Resource pack 1: Background for prescribing a gabapentinoid in chronic pain

Key messages – Resource pack 1: Background for prescribing a gabapentinoid in chronic pain

Deciding whether to start a gabapentinoid

- Decisions to start a gabapentinoid for pain should be made collaboratively between prescriber and the person.
- Non-pharmacological approaches should be considered first.
- Gabapentinoids should be used only where clearly indicated and after alternative medicines have been explored.
- The expected benefits, limitations, and risks should be discussed before treatment is started.
- Make the person aware that these medicines carry risks of addiction, dependence, tolerance, and withdrawal, and that anyone can become physically dependent.

Safety and risk considerations

- Gabapentinoids can cause a wide range of adverse effects, from mild to clinically significant harm.
- Risks are higher in older people, people with respiratory disease, and those taking opioids or other sedating medicines.
- Monitor closely for signs of dependence and misuse, including early refill requests, dose escalation or multiple prescribers.
- Avoid prescribing gabapentinoids to people with current or past alcohol dependence or substance use disorders.
- As gabapentinoids are classified as controlled drugs, they must be prescribed, supplied and stored in line with legal requirements.

Principles for treatment and review

- Set clear functional goals with the person before starting treatment.
- Establish a plan with the person for review and stopping at the outset, including how treatment would be reduced or stopped if it is no longer needed.
- Start treatment as a therapeutic trial, recognising that effectiveness is often limited, and review regularly to ascertain whether there is an ongoing need for continued treatment.
- If there is no meaningful benefit, taper and discontinue gradually in collaboration with the person.
- Document all assessments, discussions, decisions, and review plans clearly in the clinical record.

1.0 Background for prescribing a gabapentinoid in chronic pain

This background section provides an overview of the evidence, clinical context and key considerations relevant to the use of gabapentin and pregabalin (gabapentinoids) in the management of chronic pain. It provides a foundation for the practical guidance set out in subsequent resource packs.

1.1 Patient population

This guidance is applicable to adults who are receiving or considering gabapentinoids, with the exception of those prescribed gabapentinoids for epilepsy or generalised anxiety disorder. Where people are receiving palliative care, some aspects of the guidance may require tailoring to their individual needs (see section 1.1.1 People receiving palliative care).

1.1.1 People receiving palliative care

Palliative care may be provided to people approaching the end of life, as well as to those with longer or uncertain prognosis, and may extend over months or years. In people with longer or uncertain prognosis, pain management may involve long term prescribing.

Where gabapentinoids are prescribed for ongoing pain, people receiving palliative care will be exposed to the same risks of harm as those recognised in chronic pain prescribing, including sedation, respiratory depression, cognitive impairment, dependence and falls. These risks are increased when gabapentinoids are used alongside opioids, benzodiazepines, Z-drugs or other CNS depressants, or in the presence of frailty, renal impairment or multimorbidity.

For people receiving palliative care whose prognosis is uncertain or extended and whose symptoms are being managed over time, the principles of treatment outlined in section 1.4 should be applied in an individualised and proportionate manner, balancing potential benefit against risks. Prescribers should consider whether specialist palliative care or pain services are involved and seek advice where appropriate, particularly for complex cases or higher-risk combinations of medicines.

For people receiving end-of-life or terminal care, where the primary focus is comfort in the context of limited prognosis, the approaches described in these resources may not be appropriate.

1.2 Place in therapy

1.2.1 Licensed indications

Gabapentinoids are licensed in the UK for the management of epilepsy and neuropathic pain, with pregabalin also approved for the treatment of generalised anxiety disorder[1-5]. When used in pain management, gabapentinoids should be prescribed only where there is a clear clinical rationale and where the potential for benefit outweighs the known risks.

Neuropathic pain

Gabapentin is licensed for the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults. Even when neuropathic pain is confirmed, only a small proportion of people experience meaningful improvement. Treatment should therefore be initiated as a therapeutic trial and continued only if there is functional improvement.

Epilepsy
While the use of gabapentinoids for epilepsy is outside the scope of these resources, it is important to note that these medicines must not be reduced or stopped abruptly when used for seizure control, as this may lead to a deterioration in seizure stability. Some people may be prescribed a gabapentinoid for neuropathic pain while also receiving other anti-seizure medicines.

