.**
- **If a patient reports reasonable pain relief from a medication regimen in the longer term, it is also necessary to taper medications intermittently to assess whether the symptoms have resolved spontaneously or whether the patient is relatively pain free because of continued efficacy of medication**
- **Certain pain conditions such as cancer pain and sickle cell crisis might need more specialist involvement and opioid management can vary**

Assessment of long-term pain

Assessment of pain

The experience of pain is complex and influenced by the degree of tissue injury (even when no longer present or identifiable), mood, previous experiences of pain and understanding of the cause and significance of pain. Previous thoughts, emotions and experiences can also contribute to the current perception of pain, and, if unresolved, can act as a barrier to treatment.

A pain assessment, like all medical evaluations, serves two main purposes:

[1] To understand the nature of the pain problem and its confounding factors

[2] To provide a baseline against which the effect of treatments can be measured.

This second aspect is often more difficult than for many medical problems where outcomes are often simpler to recognise.

For pain problems, improvement in ‘pain’ may, paradoxically, not be the main endpoint, but improving how the pain is understood and managed may be the essential outcomes.

Primary Assessment.

Assessment should include patient education, understanding and expectations about chronic pain. Unrealistic expectations need to be recognised and addressed sympathetically and informatively

Coloured Flags

Various aspects of the history recognised as potentially important when considering investigative or treatment plans. Though widely adopted, and useful clinically. they have a limited research base.

The most common concepts are of RED and YELLOW flags. The former indicating possible pathology needing investigation, and the latter psychosocial aspects of beliefs around pain, coping and function. Various other colours have been suggested but are not widely used.

Core Details of a Pain Assessment

- Where is the pain?
- Description of pain
- Does it radiate elsewhere?
- How does it vary in intensity?
    - What makes it worse?
    - What is the effect on sleep?

- What makes it better?
- Current medications and response
- Response to previous medications and any other interventions.
- General Medical History including operations and illnesses – consider co-morbidities that may impact on drug considerations e.g., renal, hepatic, sleep apnoea.
- What is the effect on mood?
    - Try to differentiate between pre-existing and pain-related issues – difficult and not always possible or clear.
- What is the effect on physical function?
    - Employment / Daily / Social

Brief psychosocial screening: ACT-UP[1]

1. **A**ctivities: how is your pain affecting your life (i.e., sleep, appetite, physical activities, and relationships)?
2. **C**oping: how do you deal/cope with your pain (what makes it better/worse)?
3. **T**hink: do you think your pain will ever get better?
4. **U**pset: have you been feeling worried (anxious)/depressed (down, blue)?
5. **P**eople: how do people respond when you have pain?

- Mental health including emotional trauma, previous and current mood, contact with mental health circumstances. Mental health comorbidities and a history of significant emotional trauma are not a contraindication to opioid therapy but:
    - are a risk factor for opioid therapy becoming prolonged and for high doses to be used
    - patients may use opioids to blunt unpleasant thoughts and experiences: this may make opioids difficult to stop
    - are a risk factor for addiction to prescribed opioids
    - will be contributory to the current pain experience so need to be identified and managed separately.
- Be aware that Mental Health issues may become apparent that need management beyond or in parallel with the pain problem. Consideration should be made of suitable contacts for urgent or routine advice.
    - Be wary of assuming either that pain is a symptom of - or a direct cause of - mental health issues.
- Current or previous history of substance misuse to drugs or alcohol. Patients with a current or past history will need careful management and support in collaboration with specialists with expertise in addiction (for more information click here).
- Patient circumstances and context (employment, family responsibilities, sources of support). Patients with a family/household member with problems will need additional support and counselling about risks of diversion of controlled drugs.

- Relevant physical examination including observation of patient mobility, distress.

- Imaging and other diagnostics (x-rays, scans, blood tests and electrophysiology).
- **Patient's understanding of pain and expectations of outcome.**
    - **This often needs addressing to create a viable contract of expectations between the clinician and the patient.**
    - **Unrealistic expectations need to be recognised and addressed sympathetically and informatively.**

Pain Assessment Tools

Pain cannot be measured with any objective tool. No blood test, Xray, or other test will give a figure against which treatment can be measured.
Pain is a personal experience and is expressed as such. Pain Assessment Tools can however give an indication of the experience and can be helpful in assessing various aspects of suffering. Improvements are a useful indicator of treatment efficacy. Tools are based around various aspects of the pain experience:

- Pain Intensity
- Pain Interference
- Physical Functioning
- Emotional Functioning
- Quality of Life
- Patient reported global rating

Simple tools used for acute pain are not useful without context

The FPM guide on Outcome Measures [2] provides detailed guidance on the use of various tools.

Review Appointments

With the issues outlined above, the multifocal nature of the review of treatment needs to be considered. A clear history, with a focus on the aims of treatment will make ongoing reviews easier to understand in terms of the chronicity of disease, what has – or has not – been achieved and how future therapeutics fit into the possible options, avoiding, both, blind optimism and pessimism

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2. FPM Outcome Measures document

The role of medication in pain management

Key Points

- Acute pain is the body's normal response to tissue damage.
- Many types of cancer pain are also related to tissue damage or nerve compression.
- Persistent non-cancer pain serves no physiological purpose and is influenced not only by tissue injury but by a number of emotional, social and cognitive variables
- Medicines are generally less effective for persistent pain than for other types of pain. When medicines are prescribed, they should be used in combination with other treatment approaches to support improved physical, psychological and social functioning.
- Initial prescribing of opioid medicines for pain should be considered for a trial period, with outcomes of treatment agreed with the patient.
- If, at the end of the trial, agreed outcomes have not been achieved or progress made towards them, then the patient and prescriber need to discuss whether to continue treatment.
- Side effects are relatively common – consider adjuvant drugs such as laxatives and anti-sickness medications if needed. Side effects need to be considered and balanced with potential benefits. If patients continue to take medicines that provide limited analgesic benefit, then they are exposed to harms unbalanced by the benefit that the medicines provide. When medicines do not give sufficient analgesia there is a risk of dose escalation. This is rarely helpful.

A targeted approach to pain prescribing

- **The analgesic ladder: History**

In 1986 the World Health Organization proposed a stepwise approach to 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., for mild pain non-opioid medication should be prescribed, with weak opioids for moderate pain and strong opioids for severe pain. The 'ladder' approach encouraged use of adjunctive medicines at each rung of the ladder and use of strong opioids only at the top of the ladder. The analgesic ladder was validated as a tool for improving the treatment of cancer pain. The recent guidelines emphasise on individualised approach with key concepts maintained.

- **Why the analgesic ladder is unhelpful for persistent pain**

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: substantial reduction in pain intensity is rarely an achievable goal. Additionally, persistent pain may be generated by a number of different pathophysiologic mechanisms that may require different approaches to treatment. In particular, reported intensity of pain relates poorly to the degree of tissue injury and is heavily influenced by a number of factors including thoughts, emotions, understanding of the meaning of pain, previous experience of pain and the patient's current distress. The contributors to the patient's current experience of pain need to be explored and will influence the pain management plan.

- **A stepped approach**

When making medication choices to support patients with persistent pain, it may be rational to use a stepped approach, but this should not necessarily be determined by reported pain intensity (which is the underlying principle of the analgesic ladder). Medications are usually a small part of the pain management plan and should be used in conjunction with non-pharmacological interventions such as advice regarding activity, physiotherapy and an explanation that pain may be resistant to medication and complete relief of symptoms is not a goal of therapy. Regardless of pain intensity, it is rational to start with non-opioid drugs, where these have some demonstrated efficacy for the condition being treated. Trials of both weak and strong opioid therapy may be considered for some patients with well-defined pain diagnoses in whom symptoms persist despite first line interventions. 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.

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B. Clinical use of Opioids

Opioids and Acute Pain Management

The treatment of acute pain is essential to facilitate recovery from surgery and trauma by enabling early mobilisation and reducing the risks of complications including venous thromboembolism, pulmonary embolism, pressure sores and pneumonia. [1]

Severe untreated acute pain may also predispose to the development of chronic post-surgical pain or chronic pain post trauma.

Opioids remain important in the treatment of moderate to severe acute pain.

Opioids should always be used as part of a multimodal and multidisciplinary approach. Paracetamol, NSAIDS and local anaesthetics should also be used if there are no contraindications. Psychological interventions and the allaying of anxiety can reduce pain in this context. Non pharmaceutical methods e.g., ice, rest, heat, TENS should be considered where appropriate. [2,7]

NSAIDS, gabapentin, pregabalin, systemic lidocaine and ketamine are opioid sparing and reduce opioid related adverse events. [3]

Evidence-based, procedure-specific analgesic techniques should be used when evidence is available, for example PROSPECT (Procedure specific analgesic techniques) recommendations for analgesia. [6,7]

Avoid modified release opioids for the treatment of acute pain. Modified release opioids confer no benefit in the management of post operative pain and have a higher risk of opioid induced adverse events including OIVI (opioid induce ventilatory impairment). The prescribing of modified release opioids is a risk factor for the development of persistent post operative opioid use (opioid use more than three months after surgery or trauma). [4,5,6,7]

Age, rather than weight, is a better determinant of the dose of opioid needed. Dose requirements decrease 2-4-fold as age increases.[8,9]

Acute pain management should be individualised with regular assessments of the adequacy of analgesia and documentation of any adverse events. Inpatient pain teams should be involved in the care of any patient with difficult to manage pain.[2].

The efficacy of analgesia should not be assessed using a numerical pain score in isolation. Patients should also have their function assessed for example with the

Function Assessment Score (FAS). Overreliance on a unidimensional pain score may lead to overuse of opioid analgesia.[10]

The complications of OIVI include respiratory depression, raised PaCO2, decreased consciousness level and airway obstruction. These can be fatal. Respiratory rate alone is a poor predictor of OIVI. Sedation is a far better predictor. Concurrent gabapentinoid use increase the risk of OIVI. [11,12]

Opioid doses should always be titrated to effect, with the lowest effective dose for no longer than the expected duration of pain severe enough to require opioids. [7]

Patients started on opioids should be given verbal and written information, this should include discussion around:

- The risks and benefits of opioid analgesia
- A plan to deescalate and stop opioids once the acute phase is over
- Driving and opioids
- The safe storage and disposal of medication.

An example of this is the British Pain Society "Managing pain after surgery" leaflet.

There is evidence that preoperative education is associated with reduced opioid use and reduced pain intensity post operatively.[7,13, 14]

While taking opioids the patients should be assessed regularly for opioid related harm.

Patients discharged on opioids should be prescribed no more than 5-7 days medication. Primary care should be informed that this is an acute prescription and not to continue opioids without review. The discharge letter must explicitly state the recommended opioid dose, amount supplied and planned duration of use. [6, 15]

Patients transitioning from acute to chronic pain, who are requiring opioids, should be managed as per FPM guidance on the management of chronic pain.

