

Helping patients with epilepsy adhere to their medicines

People with epilepsy require good adherence to anti-epileptic medicines for optimal seizure control. However, maintaining good adherence long-term can be difficult. The primary care team can provide education, support and practical assistance to patients with epilepsy and their families, such as helping to simplify medicine regimens and putting schedules and routines in place. Assistance is also available from epilepsy support organisations and specialist nurses.

KEY PRACTICE POINTS:

- Good adherence to anti-epileptic medicines is necessary to maximise a patient's chance of being seizure free. However, poor adherence is reported in up to half of patients with epilepsy.
- Forgetfulness is a major contributor to patients, or their caregivers, missing doses
- Encourage patients and caregivers to set a routine for taking medicines and to use reminder techniques such as alarms, smart phone apps, medicine blister packs, pill boxes or a diary so that doses are not forgotten
- Education is a key part of helping patients and caregivers understand the need for regular dosing of anti-epileptic medicines
- Simple medicine regimens and 90-day dispensings of medicines can help improve adherence; review a patient's prescriptions and how often they need to visit a pharmacy to see if changes can be made

Assessing adherence: assume missed doses

Patients with epilepsy require ongoing use of anti-epileptic medicines to optimise seizure control. Missing occasional doses is to be expected for patients with any long-term condition. However, there is evidence that poor adherence is a particular problem for patients with epilepsy. Studies report that 20–50% of patients with epilepsy have poor adherence to their medicines, depending on the definition of adherence and length of follow-up.¹ Poor adherence in the first month of initiating an anti-epileptic medicine is a predictor of reduced adherence long term,² therefore early follow-up is recommended to assist with any issues.

When asking about adherence to medicines, reassure patients and caregivers that missing doses is normal. For example, instead of asking "do you forget to take your medicine?", ask "could you have missed some doses" or "how often do you forget to take doses?". Asking the same question

in different ways can be a good technique to elicit a more accurate response.

Patients may not take a medicine as intended for a number of reasons (Table 1). For children with epilepsy, caregivers are responsible for adherence to medicines rather than the patient themselves. Understanding the reasons why medicines are not being taken is essential for putting processes in place to overcome any barriers.

Strategies to improve adherence: use multiple approaches

People of all ages are affected by issues such as forgetting to take a dose. However, other problems with adherence are likely to differ depending on a patient's stage of life. Research suggests the biggest improvements in adherence to anti-epileptic medicines occur if multiple strategies are used at once, such as education about epilepsy and anti-epileptic medicines combined with reminders or alerts when doses are due, and additional intensive follow-up such as increased appointment frequencies or phone calls between appointments.^{4,5} Involving a patient's entire health care team, and their family, is likely to maximise the chances of improving adherence.

Outsmarting forgetfulness

Forgetfulness is a key reason for people with epilepsy or their caregivers missing doses. Remembering to take doses can be more difficult for patients with epilepsy due to:

- Problems with cognitive function or memory; reported in up to 30% of people with epilepsy⁶
- The adverse effects of anti-epileptic medicines, which can cause patients to feel "slower" and can alter their mood or cognition
- Temporary cognitive difficulties following a seizure
- Conditions which cause cognitive difficulties in addition to epilepsy, e.g. epilepsy following a stroke
- Having to rely on someone else to remember, e.g. caregivers


N.B. Referral to or discussion with a neurologist is recommended if patients have a new onset of memory difficulties, or a decline in pre-existing cognitive impairment.⁷

Strategies for reducing missed doses due to forgetfulness include:³

- Linking the medicine regimen to aspects of a patient's/family's daily routine
- Using reminder tools, e.g. an alarm, medication diary, smart phone application, chart, calendar, post-it notes
- Medicine packaging to encourage adherence, e.g. daily pill boxes (see: "Packaging to improve adherence")
- Including others in the treatment plan, such as a family

member, close friend or relative, especially if the patient has a degree of cognitive impairment


- Telephone calls from the general practice team or pharmacist between appointments or dispensings to check medicine use and encourage adherence

 Further information:

- Strategies for remembering doses: www.healthnavigator.org.nz/health-a-z/m/medicines-tips-to-remember-to-take-them/
- List of smartphone apps: www.epilepsysociety.org.uk/memory-apps

Help patients and caregivers to understand epilepsy

Epilepsy is associated with stigma and misconceptions in the community about its causes and effects.^{9,10} Across different cultures epilepsy has been, and in some cases still is, seen as a mental illness, contagious, a curse or evil spirit.¹¹ Clinicians may need to discuss erroneous beliefs to help parents come to terms with their child's diagnosis. Some people may be in denial of the diagnosis and not wish to administer anti-epileptic medicines as doing so would be an acknowledgement of their or their child's condition. Engaging with an epilepsy support organisation may help.