Gabapentinoids contributing to seizure control

Where a person prescribed gabapentinoids for pain is identified for **dose reduction or discontinuation**, prescribers must first **confirm that the medicine is not being used for epilepsy or contributing to seizure control**.

If there is uncertainty, or if concerns arise regarding safety or interactions, advice should be sought from the person's neurologist before any changes are made.

Generalised anxiety disorder
Pregabalin is an option for generalised anxiety disorder when first-line treatments such as selective serotonin reuptake inhibitors (SSRIs) or serotonin–noradrenaline reuptake inhibitors (SNRIs) are unsuitable or ineffective[6]. Although the management of anxiety is outside the scope of this document, some people may be prescribed pregabalin for both anxiety and neuropathic pain. Where pregabalin is providing benefit for both conditions, treatment may continue provided it remains safe and effective. If pregabalin was initiated by mental health services, the original prescriber should be contacted if concerns arise regarding ongoing use, emerging harms or interactions. See section 6.0 Frequently asked questions for more information.

1.2.2 Off-label use

While gabapentinoids are often prescribed off-label for a range of clinical conditions including non-neuropathic pain syndromes, the supporting evidence for this use is limited[7-10].

Chronic primary pain

Chronic primary pain is a complex multifactorial condition for which **gabapentinoids offer minimal or no meaningful benefit**.

National Institute for Health and Care Excellence (NICE) guideline NG193 recommends that prescribers should not initiate gabapentinoids to manage chronic primary pain, as the evidence does not support their effectiveness[9]. Treatment of these conditions should focus on supported self-management, psychological approaches, physical activity, and lifestyle interventions.

Low back pain with or without sciatica

NICE guideline NG59 recommends **gabapentinoids should not be offered for low back pain, with or without sciatica**[11].

Evidence from clinical trials shows that these medicines provide no meaningful improvement in radicular leg pain compared with placebo, while adverse effects may impair mobility and participation in rehabilitation[12,13]. People who have been prescribed gabapentinoids for low back pain with or without sciatica should be reviewed and gradual discontinuation should be encouraged, with ongoing support

and access to appropriate non-pharmacological services. See section 6.0 Frequently asked questions for more information.

Do not use gabapentinoids to replace opioids

Gabapentinoids **should not be used to replace opioids** or as a way of reducing opioid use, as the evidence does not support this practice.

Summary: When gabapentinoids should and should not be used

Use gabapentinoids only when:

- There is a clear diagnosis of neuropathic pain.
- Alternative pharmacological options (e.g. amitriptyline and duloxetine) have been tried and were ineffective, not tolerated, contraindicated, or unsuitable.
- Shared decision-making has taken place and goals are agreed.

Do NOT use gabapentinoids when:

- The indication is low back pain with or without sciatica.
- Pain is non-neuropathic or unexplained.
- The person is at high risk of misuse, diversion or sedation-related harm.

Key message:
Gabapentinoids have limited efficacy and should only be initiated when benefits clearly outweigh risks.

1.3 Risks

Gabapentinoids are associated with a range of risks that must be considered before initiation and throughout treatment. These include common adverse effects that may affect day-to-day functioning, as well as more serious harms such as respiratory depression, dependence and misuse. The Medicines and Healthcare products Regulatory Agency (MHRA) has issued multiple Drug Safety Updates highlighting reports of severe respiratory depression, in some cases without concomitant opioids use[14-17].

1.3.1 Adverse effects

Gabapentinoids are associated with a range of adverse effects. While it is not practical to discuss every possible adverse effect during an initial consultation, it is important to highlight those that are common, clinically significant or likely to affect safety and quality of life.

Common adverse effects include drowsiness, dizziness, fatigue, weight gain or increased appetite, and changes in mood or behaviour. Some of these adverse effects may impair balance, concentration, driving ability and ability to carry out daily activities. Other important effects include erectile dysfunction and cognitive problems which can impact quality of life and treatment adherence.

Severe respiratory depression

Gabapentinoids are associated with **a rare risk of severe respiratory depression even without concomitant opioid medicines**.

Older people and people with compromised respiratory function (e.g. chronic obstructive pulmonary disease (COPD), respiratory or neurological disease, or renal impairment at higher risk of experiencing severe respiratory depression.

Table 1 summarises the key adverse effects, grouped by how frequently they occur according to the Summary of Product Characteristics (SmPC)[4,5]. Some people may experience no side effects at all, while others may notice several occurring together, especially when treatment is first started or when doses are increased. The table can be used as a guide for discussion, helping to explain which effects are more likely and which are less common.