There will be a subset of patients with acute pain that have pre-existing chronic pain. If they are coming for elective surgery consider optimising management of pre-operative pain and psychological risk-factors before admission, including weaning of opioids where possible.[6]

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Opioids for long term pain

The effectiveness of opioids for long term pain

Clinical evidence regarding the effectiveness of opioids for long term pain is unclear. Indeed, there is insufficient evidence to determine the long-term benefits of opioid therapy for chronic pain and there is an increased risk of harms with long-term opioid therapy. This is partly due to few placebo-controlled trials investigating opioid therapy in long term pain in the medium- (6 to <12 months) and long-term (≥ 12 months). A 12 month follow up study comparing opioid to non-opioid drugs in patients with chronic back pain or knee and hip pain showed no difference in improving pain related function [1]. Regarding the short-term effectiveness of opioids for chronic pain (1 to <6 months), there is some tentative evidence to suggest that opioids may have small improvements in pain intensity, but these may be dependent on a number of factors e.g., chronic pain condition and co-morbidities of the patient.

It is also important to keep in mind that patients participating in these randomised controlled trials have been selected based on strict inclusion and exclusion criteria, have discrete pain diagnoses and lack many of the physical and emotional co-morbidities of patients seen in clinical practice. Furthermore, progress of therapy in clinical trials is monitored more closely than in usual clinical practice and dose titration is closely supervised. As a result, it is challenging to generalise the findings from these randomised controlled trials to everyday clinical practice. Although this may indicate the need for case series and open-label research, data from research using these designs does not enable firm conclusions regarding improvement in pain intensity, function or quality of life due to the influence of confounding variables and the inability to infer causality between opioids and reported outcomes.

Taken together, this means that non-pharmacologic and non-opioid treatments should be optimised first as appropriate for the specific condition and the patient considering the biopsychosocial aspects of the patient's pain (e.g., exercise, physiotherapy, psychological therapies, acupuncture). Initiating a trial of opioid therapy should only be considered if established non-pharmacologic and non-opioid treatments are not effective, not tolerated, contraindicated and/or not available, and if expected benefits for pain and function are anticipated to outweigh the associated risks to the patient. Given the harms associated with opioid treatment and the probability of therapeutic disappointment in the long term, exploration of opioid therapy for a patient with long-term pain should be carefully planned and closely monitored. This should include clinicians having a discussion with the patient of the realistic benefits and known risks of opioid therapy, working with patients to establish treatment goals for pain **and** function and how these goals will be evaluated, monitored and documented, and identifying next steps if the opioid therapy is discontinued due to the benefits not outweighing the risks.

With the evidence we have, there should be no trial of traditional opioids in chronic pain beyond modest doses over about 2-4 weeks and the therapeutic trial should be informed by important practice points:

Important Practice Points

Always consider broad dose guidance and the value of specialist input

1. Patients who do not achieve useful pain relief or improved function from opioids within 4 weeks are unlikely to gain benefit in the long term.
2. There should be an exit strategy; jointly decided between the clinician and patient at the outset if the opioid therapy is unsuccessful in improving pain and function.
3. Patients who may benefit from opioids in the long term will demonstrate a favourable response within 4 weeks. However, see point 4
4. Short-term efficacy does not guarantee long-term efficacy. Outcomes should therefore be regularly evaluated and documented by both the patient and clinician.
5. An optimal dose is reached when there has been a demonstrable improvement in pain or function, and further increases have not further improved these.
6. Dose increases after a period of stability, or when a high dose has already been reached without significant benefit, need to be considered carefully and are usually not indicated. Exceptions may include a new acute pain problems for which a temporary increase may be trialled.
7. If the benefits of increasing the dose are considered to outweigh the risks, clinicians should work closely with patients to devise a plan for increasing the dose in a stepwise manner to reach the therapeutic goals, and, in the case of an acute pain for a reduction when the acute issue has resolved.

Side effects of opioids

Side effects are extremely common with opioid therapy and frequently lead to discontinuation[2]. It is therefore important to set the expectations of patients. Indeed, before the first prescription, opioid-associated side effects should be anticipated and appropriate counselling about common side effects and their management should be provided to patients. Furthermore, patients should be warned of the likelihood of enhanced effects and risks associated with concomitant use of other medicines and substances with sedative properties, including alcohol. Inadequate management of side effects and consequences of opioid treatment may contribute to unplanned hospital admissions and contribute to the overall costs associated with opioid treatment. There is little evidence that, in equianalgesic doses, commonly used opioids differ markedly in the incidence of their side effects. Patients using intermittent opioid dosing regimens might not become tolerant to side effects.

Manageable side effects

The most common side effects are predictable consequences of opioid pharmacological actions and include:

1. Constipation. 60%–80% of patients in opioid therapy have gut-related side effects. Constipation is the predominant complaint, but nausea (see below), vomiting (see below), abdominal pain, and distension are also frequently observed [3]. Straining, gas production, hard consistency of stools and abdominal discomfort should be considered (as well as number of bowel movements). Gastrointestinal side effects do not tend to improve after initiation of treatment or following an intended dose increase and may require long-term management. Where appropriate, treatments for gastrointestinal side effects should be considered:

    a. A small supply of an anti-emetic (e.g., cyclizine, prochlorperazine) may be beneficial when providing the initial prescription of an opioid.
    b. Encouraging the patient to drink lots of fluid, and to eat additional fruit and fibre may minimise constipation. However, a combination of stool softener (e.g., docusate sodium) and a stimulant laxative (e.g., senna or bisacodyl) may be necessary.
    c. Peripherally restricted opioid antagonists (such as oral naloxegol)) has modest benefit for improving constipation when compared with placebo. However, there are few data compared with regular optimal laxative therapy and lifestyle advice. These products have a limited place in the management of opioid induced bowel symptoms and constipation after an adequate trial of other options.

2. Nausea and vomiting. Opioid-induced nausea and vomiting are experienced by up to 40% of pain patients with no history of emesis. However, as opioid-induced nausea and vomiting are inconsistent consequences of opioid therapy, prophylactic antiemetics are generally not prescribed. In most patients, tolerance to the emetic effect of opioids develops after 2–4 weeks. Routine administration of antiemetics is therefore not necessary [4].

3. Pruritus. Opioids are considered the best-known medicine to evoke pruritus [5]. Pruritus tends to persist throughout treatment and may require long-term management. Several treatment options have been tested for opioid-induced pruritus, but none have been found fully satisfactory [5]. A reduction in opioid dose or switching to another opioid should therefore be considered if opioid-induced pruritus occurs [4].

4. Dizziness and sedation. Central side effects, such as dizziness and drowsiness, tend to improve gradually after opioid initiation. However, patients should be counselled about the possible effects on driving and other skilled tasks involving co-ordination and concentration when initiating or increasing an opioid dose. If these effects persist, dosages should be considered for reduction or consideration should be made to switch to another opioid [4].

5. Myoclonic movements. Myoclonus can occur in patients on chronic opioid therapy [6]. If this does happen, opioid doses should be considered for reduction or consideration made to switch to another opioid [4].

6. Increase in pain severity. For some patients in opioid therapy, their pain severity may increase. It is important to ascertain why this occurs through close monitoring of dose reduction. There are a number of reasons why a patients may report an increase pain intensity:

    a. Tolerance. After ongoing exposure to opioid therapy, some patients may develop tolerance (the same dose of drug produces less analgesic effect over time).

    b. Disease progression. In some chronic pain conditions, the symptoms can deteriorate as a result of progression of the syndrome.

    c. Opioid-induced hyperalgesia. This is characterised by a worsening of symptoms despite an increase in opioid dose.

7. Dry mouth. Opioids can cause dry mouth as a result of affecting the production of saliva. This tends improve shortly after initiation of treatment or following an intended dose increase.

8. Urinary retention. Opioids can be associated with urinary retention, particularly in elderly patients due to existing comorbidities [7]. If this occurs, a reduction in opioid dose or a switch to another opioid should be considered [4].

Harmful side effects

- Respiratory-related:
    - Opioids have multiple effects on respiratory physiology, including decreased central respiratory drive, respiratory rate, and tidal volume. They also increase airway resistance and decrease the patency of the upper airways. The consequence of all of these effects may lead to ineffective ventilation and upper airway obstruction in susceptible individuals.
    - Respiratory depression is a much-feared harm associated with the use of opioids. It is mostly a concern in acute pain management where patients have not developed tolerance. For chronic pain, it is most likely to be a potential problem if there has been a large, often unintended dose increase, or changes in formulation or route of administration.
    - Opioids can cause irregular respiratory pauses and gasping may lead to erratic breathing and significant variability in respiratory rate. The respiratory effects of opioids are more pronounced during sleep. Fatalities have been reported in patients with obstructive sleep apnoea who are prescribed opioids, and sleep apnoea may be a relative contraindication to opioid therapy. This is particularly important if patients are taking other central respiratory depressants such as

benzodiazepines. If opioids are prescribed to patients with obstructive sleep apnoea, they will need up to date assessment of nocturnal respiratory function and should be compliant with therapy for this e.g., continuous positive airway pressure. Patients with sleep apnoea being prescribed opioids will need regular and detailed assessment of treatment.

- Opioids should only be started in patients with sleep-related breathing disorders after very carefully balancing potential benefits and risks. Opioid treatment should be considered for discontinuation if sleep-disordered breathing occurs and does not improve despite optimisation of breathing therapy and/or reduction or cessation of other medications which negatively affect respiration (hypnotics, antipsychotics) [4].

- Increased absorption may occur from transdermal opioid formulations with a fever or other intercurrent illness, and if the patient is exposed to external heat, for example a hot bath or sauna. If concerns arise, closer patient monitoring will be required.
- Hypogonadism. Long-term opioid therapy can lead to hypogonadism which is characterised by sexual dysfunction and infertility. The management of hypogonadism can include a reduction in opioid dose, opioid rotation and hormone replacement [4].
- Falls and fractures. Opioid use increases the risk of falls and fractures. [2].
- Cardiovascular events. Although there is limited research into the cardiovascular events associated with long-term opioid use, preliminary evidence has identified an associated between long-term opioid use for chronic pain and an increased risk of myocardial infarction [2].
- Opioid use disorder and dependence. Long-term opioid use has been associated with a significantly increased risk of abuse or dependence for all doses of opioids [2]. It is thought that any current or previous substance use, any mental health diagnosis, younger age and male sex are predictors of the development of misuse among patients with outpatient opioid prescriptions [8]. If opioid use disorder is suspected, clinicians should discuss their concern with their patient in a non-judgmental manner and provide an opportunity for the patient to disclose related concerns or problems. Collaboration with an opioid use disorder treatment specialist should be considered for the management of opioid use disorder. Treatment options could include opioid tapering, continuation of therapy with a stable opioid dose, psychological therapies and buprenorphine or methadone therapy [4].
- Long term opioid use is associated with endocrine effects such as sex hormone and adrenal insufficiency [9,10]
- Overdose. Observational studies in North America have reported important risks of non-fatal and fatal unintentional overdose from long-term opioid use. This is contrast to the low rates reported in randomised controlled trials and may be due to strict inclusion and exclusion criteria, close monitoring of patients, short follow up duration and non-systematic assessment of opioid use disorder or dependence. Nevertheless, overdose is a serious side effect of opioid therapy, particularly in long-term opioid therapy. To reduce the risk of overdose, patients should be educated on overdose prevention, including when opioids are combined with other drugs or alcohol, naloxone use and be

monitored frequently. For patients who have a non-fatal overdose, they should be evaluated for opioid use disorder and/or dependence and have appropriate treatment [11].