 Patient and caregiver support is available from:

- Secondary care:
 - Some DHBs will have epilepsy or neurology Nurse Specialists who can assist with adherence
- National organisations:
 - Epilepsy New Zealand: www.epilepsy.org.nz
 - The Epilepsy Foundation of New Zealand: www.epilepsyfoundation.org.nz
- International organisations:
 - The Epilepsy Foundation (United States): www.epilepsy.com
 - Epilepsy Action (United Kingdom): www.epilepsy.org.uk

Discuss the need for regular use of anti-epileptic medicines

Anti-epileptic medicines generally have half lives less than 24 hours.¹² Regular dosing is therefore necessary to maintain therapeutic levels and maximise seizure control. All anti-epileptic medicines are prescribed with daily dosing regimens.¹³


 Patient education about how anti-epileptic medicines work is available from: www.healthnavigator.org.nz/medicines/a/anti-epileptic-medication/

Table 1: Common reasons for lack of medicine adherence in people with epilepsy.³

Unintentional causes	<ul style="list-style-type: none">■ Forgetfulness■ Poor understanding of their/their child's epilepsy, and the need for ongoing medicines■ Misunderstanding over prescribed medicine doses or frequencies, e.g. complicated treatment regimens
Causes for intentional reductions in dose or dose frequency	<ul style="list-style-type: none">■ Concerns over adverse effects■ Believing they have a low risk of seizure■ Believing they no longer need treatment■ Feeling the inconvenience and adverse effects of treatment are not worth the benefit
Other physical, cognitive and psychological causes	<ul style="list-style-type: none">■ Difficulty swallowing or palatability issues■ Cognitive impairment, including medicine-induced or post-ictal impairment■ Problems with motor function■ "Pill burden": the number and frequency of tablets or volume of liquid prescribed■ Feelings of stigma and embarrassment■ Depression■ Lack of clear responsibility in the family for who should ensure children take medicines■ Rebellion/refusal to take medicines

Highlight the risks of lack of adherence

Missing doses of epilepsy medicines increases the risk of a seizure occurring. Good adherence is recommended as a key strategy for reducing the risk of sudden unexpected death in epilepsy (SUDEP), which can be triggered by tonic-clonic seizures (see: "Sudden unexpected death in epilepsy [SUDEP]").^{14, 15} A lack of adherence can also result in more hospital visits and longer-term effects on health. A study of over 33,000 people with epilepsy in the United States found that patients who collected less than 80% of their prescribed anti-epileptic medicines had a 20% higher rate of emergency department visits, 40% higher rate of hospitalisation and three-fold higher risk of mortality than patients who collected over 80% of their medicines.^{16, 17}

Therefore, being adherent to their medicine regimen can help to reassure patients who are fearful or embarrassed about experiencing a seizure. It can also ease anxiety which may prevent the patient from engaging in social or sporting events, or affect their focus at school or work.¹⁰

Missing one or two doses does not necessarily mean a patient will experience a seizure, and conversely being adherent to medicines does not guarantee that a patient will be seizure-free. This may lead to patients or caregivers thinking they can "get away with" skipping a dose or that regular dosing is not worthwhile. Emphasise that good adherence will decrease their risk of a seizure, and that having a seizure, despite good adherence, is not a "failure".¹

Packaging to improve adherence

Pharmacies can repackage some medicines from the original manufacturer's packaging into dose administration aids. These aim to improve adherence by addressing specific problems a patient may have, such as:⁸

- Complex regimens with multiple medicines
- Difficulty removing medicines from the original packaging
- Difficulty recalling if a medicine has been taken or not


Common repackaging options include blister packs or pill boxes with all the medicines a patient needs to take at one time, e.g. Tuesday morning at breakfast, included in one compartment. Packaging is usually see-through so that patients or caregivers can easily tell if doses have been taken. Medicines can also be repackaged into rolls of individual tear-off sachets, where each sachet contains the medicines to be taken at one time with a printed description on the sachet of the time of dosing and medicines included.⁸ Availability and costs of these packaging options will differ between pharmacies.