Table 1. Adverse effects associated with gabapentin and pregabalin

(SmPC frequency categories indicate the following numeric ranges: Very common ≥ 10%, Common 1–< 10%, Uncommon 0.1–< 1%, Rare 0.01–< 0.1%)

Adverse effect	Gabapentin	Pregabalin	Clinical relevance
Dizziness, somnolence	Very common	Very common	Contributes to sedation, impaired driving and falls
Ataxia (unsteadiness)	Very common	Common	Risk of falls due to poor balance
Fatigue	Very common	Common	May affect daily functioning
Headache	Common	Very common	May limit tolerability
Euphoria *(feeling unusually "high")*	Not a recognised common effect	Common	Recognised with pregabalin. May produce a sense of wellbeing or "high", which can contribute to misuse or non-medical use in some patients
Cognitive effects (confusion, memory impairment/amnesia)	Common	Common	May impair concentration, memory and daily functioning
Gastrointestinal effects *(nausea, vomiting, constipation, diarrhoea, flatulence, dry mouth)*	Common	Common	Usually mild but may affect adherence
Weight gain/increased appetite	Common	Common	Relevant with longer-term use (metabolic impact, adherence)

Table 1. Adverse effects associated with gabapentin and pregabalin (continued)

Adverse effect	Gabapentin	Pregabalin	Clinical relevance
Visual disturbance *(blurred vision, diplopia)*	Common	Common	May contribute to falls and affect driving
Mood and behavioural changes	Common (emotional lability)	Common (irritability)	Can affect adherence and signal psychiatric adverse effects
Tremor	Common	Common	May affect fine motor tasks (e.g. writing)
Peripheral oedema	Common	Common	Can worsen heart failure or cause discomfort
Erectile dysfunction/ impotence	Common	Common	May affect quality of life and adherence
Suicidal ideation/ behaviour	Not known	Rare	Low frequency but serious class effect; important safety consideration
Respiratory depression	Rare	Not known	Uncommon but serious; risk increases with opioids and other sedatives

1.3.2 Populations at increased risk of adverse effects

Certain groups are at increased risk of significant harm from gabapentinoids and therefore require caution when these medicines are prescribed. These include older people, people taking opioids or other sedating medicines and those with respiratory disease. For more details see Table 2.

Table 2. Populations at increased risk of adverse effects with gabapentinoids

Older people
• More vulnerable to the sedative and cognitive effects of gabapentinoids. • Age-related physiological changes increase the likelihood of confusion, memory disturbance, impaired coordination, falls and functional decline[4,5,18]. • Cognitive symptoms often improve when gabapentinoids or other CNS depressants are reduced or discontinued. • Risk of respiratory depression increases, particularly at higher doses or when gabapentinoids are used alongside other sedating medicines[16].
People using other CNS depressants
• Co-prescribing gabapentinoids with opioids, benzodiazepines, Z-drugs, or other CNS depressants should be avoided where possible, as it substantially increases the risk of sedation, respiratory compromise, toxicity and confusion[16]. • If co-prescribing cannot be avoided, these people require close monitoring, and dose adjustments should be considered, particularly where renal function is reduced.

Table 2. Populations at increased risk of adverse effects with gabapentinoids (continued)