The Cost of Opioid Related Side Effects

- Direct costs associated with opioid related side effects accumulate as a result of the need for prescribing medicines to prevent or minimise side effects and increased healthcare use (GP consultations, Emergency Department visits, unplanned hospital admissions).
- Impaired physical, psychological and social functioning (assessed by reduced quality of life), and work absences contribute to indirect costs.
- Given the high incidence and large economic burden of opioid-related side effects, prevention rather than treatment may be cost-effective.
- Opioid-related side effects are common in hospitalised patients and may contribute to increased length of stay and costs of admission.

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Management of Opioid Related Side Effects

Most common side effects are predictable consequences of opioid pharmacological actions and include nausea, vomiting, constipation, pruritus, dizziness, dry mouth and sedation

- Opioid-associated side effects should be anticipated and appropriate counselling about common side effects and their management should be provided to patients before the first prescription.
- Tolerance to many side effects usually occurs within the first few days of initiating treatment; however, unlike other side effects pruritus and constipation tend to persist throughout treatment.
- Common gastrointestinal side effects should be predicted, and prophylactic treatments considered if appropriate
- A small supply of an anti-emetic (e.g., cyclizine, prochlorperazine) may be beneficial when providing the initial prescription of an opioid.
- Encouraging the patient to drink lots of fluid, and to eat additional fruit and fibre may minimise constipation, however a combination of stool softener (e.g., docusate sodium) and a stimulant laxative (e.g., senna or bisacodyl) is often necessary.
- Peripherally restricted opioid antagonists (such as oral naloxegol, oral prolonged release naloxone in combination with prolonged release oxycodone, and subcutaneous methylnaltrexone) have modest benefit for improving constipation when compared with placebo, however there are many fewer data compared with regular optimal laxative therapy and lifestyle advice. These products have a limited place in the management of opioid induced bowel symptoms and constipation after an adequate trial of other options.
- Central side effects, such as drowsiness and dizziness, also tend to improve gradually after opioid initiation, however patients should be counselled about the possible effects on driving and other skilled tasks involving co-ordination and concentration when initiating or increasing an opioid dose.
- Patients should be warned of the likelihood of enhanced effects and risks associated with concomitant use of other medicines and substances with sedative properties, including alcohol.

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Long term harms of opioids

Recognised long term harms of opioids include:

- **fractures and falls**
- **endocrine dysfunction**
- **immune system**
- **opioid induced hyperalgesia**
- **cardiovascular events**
- **gastrointestinal complications and bleeding**

Controlled studies on long-term (≥1 year) opioid therapy are very limited, but evidence suggest that the increased risk of serious harms appears to be dose dependent.[1,2]

The risk of these adverse events is not unique to substance misuse, with one study finding the risk of adverse events being 23.7 fold more common from opioid use than misuse.[2] Compared to days without opioid exposure, the authors found current opioid exposure (not substance misuse) was associated with a 2.5 fold higher risk of a serious adverse drug event.

Fractures and Falls

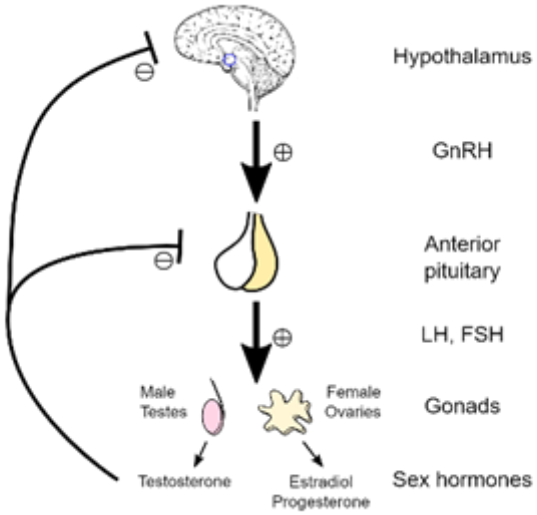
- Opioid use increases the risk and incidence of falls;[3] 30% of people over 65 and 50% of people older than 80 will have at least one fall per year.[4]
- A meta-analysis of 30 studies found an **increase in risk of falls, fractures and fall injuries among older people who use opioids**.[5] One study based in the USA, regarding elderly patients with a diagnosis of osteoarthritis, found that the incidence of falls was greater for patients prescribed opioids, than for those prescribed COX2 inhibitors or NSAIDs (OR 3.3 and 4.1).[6]

- Not only is the risk of falling increased, **but also the risk of fracture**. In a study looking at patients treated for falls, matched against controls, adults aged over 65 years with hip fractures were more than four times more likely to be treated with opioids prior to the fall (OR 4.497, 95% CI 2.724 o 7.424) than patients without fracture[7]. Falls occur mostly at initiation or following a dose escalation[29].

Endocrine System

- Long-term administration of opioids is associated with endocrine abnormalities, including:
    - **Sex hormone dysfunction**
    - **Adrenal dysfunction**

The most commonly observed endocrine disorder with long term use of opioids is **secondary hypogonadism, or opioid-induced androgen deficiency (OPIAD)**[8] due to suppression of the hypothalamic-pituitary gonadal (HPG) axis, altering the sex hormone-hypothalamic feedback loop. The dosage or duration of opioid treatment required to cause these may be as short as one week[9], and occurs with both intrathecal, oral and transdermal use.[8,10,11] One systematic review and meta-analysis found that hypogonadism is present among approximately 63% of male patients on long-term opioids.[12]



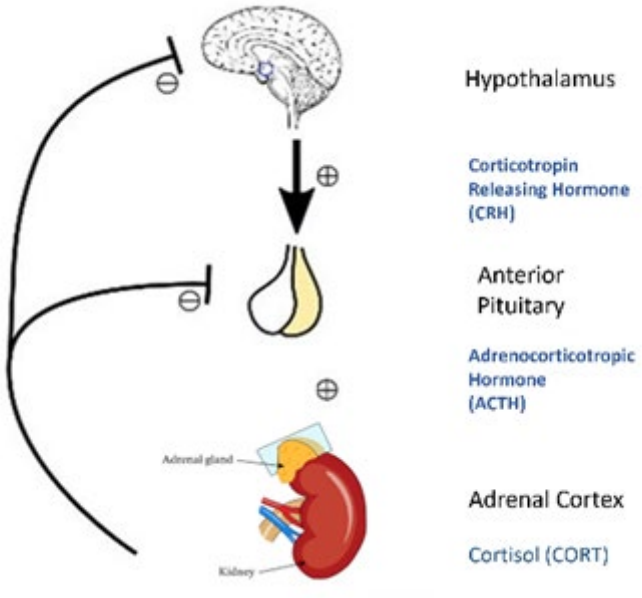
GnRH: gonadotropin-releasing hormone; LH: luteinizing hormone; FSH: follicle-stimulating hormone[13]

Sex hormone deficiency can lead to[14]:

- anaemia
- decreased libido
- decreased muscle mass

- depression
- erectile dysfunction
- fatigue
- menstrual irregularities
- osteoporosis
- vasomotor instability
- weight gain

- **Adrenal dysfunction**



Suppression of the hypothalamic-pituitary-adrenal (HPA) axis results in adrenal insufficiency, leading to lower blood cortisol and adrenocorticotropic hormone (ACTH) levels due to opioid use can present with symptoms including[12,15]

- fatigue
- malaise
- abdominal discomfort, anorexia
- orthostatic hypotension

Hypocorticism has been seen to present in about 15%[16] of patients.
NICE advises reducing the dose in persons with adrenocortical insufficiency.[17]

Screening and diagnosis:

- **Inform** patients about side effects of **endocrine dysfunction** before starting treatment.
- Routinely **ask** about symptoms suggestive of sex hormone deficiency at regular follow-up visits.
- *If symptomatic*, **test** serum testosterone, sex-binding globulin, LH/FSH, DHEAS in both men and women, oestradiol levels in women and early morning cortisol levels.
- **Monitor** blood pressure.

- If endocrine impairment is demonstrated, **refer** the patient to an endocrinologist for advice regarding the benefits of hormonal replacement therapy.

Immune System

- A well reported side effect of opioid use is the suppression of the immune system, which can impact on disease progression including HIV[18] and cancer. Morphine decreases the effectiveness of both natural and acquired immunity, with potential effects on outcomes of surgery or disease processes or increase in prevalence of other opportunistic infections.[19]
- Opioids modulate the immune system directly by binding to μ-opioid receptor on immune cells, or indirectly by binding to receptors within the central nervous system.[20] By activating the descending pathways of the HPA axis and the sympathetic nervous system, glucocorticoids are released, along with noradrenaline, both acting on leucocytes resulting in reduction of immune response.[20]
- One controlled retrospective study showed that opioid use was associated with lower response rate to treatment, and a shorter median progression-free survival as well as overall survival in patients treated with nivolumab for non-small-cell lung cancer.[21] However, an observational study found no evidence between post diagnosis opioid use and cancer reoccurrence.[22]
- Different opioids have different effects on the immune system, with different results obtained from *in vitro* and *in vivo*. [23] Not all opioids have the same effect, with tramadol,[24] tapentadol and buprenorphine having a weaker immunosuppressive action.[23]

Individual risk factors in those with an **immunosuppressed status, due to frailty, disease such as cancer or HIV, or those who have undergone invasive surgery** should be considered when treating with opioids.

Opioid Induced Hyperalgesia

- Prolonged use of opioids can lead to a state of abnormal pain sensitivity, called *opioid induced hyperalgesia* (OIH), where patients receiving opioid therapy become more sensitive to pain[25], pre-existing pain may be aggravated[26], or the pain may be different from the original pain being treated.[25]

- The exact mechanisms for developing OIH are not fully understood, but OIH may be diagnosed if the patient on long-term opioid therapy presents with increased pain. OIH should not be confused with breakthrough pain resulting from development of opioid tolerance. Opioid tolerance responds to increase in dose, whereas with OIH pain increases with increasing dosage.[27]

- Pain related to **disease progression must be ruled out** before a diagnosis of OIH is made.
- Management of opioid induced hyperalgesia is challenging and requires time and patience, and understanding from the patient and their family.[25] It requires opioid dose reduction or weaning[27], or changing to an alternative opioid preparation (switching).[28]

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Current UK data on opioid misuse

Office for National Statistics Data

The Office for National Statistics (ONS) produces data annually on deaths related to drug poisoning in England and Wales, giving the cause of death, sex, age and substances involved in the death. For example, in the 2021 registrations edition, current tramadol deaths are down from 240 in 2014 to 195, although all opiate deaths are up to 2219 from 1786. Reports from previous years are also available.