Provide clear, simple medicine regimens

Guidelines for the pharmacological treatment of epilepsy recommend monotherapy as the first-line approach,⁷ which is also likely to improve medicine adherence.³

Ensure patients and caregivers have written instructions for their medicine regimen

Medicine regimen instructions are usually provided by the patient's epilepsy care team and should include advice on what to do if a dose is missed, how to manage adverse effects and when to seek medical assistance.¹ Check that patients and caregivers understand these instructions and clarify any areas of confusion.

 Further information on taking anti-epileptic medicines is available from:

- The New Zealand Formulary for Children: www.nzfchildren.org.nz/nzf_70291
- Health Navigator: www.healthnavigator.org.nz/medicines/c/carbamazepine/

Check if any changes have been made to a patient's medicine regimen

If adherence has recently decreased, check if the prescribed medicine has changed; a different brand name and appearance of a medicine may lead to confusion about dosing or concerns regarding adverse effects or efficacy, which may require reassurance. Encourage patients and caregivers to refer to medicines by their generic name, i.e. active ingredient, so they are more confident with any brand changes.

See if simple changes to the regimen would help

In some cases simple changes can help make a regimen more practical and easier to adhere to, e.g. a volume of liquid rounded to the nearest simple unit or dosing intervals changed

to more convenient times, e.g. outside of school or work, to coincide with mealtimes.

Make it easier for patients to get medicines

Less frequent dispensings may improve adherence, particularly for patients or caregivers who have difficulty accessing a pharmacy due to location or transport issues. Ideally anti-epileptic medicines should be dispensed in 90-day lots whenever possible and the dispensing of any other medicines the patient is taking can be co-ordinated to reduce the overall number of trips they need to make to the pharmacy.¹

The following anti-epileptic medicines are normally dispensed "stat" in 90-day lots:¹⁸

- Carbamazepine
- Sodium valproate, liquid formulation
- Phenytoin sodium
- Phenobarbitone
- Primidone

Clonazepam and clobazam are safety medicines which means that they can be dispensed in less than 90-day lots if there is a safety concern. The prescriber can determine the dispensing frequency by indicating this on the prescription.

The following anti-epileptic medicines are dispensed in monthly lots, but prescribers can endorse prescriptions with "certified exemption" in order for them to be dispensed in 90-day lots where appropriate:¹⁸

- Gabapentin
- Lacosamide
- Lamotrigine
- Topiramate
- Vigabatrin

Sudden unexpected death in epilepsy (SUDEP)

Good adherence to anti-epileptic medicines is recommended to reduce the risk of seizure, which in turn reduces the risk of SUDEP.^{7, 15} SUDEP is not yet fully understood and it is unclear why some seizures in some patients result in sudden death. The risk is associated with severity of epilepsy and frequency of tonic-clonic seizures, with the highest rates reported in patients who have been referred for, or undergone, surgery to treat their epilepsy.¹⁴

Incidence rates in people treated in the community range from < 1–20 cases per 10,000 patients, per year.¹⁴ Most cases of SUDEP occur in the context of a tonic-clonic seizure, often at night.^{14, 15} Data from isolated cases which occurred while a patient was being monitored show that sudden death may be caused by cardiac arrest, apnoea or cerebral shutdown.

The remaining anti-epileptic medicines, such as sodium valproate tablets, levetiracetam and ethosuximide are dispensed in monthly lots. However, patients who meet access exemption criteria can obtain 90-day stat dispensings of these medicines. To do this, the patient or a representative such as a parent signs the back of the prescription, indicating that they meet one of the following access exemption criteria:¹⁸

- They have limited physical mobility
- They live and work more than 30 minutes from the nearest pharmacy by their normal form of transport
- They are relocating to another area
- They are travelling extensively and will be out of town when the repeat prescriptions are due

Helping with costs

Patients who have a high use of general practice services and are not eligible for a Community Services Card may obtain reductions on the costs of some visits to the doctor and some prescriptions with a High Use Health Card (see: "The High Use Health Card"). Remind patients and caregivers that they only need to pay the prescription fee for a maximum of 20 prescriptions per family per year. Patients will need to keep receipts if they collect prescriptions from different pharmacies.