People with respiratory problems
• People with existing respiratory conditions, such as COPD or sleep apnoea, are at increased risk of severe exacerbations or respiratory depression when taking gabapentinoids[15]. • Risk is further increased if gabapentinoids are used in combination with opioids or other sedating medicines[15]. • Prescribers should start at low doses, avoid unnecessary co-prescribing of opioids or other CNS depressants and ensure appropriate monitoring.
People with mental health conditions
• Increased risk of worsening mental health, self-harm, suicide, or misuse in those with depression, suicidal ideation or behaviour, or substance use. • Gabapentinoids may worsen mood symptoms in some people and may cause emotional blunting, reduced motivation or behavioural disinhibition[19]. • Before prescribing, screen for depression and suicidal risk. • Avoid initiating in people with known or suspected substance use disorders[20]. • Where concerns are identified, seek advice from mental health services to support decision-making.
People with renal impairment
• Gabapentin and pregabalin are eliminated unchanged by the kidneys. Reduced renal function increases the risk of accumulation and toxicity (e.g. sedation, dizziness, confusion or respiratory depression). • According to the SmPCs, dose adjustment should be guided by creatinine clearance (CrCl) calculated using the Cockcroft–Gault equation[4,5], and therefore CrCl is used throughout this document when referring to renal dosing. However, in clinical practice, estimated glomerular filtration rate (eGFR) can be used when the information needed to calculate CrCl is not available. • Renal function should be assessed before initiation and monitored at least annually. • Monitoring should be undertaken more frequently if renal function declines or if clinical circumstances indicate an increased risk of drug accumulation, with the frequency determined by clinical judgement. See section 6.0 Frequently asked questions for more information.
Pregnant and breastfeeding people
• The MHRA has warned of a possible increased risk of congenital malformations with pregabalin use during pregnancy and recommends effective contraception for women of childbearing potential[21]. • For gabapentin, the SmPC advises that it should be used during pregnancy only if the potential benefit outweighs the risk to the foetus. Routine contraception is not specifically recommended; however, pregnancy planning and potential risks should be discussed with people of childbearing potential[2,4,5]. • Both gabapentin and pregabalin are excreted into breast milk. Use during breastfeeding should be considered on an individual basis, taking into account the potential risks to the infant and the clinical need for treatment[1-5]. If treatment is required, the lowest effective dose should be used, and the infant should be monitored for adverse effects such as sedation or poor feeding.

Summary: Who is at highest risk of harm?

People at greatest risk of significant adverse effects include:

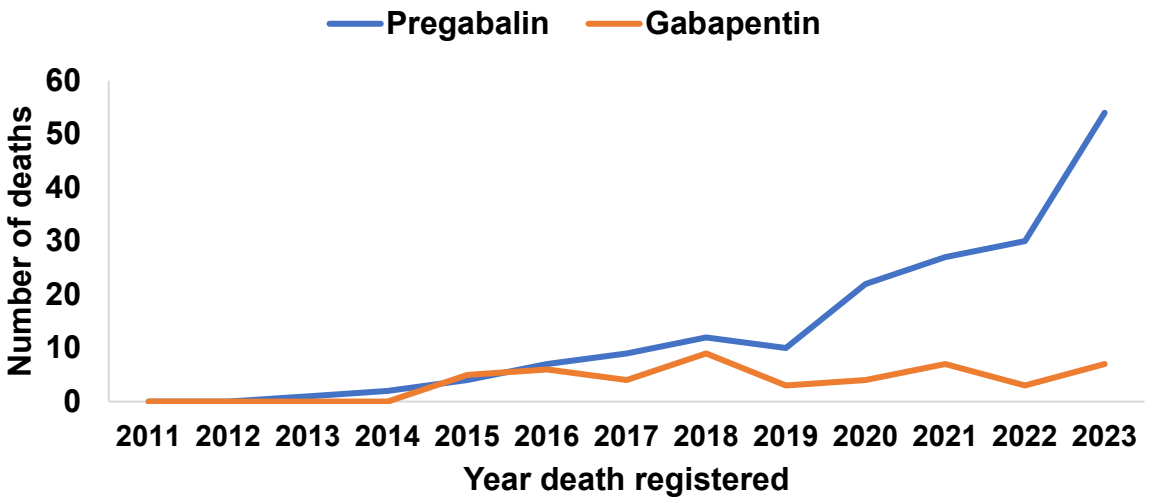
- **Older people**: increased susceptibility to sedation, confusion, falls and respiratory depression.
- People with **respiratory disease** (such as COPD): increased risk of severe exacerbations and respiratory depression.
- People taking **CNS depressants** such as opioids, benzodiazepines, Z-drugs or alcohol.
- People with **renal impairment**: risk of accumulation and toxicity without dose adjustment.
- People with **mental health conditions** or **substance use disorders**: higher risk of misuse, disinhibition or worsening mood symptoms.

Clinical action: Use the lowest effective dose, review regularly, and avoid unnecessary co-prescribing of opioids, benzodiazepines, Z-drugs or other CNS depressants.