The ONS does not distinguish between prescribed, over the counter and illicitly obtained medicines. The drug misuse figures only include drugs controlled under the Misuse of Drugs Act but, as additional drugs are controlled under the Act, the data is backdated. The published data only breaks down poisoning (and not drug misuse) deaths by substance.

C. A structured approach to opioid prescribing

Type of pain and timing of therapy

Opioids are not the first line of therapy. Other alternative drugs and non-drug therapy should be tried before prescribing opioids. There is evidence for effectiveness of opioid therapy for acute pain management. Similarly, opioids have a circumscribed role in the management of cancer pain, particularly towards the end of life.

- In general, poorly defined pain of uncertain aetiology with no abnormal findings on imaging investigations would be less likely to respond to opioid therapy.

- Clearly defined pain associated with identifiable organic disease may respond to opioids but even well-defined syndromes including major joint osteoarthritis demonstrate a disappointing response to opioids when used over a long period of time.

- Paroxysmal pain where the patient experiences episodes of pain with rapid onset and of short-lived duration is difficult to manage with opioid drugs or other medications.

The decision to prescribe opioids for long-term pain should be carefully considered. It is important to consider:

- the importance of shared decision making in relation to opioid treatment: this should include the patient, the prescriber, the patient's GP (if not the prescriber) and other key individuals involved in the patient's care
- when to start opioids in relation to other therapies: non-opioid interventions (pharmacological or non-pharmacological) should be considered before opioid therapy where there is good scientific rationale for these interventions. It will usually be appropriate to continue effective or partially effective interventions in parallel with opioid therapy

the specific problems of using opioids to support discharge from hospital. 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. (Ref https://fpm.ac.uk/sites/fpm/files/documents/2021-03/surgery-and-opioids-2021_4.pdf)

The opioid trial

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. The opioid trial establishes whether the patient achieves any reduction in pain with use of opioids. It is important to remember that short term response to opioid therapy does not predict long term effectiveness, which may be limited by adverse effects or declining efficacy. Achieving optimal doses and managing side effects of opioids is not the purpose of the trial; these can be explored once it has been shown whether opioids are helpful for the patient. Consider an opioid contract and a pain, sleep and function diary.

Starting the trial

The patient and prescriber should agree some readily assessable outcomes that indicate that opioids may play a role in the patient's management. These will usually include reduction in pain intensity and ability to achieve specific functional improvement facilitated by the medication. For patients in whom sleep is significantly impaired by pain, improved sleep would be a reasonable outcome.

Duration of the opioid trial

This will depend on the periodicity of the patient's pain. If the patient has constant pain, the opioid trial may be concluded in one or two weeks. If the patient has intermittent disabling flare ups of pain on a background of more manageable symptoms, the trial should be long enough to observe the effect of opioids on two or three episodes of increased pain.

Choice of opioid formulation and dose

Where possible, the usefulness of opioids should be explored by prescribing a short (1-2 week supply) of immediate release morphine tablets or liquid. The patient may be advised to explore different doses within a specified range e.g., morphine 5-10mg. If a reduction in pain is not achieved following a single dose of immediate relief morphine 20mg, opioids are unlikely to be beneficial in the long term.

Assessing whether the opioid trial is a success

The patient should keep a diary during the opioid trial. This should include a twice-daily report of pain intensity, comment on sleep, note of activity levels and how any of these are changed following a dose of opioid. All doses of opioid should be recorded in the diary with a comment on side effects. If the opioid trial is not successful, the drugs should be tapered and stopped within one week.

If the patient reports no improvement in symptoms following the trial, it is very unlikely that long-term opioid therapy will be helpful.

Documentation

All stages of the opioid trial should be clearly documented and if appropriate, a copy of the agreed aims of therapy and how these may be monitored should be given to the patient. Documentation should also include the agreed starting dose and formulation of drug and details of planned dose escalation. If the opioid trial demonstrates that the medicines are unhelpful, the reasons for this (lack of efficacy/intolerable adverse effects) should also be clearly documented. If the patient reports reduction in pain but at the cost of side effects that preclude achievement of functional goals, it is reasonable to explore different dosing regimens with active management of side effects to see if a useful balance between benefits and harms can be achieved.

If the opioid trial demonstrates some benefit from opioids, further exploration of opioid treatment may be helpful. A successful short-term opioid trial does not predict long-term efficacy.

Long term prescribing

Choice of Drug

- Choice of opioid depends on clinical circumstance, local formularies and guidance and individual knowledge and competence.
- There is little evidence that one opioid is more effective and associated with fewer side effects than others [1].
- Oral morphine should be the drug of first choice.
- There is a theoretical rationale for trying an alternative opioid if the first drug tried is helpful but causes intolerable side effects.
- Pethidine is particularly unsuitable for patients with persistent pain. Its high lipid solubility and rapid onset/offset may predispose patients to problem drug use. Its active metabolite norpethidine can lead to serious central nervous system side effects. It does not produce less smooth muscle spasm than equivalent doses of other opioids and so has no advantage for patients with visceral colic or pain.
- It is helpful to calculate total daily dose of opioid in morphine equivalents, particularly when more than one opioid is used.
- Drugs should be used for their licensed indication only.

Choice of Formulation/Route

- The oral route is the preferred route of administration.
- In most settings an initial opioid trial is probably best achieved using an immediate release opioid formulation for a very short period (between one and two weeks). When choosing a formulation for an individual patient, the temporal characteristics of his/her pain should be considered and matched to the release profile of the opioid chosen.
- 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 throughout the day and night. This should only be considered for patients who have received certain fixed doses of immediate release opioids daily.
- Use of opioid formulations with a rapid onset, such as fentanyl for transmucosal or sublingual administration are inappropriate for the management of persistent pain.
- Injectable opioids should NOT be used in the management of patients with persistent non-cancer pain.

- For a small number of patients, the transdermal route may be a suitable alternative.
- Buprenorphine as a transdermal patch has an advantage of lower potential of misuse. It also has increased safety margin and very low physical dependency making it easier to withdraw.

Agreeing Outcomes

The goals of opioid therapy should be agreed between the prescriber, the patient and their carer(s). If the prescription is initiated in secondary care, the patient's general practitioner should be in agreement, with the prescribing plan. It is usually expected that a reduction in pain of at least 30% should be demonstrable to justify longer term prescribing. Functional goals should also be agreed with the patient.

Arrangements for Review

Where practicable, review of long-term opioid therapy should be carried out by the initial prescriber. Until an agreed long-term regimen has been established, the patient should be reviewed within four weeks of initiation of opioid treatment. The frequency of review once the opioid regimen has been established will depend on the early effectiveness of treatment, the frequency of troublesome side effects, the timing of additional interventions to control pain (e.g., surgery) and the presence of concerns in relation to problematic use of opioids. When a regimen is stable and the patient reports substantial relief of symptoms and where additional concerns do not dictate otherwise, opioid treatment should be reviewed at least six monthly.

Repeat Prescribing

- The ability to create computer-generated prescriptions for Controlled Drugs has made the actual process of prescribing opioids much easier and opioids may be entered into opioids onto repeat prescribing systems. However, this practice is discouraged.
- In general, opioids should not be added to the repeat prescribing system but should be generated as acute prescriptions.
- If an opioid has a demonstrable positive benefit for an individual patient and there is a robust system for monitoring use, then consideration may be given for short-term authorisation of repeat prescriptions.
- The prescriber and patient together should review the continuing benefit of opioid therapy and potential harms at regular intervals (at least twice each year).

Documentation

The plan for long-term prescribing should be clearly documented and if appropriate, a copy of the agreed aims of therapy and how these may be monitored should be given to the patient. Documentation should also include:

- Relevant clinical findings that support the decision to prescribe opioids.
- Agreed outcomes of opioid therapy.
- The choice of drug, formulation, dose and duration of treatment.

- Consider specialist involvement if higher doses are being considered.
- The circumstances under which opioid therapy should be discontinued.
- Arrangements for review.
- The information given to patients.

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Informed decision making on prescription

What to discuss with the patient when considering opioid treatment

- Explain that the evidence for the use of opioids as analgesics is best when used in the management of acute pain, over a period of hours from onset but tapering dose over days to a few weeks.
- Explain that opioids are poorly effective for long-term pain. For a small proportion of patients, opioids may be successfully used as part of a broader plan including non-medication treatments and self-management.
- Discuss the degree of pain relief that might be expected and understand the aim is not complete pain relief but rather reducing pain sufficiently to engage in self-management.
- Agree specific functional goals that might be achieved.
- Discuss the potential harms of opioid treatment including: -
    - Sedation
    - Nausea
    - Constipation
    - Effects on hormones
    - Effects on the immune system
    - Potential for the drugs to worsen pain
    - Potential for problematic drug use and addiction
- Discuss opioids and impairment of driving skills.
- Discuss the opioid trial.
- Discuss the circumstances in which opioid therapy will be stopped.
- Discuss arrangements for review.

Documentation

Clinical records should include:

- Relevant clinical findings that support the decision to prescribe opioids.
- Agreed outcomes of opioid therapy.
- The choice of drug, formulation, dose and duration of treatment.
- The circumstances under which opioid therapy should be discontinued.
- Arrangements for follow up.
- The information given to patients.

Formal patient contracts have no legal validity. A written, structured agreement detailing agreement on outcomes of treatment, frequency of review, dose prescribed and circumstances in which opioid treatment may be stopped should be part of

routine practice and can act as a helpful starting point when discussing progress of therapy (e.g., an opioid treatment agreement).

Responsibility for Prescribing

Where practicable, the patient should receive prescriptions from a single prescriber and the drugs dispensed from a specified pharmacist. Documentation should be clear and accurate to support consistency of safe care if the patient needs a prescription from other than the usual prescriber.

Arrangement for Review

Where practicable, review of long-term opioid therapy should be carried out by the initial prescriber until an agreed long-term regimen has been established the patient should be reviewed within four weeks of initiation of opioid treatment. The frequency of review once the opioid regimen has been established will depend on the early effectiveness of treatment, the frequency of troublesome side effects, the timing of additional interventions to control pain (e.g., surgery) and the presence of concerns in relation to problematic use of opioids. When a regimen is stable and the patient reports substantial relief of symptoms and where additional concerns do not dictate otherwise, opioid treatment should be reviewed at least six monthly

Dose equivalents and changing opioids

- Switching from one opioid to another should only be recommended or supervised by a healthcare practitioner with adequate competence and sufficient experience. If uncertain, ask for advice from a more experienced practitioner.
- Opioid rotation or switching may be considered if a patient obtains pain relief with one opioid and is suffering severe adverse effects.
- Opioid rotation is not recommended if a patient has responded to one opioid.
- When converting from one opioid to another, the initial dose depends on the relative potency of the two drugs and route of administration.
- An individualised approach is necessary.
- Conversion factors are an approximate guide only because comprehensive data are lacking and there is significant inter-individual variation.
- In most cases, when switching between different opioids, the calculated dose-equivalent must be reduced to ensure safety. The starting point for dose reduction from the calculated equi-analgesic dose is around 25-50%.
- A dose reduction of at least 50% is recommended when switching at high doses (e.g., oral morphine or equivalent doses of 500mg/24 hours or more), in elderly or frail patients, or because of intolerable undesirable effects.
- The half-life and time to onset of action of the two drugs needs to be considered when converting so that the patient does not experience breakthrough pain or receive too much opioid during the conversion period.
- Once the conversion has occurred, the dose of new opioid should be titrated carefully according to individual response and the patient monitored closely for side effects and efficacy, especially when switching at high doses.
- Withdrawal symptoms (e.g., sweating, yawning and abdominal cramps, restlessness, anxiety) occur if an opioid is stopped/dose reduced abruptly.