👁 N.B. Patients with epilepsy who are having problems with adherence can be referred to the pharmacy to assess whether they are eligible for Long Term Condition service review.

Reduced adherence may be due to adverse effects

Patients who worry about adverse effects are more likely to be non-adherent to their prescribed anti-epileptic medicines.¹⁹ Anti-epileptic medicines can be associated with a range of cognitive and psychological adverse effects which can make adherence more difficult, such as:²⁰

- Sedation and dizziness
- Mood changes: depression and changes in behaviour or personality
- Cognitive difficulties

Clinicians may find it difficult to distinguish adverse effects of the medicines from symptoms associated with a patient's underlying condition. Many adverse effects of anti-epileptic medicines are dose-related and can be minimised by slow upwards titration.¹⁵ If adverse effects are intolerable, consult with the clinician overseeing the patients treatment to see if a dose reduction, possibly followed by slowly increasing back to the same dose, is appropriate.¹⁵ For some medicines a change in formulation may alleviate dose-related adverse effects, e.g. a modified release formulation of carbamazepine minimises the incidence of dizziness and blurred vision associated with peak carbamazepine levels.^{7, 15}

The High Use Health Card

When patients have seen their general practitioner 12 times or more in a year for the same condition, they become eligible for the High Use Health Care. General practitioners must apply for the card, which allows the practice to receive a higher subsidy for patients with high health needs. The card provides the patient with same benefits as a Community Services Card for prescription fees and general practitioner visits, such as reduced fees for after-hours visits or seeing another doctor, so patients who already have one of these will obtain no additional benefit from a High Use Health Card.

👁 For further information on the High Use Health Card, see: www.health.govt.nz/new-zealand-health-system/claims-provider-payments-and-entitlements/high-use-health-card-payments



Sedation and dizziness after initiating an anti-epileptic medicine typically improve with time. However, tolerance to adverse effects varies between patients and the particular medicine used. For patients with ongoing sedation or dizziness, discuss the possibility of changing medicines with the clinician overseeing their treatment.

Anti-epileptic medicines can also result in weight gain, which may influence adherence; this occurs most often in patients taking sodium valproate, carbamazepine, vigabatrin or gabapentin.²¹

Check for low mood

Depressed mood can be associated with poor adherence and several studies have documented higher rates of depression in people with epilepsy than in the general population.¹⁵ In addition, anti-epileptic medicines can increase the risk of suicidal ideation.²² This can also influence which medicines are prescribed, e.g. levetiracetam is generally avoided in patients with a history of significant depression or attempted suicide.

Regularly assessing mood can help detect problems as they develop. Discuss patients with a new onset of depression or suicidal ideation with the clinician overseeing the patient's epilepsy management; a switch in anti-epileptic medicine may be appropriate.

Improving adherence in children with epilepsy

While many barriers to medicine adherence are common to all patients, some issues are unique to certain patient groups. Medicine adherence in young children is dependent on their caregivers. Caregivers need to understand why anti-epileptic medicines are used and the importance of regular dosing, remember to administer doses, and deal with any difficulty or refusal to take medicines. In families with genetic epilepsies, adherence can be more difficult if a parent also has epilepsy and experiences similar problems with remembering doses.

Make sure caregivers and children are clear on responsibilities

Adherence may be affected by confusion over who is responsible for a child's medicines. For example, one parent may believe the other has already given the child their medicine.

As children develop, they will become increasingly responsible for taking their own medicines. Clinicians will need to respond to this by shifting the focus of epilepsy education and management to the child rather than the caregiver. Communication about responsibility becomes even more important during any transition of care. Uncertainty about who is "in charge" could mean that the child could forget their dose while the caregiver believes they have taken their medicine. In some cases, responsibility may have been given to the child too early, and they may discontinue use or miss doses without

a caregiver being aware.²³ Check that both caregiver and child are clear on responsibilities and suggest methods to check that doses are not being missed, e.g. a checking off dates on a calendar.