1.3.3 Mortality risk

Gabapentinoids contribute to drug-related deaths, particularly when used in combination with other CNS depressants such as opioids, benzodiazepines, Z-drugs or alcohol[22]. In Wales, there has been a concerning rise in the number of deaths in which pregabalin was mentioned on the death certificate, increasing from 10 deaths in 2019 to 54 deaths in 2023[23] (see Figure 1), highlighting the need for careful, responsible prescribing. Further concern is reflected in data from the Welsh National Poisons Unit (Wales data from 2015–2024, all ages), which show a notable rise in gabapentinoid-related poisoning queries over the past two years. This increase adds to the growing evidence of safety risks associated with these medicines.

Figure 1. Number of deaths in Wales for which gabapentin and/or pregabalin was mentioned on the death certificate[8]



1.3.4 Dependence

Dependence on gabapentin or pregabalin can occur when these medicines are taken at therapeutic doses[4,5].

Presentation of dependence

Dependence may present as **difficulty reducing the dose**, requests for **early repeats** or **taking more than prescribed**.

A perceived reduction in effect over time is commonly reported and usually indicates that the medicine is no longer providing benefit. In this situation, increasing the dose is unlikely to be helpful and may increase the risk of harm. All people prescribed gabapentinoids should be considered at risk of dependence, and treatment should be reviewed regularly to ensure that benefits continue to outweigh potential harms.

MHRA Drug Safety Update (January 2026)

The MHRA issued a Drug Safety Update, Improving Information Supplied with Gabapentinoids (Pregabalin/Gabapentin), Benzodiazepines and Z-Drugs, highlighting the risks of addiction, dependence, tolerance and withdrawal, associated with these medicines. MHRA advised prescribers should:

- Provide clear information about the risks of addiction, dependence, tolerance and withdrawal, communicated using non-judgemental language
- Explain that withdrawal symptoms may occur following dose reduction or discontinuation
- Advise the person not to stop treatment abruptly and to seek medical advice before doing so
- Provide the MHRA gabapentinoid patient leaflet on the risks of addiction, dependence and withdrawal
- Report suspected adverse reactions including dependence or withdrawal via the Yellow Card scheme.

1.3.5 Misuse

Gabapentinoids, particularly pregabalin, have recognised misuse potential. Misuse and dependence have been reported in the SmPCs and caution is advised when prescribing to individuals with a history of substance use[2,4,5,24-26].

Misuse is considered to be uncommon in the general population[27,28] but is more prevalent among individuals who misuse opioids[28]. There is also evidence of increasing availability through illicit supply, including online sources[29], and higher rates of misuse have been reported within substance use services and among individuals in prison and following release[30].

Misuse in pregabalin versus gabapentin

Pregabalin is **misused more frequently** than gabapentin, likely reflecting differences in pharmacokinetic profile.

The rapid absorption, faster onset of action, greater potency, and near-linear dose response curve of pregabalin can produce more intense psychoactive effects at higher doses than gabapentin[31,32]. Reported desired effects of pregabalin include euphoria, relaxation, enhanced sociability and a sense of calm[31]. These effects are

typically achieved with non-therapeutic use, with reported single doses ranging from 200 mg to 5 g[31]. By contrast gabapentin demonstrates a plateau in its dose response effect at higher doses (around 2,400–3,600 mg), which may limit further psychoactive effect with dose escalation.

Prescribers should remain alert to behaviours indicative of misuse or diversion, including stockpiling or use of doses exceeding those prescribed for psychoactive effect.

Potential red flags for misuse or dependence

- Long-term **off-label prescribing** with refusal to consider alternatives.
- **Difficulty reducing** or **stopping** use due to withdrawal symptoms.
- History of psychiatric illness, trauma, or substance use.
- Specific requests to initiate treatment, particularly post-prison.
- Frequent early prescription requests or reports of lost medication.
- Escalating dosage requests or use beyond prescribed amounts.
- Seeking prescriptions from **out-of-hours** services.
- **Concerns raised** by professionals, carers, or family.
- **Hostile behaviour** when prescriptions are delayed or withheld.
- **Non-attendance** at review or follow-up appointments.
- **Refusal to engage** with drug screening or specialist addiction services.
- Attempts to obtain medication from **multiple prescribers**, including locums.
- Procuring gabapentinoids from the **internet** or **informal sources**.
- **Sedated presentation** during appointments.
- **Decline** in work, home, or social functioning.
- Evidence or suspicion of **injecting or nasal inhalation** of the medication.
- Experiencing withdrawal effects when the medicines are stopped suddenly.
- Expression of **cravings**, even if it is causing adverse effects.