Approximate equi-analgesic potencies of opioids for oral administration

(Reviewed March 2023 to reflect current BNF figures)

	Potency	Equivalent dose to 10mg oral morphine
Codeine phosphate	0.1	100mg
Dihydrocodeine	0.1	100mg
Hydromorphone	5	2mg
Methadone	*	*
Morphine	1	10mg
Oxycodone	1.5	6.6mg
Tapentadol	0.4	25mg
Tramadol	0.1	100mg

** The relative potency of **methadone** depends on the starting dose and the duration of administration. Conversions to and from methadone should always be undertaken with specialist advice*

Transdermal Opioids

(Reviewed March 2023 to reflect current BNF figures)

A. Buprenorphine

Transdermal buprenorphine changed at weekly intervals

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

Transdermal buprenorphine changed every three or four days (twice weekly)

	35 microgram/hr	52 microgram/hr	70 microgram/hr
Morphine sulphate (mg/day)	84mg	126mg	168mg

B. Fentanyl

Fentanyl patch strength (microgram/hr)	Oral morphine (mg/day)
12	30
25	60
50	120
75	180
100	240

Further Reading

- British National Formulary.
- Wilcock A, Howard P and S Charlesworth. **PCF 8: Palliative Care Formulary**. 2022.
- Webster LR, Fine PG. **Review and critique of opioid rotation practices and associated risks of toxicity.** Pain Medicine 2012; 13: 562-70.
- Prescribing in palliative care | Medicines guidance | BNF | NICE

Tapering and stopping

It is important to taper or stop the opioid regimen if:

- The medication is not providing useful pain relief. Increasing the opioid dose is unlikely to yield further benefits and potentially 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. Consider liaising with other professionals.

Preparation for dose reduction includes:

- Explanation of the rationale for stopping opioids including the potential benefits of opioid reduction (avoidance of long-term harms and improvement in ability to engage in self-management strategies).
- Agreeing outcomes of opioid tapering.
- Deciding which patients may need admission for opioid taper/cessation informed by existing opioid dose.
- Physical co-morbidities.
- Mental health co-morbidities including significant emotional trauma.
- Monitoring during taper of pain.
- Symptoms and signs of opioid withdrawal.
- Choice of opioid reduction scheme.
- Incremental taper of existing drug.
- Conversion to methadone or buprenorphine.
- Defining the role of drug and alcohol services to support dose reduction.
- Close collaboration between the patient, his or her carers and all members of the patient's health care team.
- Arrangements for follow-up including agreed prescribing responsibilities.

The dose of drug can be tapered by 10% weekly or every two weeks.

Stopping opioids in primary care

The decision to taper/stop an established opioid regimen needs to be discussed carefully with the patient including:

- explanation of the rationale for stopping opioids including the potential benefits of opioid reduction (avoidance of long-term harms and improvement in ability to engage in self-management strategies)
- agreeing outcomes of opioid tapering
- arrangements for monitoring and support during opioid taper
- documented agreement of tapering schedule

Stopping opioids in collaboration with specialist services

Patients who are failing to derive benefit from large doses of opioids may need support from specialist services in order to reduce medication.

This must include detailed exploration of emotional and mental health history (including addiction). Opioid tapering/cessation when patients are taking high doses is more likely to succeed if patient's emotional and mental health needs are identified and an appropriate plan for support established.

Points to discuss with patients when de-prescribing:

- Remain empathic and focus the discussion on medicines only.
- Take a full medicines history and ask the patient how well the medicines are working and reflect that the patient is describing severe pain despite medicines.

- Share that the experience of many patients is that taking medicines results in no observable benefit for pain.
- Explain that we have much better ways of working out how helpful medicines really are, and we know that a lot of things that we thought were helpful in the past have proved to be disappointing and we should take responsibility for contributing to where we are now. Medicines for pain can be associated with significant harm.
- It matters a lot that the patient has confidence that all their medicines are working well.
- Usually stopping medicines makes no difference to the pain but can make people feel better (being more awake and not sleepy, more energy)
- If a tapering trial doesn't work, we can think again.

D. Opioids and Addiction

Terminology

> "When I use a word," Humpty Dumpty said, in rather a scornful tone, "it means just what I choose it to mean—neither more nor less"
>
> Alice Through the Looking Glass, Lewis Caroll 1871

There are a number of terms that are used in describing the effects, both physical and psychological, associated with opioids (and also other substances). These terms are commonly used imprecisely, often conveying incorrect or confusing messages; both between professionals and between patients and healthcare staff.

Various definitions have been suggested[1,2,3,4], but there is no universally accepted approach, and definitions are often defined by the user group for which they are developed. For the purpose of this resource, the following terms are intended to have reasonably clear and tightly defined meanings, and some terms are best avoided.

Primary Four terms:

Tolerance – this is a three-sided term.

[1] The reduction of effect that a substance has over time. This may refer to either the beneficial effect, or the side effects.

(It is possible to maintain a beneficial effect and become tolerant of the side effects).

[2] The second is often, but not uniformly, some resumption of beneficial (and/or side effects) by increasing the dose.

[3] That the doses used in a 'tolerant' individual are likely to be deleterious, or even fatal, to a substance naive individual.

When describing treatment changes in a 'tolerant' individual, it is important to clarify the change in dose, against the current dose and indicate the benefits anticipated.

Withdrawal

Withdrawal effects are the negative effects seen when the current dose of a substance has been reduced or stopped, especially if done rapidly.

These effects are commonly both physiological and psychological. They have the potential to cause harm, and must be recognised, counselled and managed appropriately.

Sudden cessation or dose reduction of opioids may cause rebound pain, which usually settles, but may be difficult to differentiate from the unmasking of pain due to a beneficial effect; and more general systemic effects such as abdominal pain/colic (which, again, might be a facet of the pain problem), diarrhoea, sweating, anxiety and acute mood changes.

Escalation

This is a two faceted term, which encompasses:

[1] The rate at which tolerance to benefit has developed.

[2] The rate at which the prescriber has increased the medication; obtaining the intended benefit, or a degree of it, again, and for it to then wane again.

Substance Misuse

There remains the difficulty of describing the use of substance without or beyond clinical indication/prescription instructions (usually in terms of dose). The description is one of judgment[5], but is partially descriptive. It is often a 'built-in' part of the term 'Addiction' – see below, and other terms.

Associated Terms

Dependence: This is a mixed term

[1] **Psychological Dependence** – This is an emotional issue. A 'longing' for the substance and its psychological effects (a sense of well-being), but not necessarily associated with physical withdrawal symptoms. It has significant psychosocial aspects.

May be confused with '**craving**' – which is a desire for the substance driven by physical withdrawal.

[2] Physical Dependence – This encompasses the concepts of; Tolerance, Withdrawal and Dose Escalation which usually provide better descriptions of the issues; with or without the additional term Substance Misuse which indicates a degree of inappropriate use.

Other terms:

Addiction

This is difficult term, frequently used in a pejorative sense, with complex psychosocial implications.

It is commonly used as a broad term to encompass components of the terms Substance Misuse, Tolerance, Withdrawal, and Psychological Dependence; but is commonly used to describe very different aspects of its component parts, and without qualification, is generally best avoided.

Pseudo-addiction

This describes the use of, or seeking for, a medicine at a dose/frequency beyond the prescription, which may indicate an inadequate initial dose or the development of tolerance.

The embedded use of 'addiction' within the term makes it an often misunderstood term, and its clinical utility is often better served with consideration to the primary terms above.

Opioid use disorder

Opioid use disorder (OUD) is defined as the chronic use of opioids that causes clinically significant distress or impairment. Symptoms of this disease include an overpowering desire to use opioids, increased opioid tolerance, and withdrawal syndrome when opioids are discontinued. OUD can range from dependence on opioids to addiction.

References

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2. https://www.cdc.gov/drugoverdose/opioids/terms.html

3. Joint Meeting of the Drug Safety and Risk Management (DSaRM) Advisory Committee

and Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC). https://www.fda.gov/media/127780/download (accessed February 2021)

4. Acute Pain Management Scientific evidence ANZCAFPM 4th ed(2015) p569. https://www.anzca.edu.au/getattachment/4c3b03b7-52bf-4c10-9115-83d827c0fc38/Acute-Pain-Management-Scientific-Evidence.aspx (accessed February 2021)

5. Access to treatment with controlled medicines rationale and recommendations for neutral, precise, and respectful language. W. Scholten et al. Public Health 153 (2017) 147-153.

Diagnosis, identification and risk populations

Diagnosis: Opioid Dependence

There are two principle diagnostic classification systems:

- ICD-11 (International Classification of Disease – eleventh revision produced by the World Health Organisation)
- DSM-V-TR (Diagnostic Statistical Manual – fifth edition, text revision produced by the American Psychiatric Association).

There are similarities between the two but for the purposes of this document we have used ICD-11, which defines opioid dependence (code 6C43) as:

A disorder of regulation of opioid use arising from repeated or continuous use of opioids. The characteristic feature is a strong internal drive to use opioids, which is manifested by impaired ability to control use, increasing priority given to use over other activities and persistence of use despite harm or negative consequences. These experiences are often accompanied by a subjective sensation of urge or craving to use opioids. Physiological features of dependence may also be present, including tolerance to the effects of opioids, withdrawal symptoms following cessation or reduction in use of opioids, or repeated use of opioids or pharmacologically similar substances to prevent or alleviate withdrawal symptoms. The features of dependence are usually evident over a period of at least 12 months, but the diagnosis may be made if opioid use is continuous (daily or almost daily) for at least 3 months.

ICD-11 states that a pattern of recurrent episodic or continuous use of opioids with evidence of impaired regulation of opioid use is manifested by two or more of the following:

- Impaired control over opioid use (i.e., onset, frequency, intensity, duration, termination, context).
- Increasing precedence of opioid use over other aspects of life, including maintenance of health, and daily activities and responsibilities, such that opioid use continues or escalates despite the occurrence of harm or negative consequences (e.g., repeated relationship disruption, occupational or scholastic consequences, negative impact on health).
- Physiological features indicative of neuroadaptation to the substance, including:

  1) tolerance to the effects of opioids or a need to use increasing amounts of opioids to achieve the same effect.