1.3.5.1 Referral and support

If misuse is suspected, people should be referred to the most appropriate local service for assessment and support. In many areas, substance use services accept referrals only where there is clear evidence of misuse or illicit acquisition. In some health boards, dedicated services support people using prescribed medicines who require structured reduction, and some primary care teams provide this support directly. Where these services are unavailable, management should follow local policies, with specialist advice sought where appropriate.

Summary: Dependence and misuse of gabapentinoids

Gabapentinoids carry a recognised risk of dependence, misuse and diversion, even when taken as prescribed.

Dependence

- Anyone prescribed gabapentin or pregabalin may develop dependence.
- Withdrawal symptoms can include anxiety, agitation, irritability, headache, tremor, insomnia, sweating, gastrointestinal disturbance, nausea, pain rebound and, in rare cases, seizures.

- A “wearing-off” effect usually indicates loss of benefit, increasing the dose rarely helps and may cause harm.
- Difficulty reducing or stopping should always prompt review and shared decision-making.

Misuse and diversion

- Misuse is more common with pregabalin due to its faster onset and greater psychoactive effects.
- High-risk groups include people with current or past alcohol dependence or substance use, people recently released from prison, and people using opioids, benzodiazepines, Z-drugs or other CNS depressants.
- An illicit market exists; some people may attempt to obtain gabapentinoids from multiple prescribers or online sources.

All people taking gabapentinoids should be monitored for signs of misuse and supported through regular review.

1.3.6 Legal status

1.3.6.1 Controlled drugs

Gabapentin and pregabalin are classified as Class C controlled drugs and placed in Schedule 3 of the Misuse of Drugs Regulations 2001 because of their potential for misuse and dependence[14]. This classification imposes specific requirements regarding prescribing, supply, record-keeping and storage. Prescribers must ensure that prescriptions meet the legal requirements for controlled drugs.

1.3.6.2 Driving

People prescribed gabapentinoids should be informed about the possible effects of these medicines on their ability to drive or operate machinery[33]. They must not drive if their performance is impaired by medication or if they are using doses other than those prescribed[34,35]. Individuals in occupations that involve operating machinery should carefully assess whether sedation, dizziness, or reduced concentration might compromise their own or others’ safety[33,35]. Prescribers must follow relevant Driver and Vehicle Licensing Agency (DVLA) guidance, provide suitable advice, and document the discussion[35].

1.4 Principles of treatment

The decision to prescribe a gabapentinoid should be made in accordance with the principles of treatment outlined here and addressed in more detail in the relevant sections.

Principles of treatment comprise:

- **Appropriate indication:** Prescribe only when there is a clear clinical rationale, such as confirmed neuropathic pain (see section 2.1).
- **Non-pharmacological approaches:** Explore non-pharmacological options before considering gabapentinoids, as these do not carry the risks associated with medicines (see section 2.2.1).
- **Alternative pharmacological options:** Consider alternative medicines, particularly those with safer profiles or stronger evidence base for the person's condition (see section 2.2.3).
- **Shared decision making:** Prescribing should follow a shared decision-making process, ensuring the person understands the potential benefits, limitations and risks of treatment (see section 2.3).
- **Setting goals:** Agree realistic, measurable treatment goals prior to initiation, focusing on improvement in function rather than complete pain relief (see section 2.4).
- **Safe prescribing considerations:** Apply safe prescribing principles, including assessment of risk factors for harm, dependence and misuse (see section 2.5).
- **Therapeutic trial:** Initiate as a therapeutic trial with a clear plan for dose titration, an agreed period for assessing benefit, and a scheduled review to determine whether continuation is appropriate (see section 2.7).
- **Reviews:** Review treatment regularly to assess effectiveness, safety and adherence. Early review should assess pain, function and tolerability. Longer-term reviews should occur every six to twelve months (see Resource pack 3).
- **Discontinuation:** Discontinue treatment if treatment goals are not met or harms outweigh benefits. Dose reduction should be gradual, with appropriate support and continuation of non-pharmacological strategies (see Resource pack 4).
- **Documentation:** Document all decisions in person's clinical record, including at initiation (see section 2.8), during review (see section 3.7) and when discontinuing (see section 4.10).

Appendix 1a: Information poster for prescribers provides a summary of these principles for display.

Appendix 1a: Information poster for prescribers – Gabapentin and pregabalin