  2) withdrawal symptoms following cessation or reduction in use of opioids (see Opioid Withdrawal), or

3) repeated use of opioids or pharmacologically similar substances to prevent or alleviate withdrawal symptoms.

The features of dependence are usually evident over a period of at least 12 months, but the diagnosis may be made if use is continuous (daily or almost daily) for at least 3 months.

ICD-11 goes on to state additional clinical features that may accompany the above essential features of opioid dependence:

- A subjective sensation of urge or craving to use opioids often, but not always, accompanies the essential features of opioid dependence.
- When present as an aspect of opioid dependence, withdrawal symptoms must be consistent with the known withdrawal state for opioids.
- Tolerance varies as a function of individual factors (e.g., substance use history, genetics) and should be differentiated from initial levels of response during intoxication, which also exhibit significant individual variability. Laboratory testing that reveals high levels of the substance in bodily fluids with no evidence of significant symptoms of intoxication may be suggestive of tolerance. Tolerance to the effects to substances as indicated by different psychophysiological responses can develop at varying rates (e.g., tolerance to respiratory depression caused by opioid intoxication may develop prior to tolerance to the sedating effects of the drug). With abstinence, tolerance effects diminish over time.
- Individuals with certain co-morbid medical conditions (e.g., chronic liver disease) typically have reduced tolerances to substances.
- Physical or mental health consequences (beyond the essential features of substance dependence) typically occur in persons with substance dependence but are not required for the diagnosis. Similarly, functional impairment in one or several domains of life (e.g., work, domestic responsibilities, child-rearing) is commonly seen in persons with substance dependence, but is not required in order to assign the diagnosis.
- Individuals with substance dependence have elevated rates of many other mental disorders, including conduct-dissocial disorder, attention deficit hyperactivity disorder, impulse control disorders, post-traumatic stress disorder, social anxiety disorder, generalized anxiety disorder, mood disorders, psychotic disorders, and personality disorder with prominent dissocial features, as well as subthreshold symptoms. The specific pattern of co-occurrence depends on the specific substance involved, and reflects common risk factors and common causal pathways. These are distinguished from substance-induced mental disorders, in which the symptoms are a result of the direct physiological effects of the substance on the central nervous system.
- A pattern of substance use that includes frequent or high dose administration occurs more often among certain subgroups (e.g., adolescents). In these cases, peer group dynamics may contribute to the maintenance of substance use. Regardless of the social contributions to the behaviour, a pattern of substance use that is consistent with subgroup norms should not be

considered as presumptive evidence of substance dependence unless all diagnostic requirements for the disorder are met.

Indicators

Indicators that suggest the possibility of dependence should be explored in those on a long-term opioid prescription:

- Long-term prescribing of opioids for non-cancer conditions.
- Current or past psychiatric illness or profound emotional trauma.
- Reports of concern by family members or carers about opioid use.
- Concerns expressed by a pharmacist or other healthcare professionals about long-term opioid use.
- Insistence that only opioid treatment will alleviate pain and refusal to explore other avenues of treatment.
- Refusal to attend or failure to attend appointments to review opioid prescription.
- Resisting referral for specialist addiction assessment.
- The repeated seeking of prescriptions for opioids with no review by a clinician.
- Repeatedly losing medications or prescriptions.
- Taking doses larger than those prescribed or increasing dosage without consulting the clinician; often coupled with seeking early replacement prescriptions. Associated with continued requests for dose escalations.
- Seeking opioids from different doctors and other prescribers. This can take place within GP practices, often identifying locum doctors or doctors unfamiliar with their case. This may be associated with attempting unscheduled visits.
- Obtaining medication from multiple different providers, NHS and private GPs, repeatedly and rapidly deregistering and registering with GPs, seeking treatment for the same condition from both specialists and GP; or seeking treatment from multiple specialists. This may be coupled with a refusal to agree to writing to the main primary care provider.
- Obtaining medications from the internet or from family members or friends.
- Resisting referrals to acute specialists about complex physical conditions or failing to attend specialist appointments.
- Appearing sedated in clinic appointments.
- Misusing alcohol or using illicit or over-the counter, internet or other prescribed drugs or a past history of alcohol or other drug dependence.
- Deteriorating social functioning including at work and at home.
- Resisting or refusing drug screening.
- Signs or symptoms of injecting opioids or snorting oral formulations.

Assessment

A comprehensive history should be taken from any patient in whom opioid dependence is suspected. It is important to understand the medical indication for which opioids were prescribed initially. As far as possible, confrontation should be avoided, as should judgement about the motivations of the patient. Important points that should be clarified include:

- Medical indication for opioid.
- Full list of all medication, routes of administration and how long prescribed.
- What other medication with addictive potential is prescribed to the patient including benzodiazepines and gabapentin/pregabalin.
- What the patient perceives as positive and negative attributes of prescribed opioids.
- Current alcohol and illicit drug use.
- Current physical health.
- Current psychological health.
- Current tobacco consumption.
- Previous history of drug and alcohol dependence and treatment.
- Physical health history and any interventions.
- History of psychiatric illness.
- Social functioning and employment status.
- Family and carer support.
- Appropriate physical examination.

Investigations

- Urine or other drug screening for prescribed opioid and commonly abused illicit drugs.
- Consider use of the Objective Opioid Withdrawal Scale (OOWS) and the Subjective Opioid Withdrawal Scale (SOWS) where relevant.
- Relevant blood tests possibly including full blood count, liver function tests, hepatitis B & C, and HIV.
- Any other relevant investigations regarding condition for which opioids were initially prescribed.

Other sources of information should be sought including:

- Discuss with other clinicians currently (or previously where relevant) involved in patients care.
- Clinic letters regarding prescription or underlying diagnosis.
- Information from family or carers.

Risk Populations

Broadly speaking three groups are at increased risk of dependence on prescribed opioids. These groups are not mutually exclusive. They are:

- Patients who find the mood-elevating effects of opioids beneficial but have underlying psychological distress or diagnosed psychiatric illness. Any patient on long-term opioids should be reviewed regarding their psychological health. This is especially true of those with a current or past history of psychiatric illness. In these cases, they warrant treatment for opioid dependence, but of equal importance is treatment of the underlying psychiatric condition.
- Those without psychological distress who find themselves dependent but are very willing to engage in reduction programs and further addiction treatment.
- Those with a history of alcohol or drug dependence who may or may not be willing to engage in further assessment or treatment.

NB: Long-term epidemiological data show that patients with co-morbid mental health diagnoses or a history of addiction are more likely to receive opioids for pain and are more likely to be prescribed high doses, multiple opioids and other psychoactive drugs (e.g., benzodiazepines). This phenomenon has been described as 'adverse selection'.

Further Reading

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- Morasco BJ, Duckart JP, Carr TP, et al. **Clinical characteristics of veterans prescribed high doses of opioid medications for chronic non-cancer pain**. Pain 2010;151: 625-32.
- Wilsey BL, Fishman SM, Tsodikov A, et al. **Psychological Comorbidities Predicting Prescription Opioid Abuse among Patients in Chronic Pain Presenting to the Emergency Department**. Pain Medicine 2008; 9: 1107-1117.

Treatment and prevention of dependence

Treatment

Once a diagnosis of dependence has been made a treatment plan should be developed. The decision on which treatment course is chosen should be a collaborative one between the patient and doctor.
Depending on the complexity of the case and the skills and training of the prescriber this may be all under one doctor or it may involve a full network of clinicians, including GPs, addiction specialists, pain specialists, psychiatric specialists and acute services, or some point in between. Clear communication between all healthcare specialists involved in the patient's care is vital as is clear documentation.
Although many patients will recognise that they have an issue with prescription opioid dependence and will be willing to work in collaboration with their doctor to develop a treatment plan, some may have difficulty recognising their symptoms and may perceive a lower need to have treatment [1].

Usually, one doctor should take over all prescribing of opioids and other potentially addictive drugs. If there is disagreement between the doctor and patient it may be beneficial if a different doctor who has not previously treated the patient takes over prescribing so that a new relationship and set of boundaries can be developed. Information about the acute and chronic risks of opioids should be given to the patient.

Any underlying physical or psychiatric condition should be identified, and appropriate treatment plans or referral made.

Principles of Opioid Substitution Treatment (OST)

If a diagnosis of dependence is made a decision needs to be reached regarding whether to maintain a patient on opioids or detoxify them. This decision involves multiple factors and should be made, where possible, in collaboration with the patient. The decision to maintain a patient versus detoxify can be influenced by factors that include patient choice, patient's motivation, past drug and alcohol dependence, psychiatric and physical history, length of time on opioids, quality of life and social support. It may involve a meeting of multiple healthcare professionals involved in the case. The patient should be provided with as much information as possible so that they can make an informed choice. It may be important to record that the patient has the capacity (within the meaning of the Mental Capacity Act 2005) to make a decision.

Maintenance

If a decision is made to maintain a patient they should generally be transferred to a longer-acting, oral opioid. These include methadone and buprenorphine. Methadone and buprenorphine should be used cautiously in those with a history of respiratory difficulties, significant liver dysfunction and obstructive bowel conditions. Higher dose

methadone is associated with prolonged QT syndrome [2].
Conversion tables should be treated with great caution. Conversion should only be undertaken with the support of a clinician experienced in opioid conversion and the use of methadone or buprenorphine. Advice should be sought from the local drug treatment provider.
It is advisable to consider a period of supervised consumption; however, a patient should not be converted to a fully supervised dose immediately as it places them at risk of overdose if they have been non-compliant.
The same doctor should regularly review the patient; the full range of treatment needs should be reviewed.
Consideration should be given to involving the patient in a wider addiction treatment programme. This may include, as an individual or in a group, motivational enhancement therapy, relapse prevention and/or mutual aid .
The patient should be regularly tested for the prescribed opioid and commonly used illicit substances. They should regularly be asked about alcohol and other drug use.

Detoxification

Detoxification will often be the preferred option. Usually this should take place on an outpatient basis (although residential treatment, either in an acute hospital or detoxification unit, is available throughout the UK). The options involve either conversion to a long-acting opioid as above or a gradual reduction in the dose of the currently prescribed opioid. This reduction should take place in collaboration with the patient.
If a patient chooses to detoxify, they should be warned of the risk of overdose if they relapse to opioid use.
In certain patients who have detoxified and do not need on-going opioids consideration should be given to prescribing naltrexone.

Naloxone

In those patients considered dependent and at risk of overdose, the provision of take-home naloxone with associated overdose training should be considered for both the patient and their family and carers.

In elderly patients with pre-existing cardiovascular disease or in those receiving potentially cardiotoxic drugs, Naloxone 400 micrograms/ml should be used with caution since serious adverse cardiovascular effects such as ventricular tachycardia and fibrillation have occurred in postoperative patients following administration of naloxone hydrochloride.

Role of specialist drug and alcohol dependence treatment services

Every local area in the UK has a specialist addiction service; in England these are commissioned by local authorities, in Scotland and Wales by the NHS and in Northern Ireland by the Public Health Agency. These services should provide advice,

assessment and support to other parties involved in the care of this patient group and, where appropriate, take over prescribing of opioids either looking towards detoxification or maintenance. In complicated patients it may be appropriate for these services to become the lead agency. Depending on the area they may be able to provide support regarding co-occurring mental health issues; however, in England psychiatric services are separately commissioned and provided.

Sources of Support

More information in Drug Misuse and Dependence: UK Guidelines on Clinical Management.

NHS Choices maintains a searchable directory of local drug and alcohol treatment services.

Naloxone dosage for opioid reversal: current evidence and clinical implications - PMC (nih.gov)

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Prevention

- Assess patients comprehensively and appropriately prior to prescribing opioids.
- Prescribe within your expertise.
- Explore and treat any underlying psychological and social distress in line with appropriate NICE guidance.
- Treat underlying physical conditions causing pain in line with appropriate NICE guidance.
- Always agree clinical outcomes with a patient and set a time frame for clinical review.
- Always review the continued need for opioids on discharge from hospital. Have a clear plan regarding duration of treatment and communicate this clearly to primary care.
- If the reason for prescription of opioids or intended prescription are uncertain, discuss and consult with the initiating prescriber/specialist.
- Ensure effective communication between all prescribers involved in a patient's care – refusal to allow healthcare professionals to communicate should in general lead to a refusal to prescribe.
- Temporary registered patients should be given at most three days' prescription of medication to allow previous notes to be obtained.
- If in doubt regarding treatment options seek a specialist opinion for the relevant underlying condition.

Patients with substance misuse: general considerations

Considerations when prescribing for patients with a current or past history of substance misuse/in recovery from addiction

Key Points

- Poor understanding of addiction and stigma amongst healthcare professionals can be a barrier to optimal pain management.
- Concerns expressed by healthcare professionals include

– Addiction relapse
– Dangers of drug overdose when there is uncertainty regarding patients' illicit drug doses
– Uncertainty in identifying drug-seeking behaviours in the substance-misusing patient.

- The addicted patient can benefit from opioid therapy for moderate/severe acute pain such as trauma, surgery etc.
- Pain and opioid addiction have neurobiological commonality.

- A patient receiving maintenance opioid therapy with methadone or buprenorphine will not derive analgesia from their maintenance dose [1].
- Patients on maintenance opioid regimens will be tolerant to the analgesic effects of opioids and may have a degree of increased pain sensitivity.
- Detailed assessment corroborated by other professionals involved in the patient's care is mandatory.
- Comprehensive communication within the health (and social) care team supports safe management.
- See also sections on diagnosis, identification and risk populations and treatment and prevention.

Pain Experience in the Opioid Addicted Patient: General Considerations

- Any drug misuse may worsen the patient's experience of pain and patients at a higher risk of opioid misuse may experience more subjective pain [2].
- The patient may have previously self-medicated to remove pain and psychological distress.
- Although patients may have poor acceptance of non-pharmacological interventions for pain control, there is some evidence that psychological therapies can aid in reducing both pain interference and opioid misuse in those who are using opioids in a harmful manner [3,4].
- Frequent episodes of intoxication/withdrawal may alter the intensity of the pain experience.
- Addiction is associated with sleep disturbance which may exacerbate chronic pain [5].
- Depression and anxiety commonly co-occur with addiction [6]. These are important influences on the pain experience and need to be identified and managed accordingly.
- Patients with addiction are more likely to suffer from accidental/non-accidental injury and medical complications related to drug use. I.e., are at high risk from physical problems that require analgesia.

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Substance misuse: acute pain management

The aim of the analgesic management of these patients is to:

- Provide safe and effective analgesia.
- Prevent withdrawal.
- Liaise with the community drugs team throughout the duration of their hospital stay and early discharge planning.
- Offer drug management referral if needed.

Key principles:

Treat all patients with empathy and reassure them that their pain will be managed. Illicit opioid users are often scared of withdrawing and have had previous bad experiences with health care providers.

Detoxification is not appropriate in the peri-operative period.

Patients on long term opioids are at risk of opioid tolerance and opioid induced hyperalgesia.

Inadequate acute pain management will not only hamper recovery but increases the risk of relapse of illicit drug use.

Sedation/overdose when tolerance to opioids is uncertain especially when patients are using additional centrally active medications. They are still at risk of opioid induced side effects including ventilatory impairment (OIVI) so careful monitoring is needed.

Diversion and misuse of drugs prescribed for acute pain is a risk but should not prevent adequate analgesia.

Early and continued liaison with their community drugs team (CDT), community pharmacist and general practitioner is important.

Multimodal analgesia is key to their pain management.

Regional analgesia can be very useful if appropriate, it can avoid or reduce opioid need.

Have a clear plan for dose tapering as acute pain subsides.

Patients on Opioid Substitution Therapy (OST)

Confirm the dose with CDT / community pharmacist.

OST should be continued if reliably taken in the last three days and there is no sign of opioid overdose.

Methadone

-If struggling with pain split the dose into a bd/tds dose

- Multimodal analgesia titrated to effective analgesia

Buprenorphine sublingually

-If struggling with pain split the dose into a bd/tds dose

-Multimodal analgesia titrated to effective analgesia

SC buprenorphine

-This can be given weekly or monthly as a depot

-Acute pain management maybe problematic

-Multimodal analgesia with regional anaesthesia techniques where appropriate

-If listed for elective surgery careful planning is needed in liaison with the patients CDT. This may include the conversion of the OST to s/l daily buprenorphine or oral methadone until the acute pain has settled

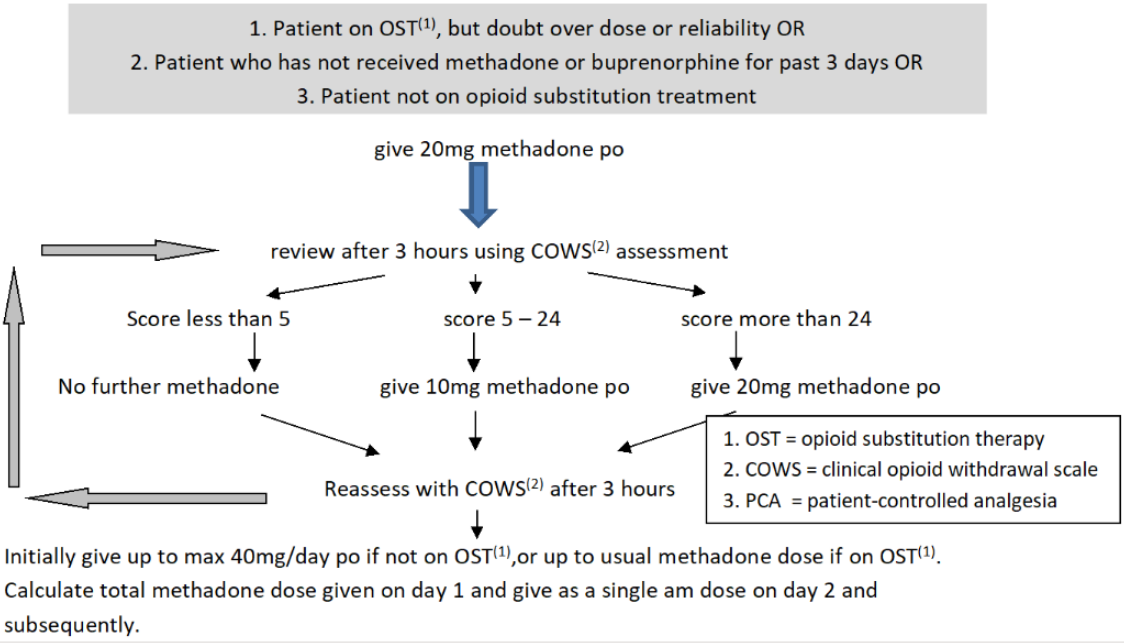
Patients using illicit opioids not on OST

Quality of illicit opioids is variable.

Score opioid withdrawal using Clinical Opioid Withdrawal Score (COWS)

COWS Score for Opiate Withdrawal (mdcalc.com)

Dose OST as per the COWS score- one example of how to do this is from Oxford University Hospitals (Dr Jane Quinlan)



OST prescriptions on discharge have to be the responsibility of the patients local CDT

Substance misuse: chronic pain management

General considerations when managing chronic pain in the opioid addicted patient

- Pain management is underpinned by good communication with the patient and reassurance that pain will be managed optimally
- Medications should be part of a wider plan to support self-management
- Mental health diagnoses and emotional difficulties need to be identified and managed
- Physical rehabilitation, exercise and psychological treatments are essential to support chronic pain management
- Close collaboration with drug services and the patient's GP is mandatory (including confirmation of substance misuse)

Long-term opioid prescribing in the opioid addicted patient: important considerations

- Patient selection
    - Patients with addiction are more likely to be prescribed opioids than non-addicted patients
    - Addiction is a risk factor for prescription opioid misuse/problematic use
- Untreated addiction is a barrier to chronic pain management
- Opioids prescribed for pain may be in whole or in part acting as maintenance treatment for opioid addiction
- Opioids may be used by a patient to attenuate unpleasant thoughts and feelings
- Opioids are poorly effective in chronic pain
- Close collaboration between primary care, secondary care and with drug addiction and recovery services is mandatory
- The risks of misuse and diversion should be assessed and monitored
- A structured approach to care is important including clear agreement regarding dose, short duration of prescriptions and frequent follow up

Chronic pain management in the patient receiving opioid substitution therapy:

- Medications should be part of a wider plan to support self-management
- Mental health diagnoses and emotional difficulties need to be identified and managed
- Physical rehabilitation, exercise and psychological treatments are essential to support chronic pain management
- Close collaboration with drug services and the patient's GP is mandatory
- Regimens should avoid prescription of multiple opioids

For patients on methadone

- Split dose and give 12 hourly

For patients on Buprenorphine

- Split dose and give 8-12 hourly

Chronic pain management for patients in recovery from addiction:

- Risk of relapse may occur both with use of opioids **AND** under-treatment of pain
- Use non-opioid interventions where possible
- Careful explanation of the risks and benefits of the proposed treatment plan should be discussed with the patient
- Anxiety should be assessed and managed, if necessary, with medication
- Patients may have strongly held beliefs regarding opioid therapy, and these should be respected

Opioid prescribing for patients in recovery from addiction:

- Agree the treatment plan with the patient and other healthcare providers
- Agree the outcomes of treatment
- Consider a short trial of opioid e.g., two weeks
- Assess risk to determine frequency of review
- For long-term prescribing use sustained release preparations e.g., MXL 30 mg daily
- Consider early involvement of specialist services where opioid analgesia is considered
- If opioids do not work **aim for tapering and stopping**

Pain emerging when methadone for OST is tapered

Particular challenges arise when patients treated with methadone for addiction experience emerging pain on dose taper. Methadone is a recognised drug treatment for pain and longer-term analgesia may be achieved by splitting the methadone dose and administering 12 hourly. If the 12 hourly methadone regimen appears to be effective as part of a broader pain management plan, there may be justification for continuing the regimen. It is important that individual management plans are generated with agreement from all local stakeholders.

In general, a pragmatic solution may be that for patients who meet the following criteria:

- The pain is related to obvious organic disease
- The symptoms have previously been masked by heroin use or methadone maintenance,
- The pain emerges on methadone taper
- The patient is compliant with treatment plans (not using on top etc)
- The patient has been assessed by a pain specialist with special interest in opioids and addiction

- The patient is deemed safe for opioid therapy and
- Other evidence based interventions are not appropriate then

The patient may be maintained on methadone split into two daily doses prescribed for convenience by their GP but with a firm guarantee from both pain and substance misuse services that if the GP has concerns, he/she has rapid access to support from pain and substance misuse services. This has to be agreed case by case within a MDT setting, although the MDT decision may be virtual. These very specific circumstances should consider the prescribing experience of local primary care teams and cases should be managed only by clinicians familiar with the pharmacology and clinical use of methadone.

E. Information for patients

About pain for patients

Most of us have experience of pain including headaches, pain from small injuries and muscle pain, for example following exercise. These pains do not last long and often do not need treatment. All pain we feel is affected by how we are feeling, our past experiences of pain and any worries we have about the cause of the pain. If we are worried and upset about how pain may affect us in the future, our pain will feel worse. Unpleasant thoughts, feelings and memories (even if these are not to do with pain) can affect how we feel pain. Anxiety, depression, Post-Traumatic Stress Disorder, previous emotional upsets or other mental health problems can worsen our experience of pain and make it more difficult to treat.

Types of pain

Pain is usually described as acute (short term) or chronic (long term or persistent, which is usually more than three months).

- **Acute pain (Short term pain)** is usually related to an obvious injury such as tooth infection, broken bone or operation. It can be severe but usually gets better quite quickly.

Chronic pain sometimes begins with an injury, but the pain does not get better as expected. Often it is not clear how a chronic pain has started. Chronic pain is usually not a sign of on-going injury or damage but may be to do with changes in the nervous system over time over time that make pain signals independently cause pain. It can cause low mood, irritability, poor sleep and reduced ability to move around. Common types of chronic pain include:

  - low back pain,
  - pain related to arthritis
  - pain related to injury to a nerve or other part of the nervous system (neuropathic pain).

Both types of pain can range from mild or severe. **Cancer pain** is usually described separately and may be short or long lasting. The pain can be caused by the cancer itself or the cancer treatment. People with cancer may experience short or long term/persistent pain unrelated to their cancer.

Neuropathic pain is a type of chronic pain associated with injury to nerves or the nervous system. Types of neuropathic pain include:

sciatica following disc prolapse, nerve injury following spinal surgery, pain after infection such as shingles or HIV/AIDS, pain associated with diabetes, pain after amputation (phantom limb pain or stump pain) and pain associated with multiple sclerosis or stroke.

Treatments for different types of pain

(You may have more than one type of pain)

- **Acute pain (short term pain)**: Treatments for acute pain usually only need to be given for a short time while healing of the injury begins. Acute pain is often easy to treat with a range of medicines and other treatments depending on how severe the pain is. Opioid medicines are useful for treating acute pain and usually only need to be given for a few days. The dose of opioid should be reduced as healing occurs.
- **Chronic pain** is difficult to treat with most types of treatment helping less than a third of patients. Most treatments aim to help you self-manage your pain and improve what you can do. Different treatments work for different people. Medicines generally and opioids in particular are often not very effective for chronic pain. Other non-medicine treatments may be used such as:
    - electrical stimulating techniques (TENS machine),
    - acupuncture,
    - advice about activity and increasing physical fitness,
    - psychological treatments such as Cognitive Behaviour Therapy and meditation techniques such as mindfulness.

Helping you understand about chronic pain is important and in particular helping you understand that physical activity does not usually cause further injury and is therefore safe. It is important that you understand that treatments tend not to be very effective and that the aim is to support you in functioning as well as possible.

- **Neuropathic pain** is usually severe and unpleasant. Medicines may be used to treat neuropathic pain but are usually not very effective and work for only a small proportion of people. You may not benefit from the first drug tried so you may need to try more than one drug to try and improve symptoms.
- **Cancer pain** is usually caused by an obvious source of tissue damage (tissues include ligaments, muscles and tendons) and may be acute or chronic. Neuropathic pain can occur with cancer diagnoses and treatments (such as radiotherapy). Because cancer pain treatment, particularly at the end of life, is often for a short duration, it is usually more successful than chronic pain treatment. People who recover from cancer or who survive a long time with cancer may have pain that is more difficult to treat.

Thinking about opioid treatment for pain

Pain is complicated and effected by many things, including:

- how you are feeling in general
- your previous experience of pain
- your understanding of why you have pain
- any worries you have about your pain
- how you deal with your pain
- how your pain affects your life

Pain that doesn't get better can often cause distress, tiredness and irritability. Your sleep may also 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.

You should discuss, with your doctor, what you expect from the treatment. It is easier to treat pain after surgery or an injury with pain relieving medicines, however it is rarely possible to relieve long-term pain completely by using such drugs. The aim of treatment is to reduce your pain enough to help you get on with your life. In trials most medicines for long-term pain only benefit around one in every four or five people and on average only provide a 30% reduction in pain. Medicines work best if you combine them with other ways of managing symptoms such as regular activity and exercise, and doing things that 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 these drugs are helping.

Why don't my painkillers work? is a commonly asked question, and often one without any easy answers. Long-term pain arises through many different mechanisms, and most drugs only target one of these making it less effective. Some pains do not seem to respond to any painkilling medicines. You can get used to painkillers, including opioids, so that you need more and more to have the same effect: This is called building up tolerance. We know that high doses of opioid medicines taken for long periods are unlikely to give better pain relief and are linked with a number of problematic harmful or unpleasant effects.

Taking opioids for pain

- **How do opioids work?**

Opioids provide pain relief by acting on areas in the spinal cord and brain to block the pain signals. They are considered to be some of the strongest painkillers available and are used to treat pain after surgery, serious injury and cancer. Opioid drugs can help manage some, but not all, types of chronic pain.

- **How are opioids taken?**

Opioid medicines come in many different forms: injections, tablets, capsules, liquids, and patches.

- **When should I take my opioid medicines?**

For continuous long-term pain you may be given a slow-release tablet or an opioid skin 'patch' which gives a steady level of medicine in the blood. Your healthcare team will find the best way to manage your pain and adjust the dose to give you pain relief most of the time. They'll also try to lessen the side effects. Fast-acting opioid medicines and opioids that can be injected are not very useful for managing continuous pain.

- **What dose of opioid should I take?**

The correct dose of any medicine is the lowest dose that produces a noticeable benefit. It is unusual to get complete pain relief from opioids.

You should always take the correct dose of prescribed medicines. If you feel the dose is not enough, or if the side effects interfere with your life, you should discuss this with your healthcare team.

- **How long will it take to work?**

This depends on the form that has been prescribed. Fast acting tablets may be used when you first start trying opioid treatment; these may work within an hour and last for around three to four hours. Slow release tablets or patches take longer, up to two days to begin to have any noticeable effect.

- **What are the possible side effects?**

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

Sometimes these side effects can go on for longer than a 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, 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 (not being able to poo regularly or having problems completely emptying your bowels).This is a common problem when taking opioids and does not tend to go away the longer you take opioid medicines. 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
- 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
- Loss of immunity

- Hormone disturbance and loss of bone density

- **What if I forget or miss a dose?**

Take it as soon as you remember!
However, if it is almost time for your next dose, skip the missed dose and take your medication as normal.
Do not take two doses together!

- **Can I drive when I'm taking opioids?**

Please see our patient information leaflet on **Driving and Pain**

- **Can I take this medicine long-term?**

Opioids can have a positive benefit for some people living with long-term pain, but they can have serious consequences when they are not providing sufficient benefit or being taken in a manner that was not intended. It is important to think about the risks and benefits of continuing opioids with your prescriber on a regular basis. Recent medical literature suggests that the risks to your health increase significantly when prescribing opioids at high doses for a long period of time. If you take opioid drugs for many months or years, it can affect your body in a few ways. 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 healthcare team. Your team will be able to tell you whether you are at risk of developing these problems.

Everyone prescribed opioid medicines in the long-term should have them reviewed by their prescriber regularly. If this does not happen ask your General Practitioner (GP).

If you want to try reducing your dose, you should discuss this with your doctor and bring the dose down slowly.

Many people find that after a few months they can reduce their opioid dose without the pain increasing. Many people can gradually reduce their opioid dose and find that their pain is no worse. As fewer side effects are experienced, quality and enjoyment of life can improve. All of this contributes to greater physical fitness.

- **Can I drink alcohol?**

Both alcohol and opioids can cause sleepiness and poor concentration. You should avoid alcohol completely when you first start on opioids or when your dose has just been increased. If you are taking opioids, you should avoid alcohol if you are going to drive or use tools or machines. When you are on a steady dose of opioid, you should be able to drink small amounts of alcohol without getting any extra unusual effects.

- **Will my body get used to opioid medicines?**

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 that include:

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

- **What about addiction to opioids?**

It is rare for people in pain to 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. It is more common if you:

- have been addicted to opioids (including heroin)
- Have been addicted to other drugs or alcohol before.

have 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. If you have had a problem with drug or alcohol addiction in the past this does not mean that you cannot take opioid medicines for your pain. However, your healthcare 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.

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

So,

- **What if I want to stop taking an opioid?**

Do not stop taking your opioid medication suddenly, you may experience withdrawal symptoms. Speak to your healthcare professional (doctor, nurse, pharmacist) who will be able to supervise a gradual reduction.

- **Is there anything else my prescriber needs to know?**
- If you are allergic to any drugs or medicines
- If you are taking any other prescribed or over the counter medicines or herbal medicines
- If you are pregnant or breast feeding, or if you are planning to become pregnant in the future
- If you have a kidney problem
- If you have or have had a history of excessive alcohol use, recreational drug use or addiction to prescribed or over-the-counter medication.

- **I am on a high dose of Opioid pain killer and my doctor wants me to stop the medication. What can I do?**

If you are on a high dose opioid, even if it is helpful for you, your doctor might want to reduce this. The long-term effects of opioids and in some cases other drugs such as gabapentin, pregabalin, diazepam can trigger a reduction. There are various services available to help with this. A discussion with your doctor might help finding the support you have local to your residence.

Examples of local support:

- GP-led medication review and optimisation.
- Advanced Nurse Practitioner, Specialist Nurse led review and optimisation.
- Community Pharmacist led medication review and optimisation.
- Community Multi-disciplinary Team (MDT) approach, in combination of the above
- MDT with liaison Pain Medicine Specialist in secondary care.
- Patient-led optimisation (with ongoing assessment and review by healthcare professionals)