Working with stigma and embarrassment

Although stigma can affect people of all ages with epilepsy, children and young people can be particularly affected, and feel embarrassed about having epilepsy and being different to their peers. As a result, they may not wish to take their prescribed medicines around friends or classmates.^{7,24} Reassure children and their caregivers that many other young people have a long-term health condition which involves daily medicines and the risk of an event, e.g. children with type 1 diabetes who take insulin and children with asthma who use inhalers, and this does not make them "abnormal". Dosing schedules which do not require taking medicines at school may help reduce stigma or embarrassment, and allow the caregivers to maintain responsibility rather than relying on the school. Discuss with children ways that they could take medicines in private while at school if this is necessary.


Ask about difficulty swallowing or palatability issues

Young children are likely to be prescribed liquid formulations of anti-epileptic medicines and gradually transition to tablet or capsule formulations at older ages. This can affect adherence if children find swallowing these medicines difficult or it causes anxiety, e.g. fear of choking.

Strategies for improving adherence in children who have difficulty swallowing tablets or capsules include:

- Tilting the head forward while swallowing; this results in a longer closure of the airway to prevent aspiration and patients report their ability to swallow medicines is improved.^{25,26}
- Training children to be able to swallow progressively larger items, e.g. using lollies.²⁷ For instructions, see: www.bpac.org.nz/Supplement/2014/September/pillswallowing.aspx
- Some formulations may be crushed or compounded into a suspension. Discuss options with a pharmacist. For children prescribed topiramate, a sprinkle capsule formulation is available; capsules can be opened and the contents sprinkled on food for easier administration.¹³

Pharmacists are well placed to initiate discussions with patients and caregivers about any difficulties in taking medicines, and to raise these issues with the medical team.

 Further information on giving medicines to children is available at: www.pharmac.govt.nz/tools-resources/print-and-pdf-resources#MedsToChildren-exp

Improving adherence in adolescents with epilepsy

As children with epilepsy develop into adolescents and become responsible for their care, it is important that they receive their own education and support with setting a routine and reminders for taking medicines. Teenagers with epilepsy can be frustrated by the limitations it places on them, such as greater difficulty in gaining a driver's licence and reduced independence, or feeling excluded from their social group as a result of being different.¹⁰ Young people in particular may be more likely to stop taking their medicines if they have not had a seizure in some time.²³

Some adolescents may refuse to take anti-epileptic medicines as a form of self-assertion as they do not want to follow instructions given to them by adults. Alternatively, as they develop their own views on their health, identity and taking medicines, this may be in conflict with their caregivers or clinicians. Emphasise to young people that taking anti-epileptic medicines is a way for them to exert control over their condition and minimise the effect it has on their life.¹⁰ As is the case with younger children, dosing schedules which allow adolescents to take their medicines at home instead of at school, university or work can help them maintain good adherence.

Improving adherence in adults with epilepsy

Seizures may affect a person's work or study, their ability to hold a driver's licence, reduce their independence and have other longer-term effects on their future health. Seizures may have a higher risk of consequences in older adults, such as an increased risk of fracture with a fall during a seizure.

Complex regimens, "pill burden" and polypharmacy

Older adults with epilepsy are more likely to be taking multiple medicines due to co-morbidities. Ask patients whether they are finding it difficult to take the number or volume of medicines

they are prescribed. Consider any other medicines a patient is taking and whether their total regimen of medicines could be simplified.

Anti-epileptic medicines may also have interactions with other prescribed medicines which increase the risk of adverse effects, and therefore may mean that patients stop taking their medicines. Switching anti-epileptic medicines may be possible to avoid interaction effects. Newer anti-epileptic medicines have fewer effects on hepatic enzymes than older medicines, such as phenytoin or carbamazepine, and therefore may be less likely to cause interactions.³⁰

If a female patient requires hormonal contraception, check for interactions with anti-epileptic medicines before initiating, as interactions can reduce the efficacy of either medicine despite good adherence. The efficacy of combined hormonal and oral progesterone-only contraceptives is reduced by a number of anti-epileptic medicines, including carbamazepine, phenytoin and topiramate.^{28,29} Lamotrigine levels are decreased by the use of combined hormonal contraceptives.²⁸ Intrauterine devices (copper or levonorgestrel) and medroxyprogesterone acetate injections are recommended for women using enzyme-inducing anti-epileptic medicines.²⁹ Women who discover they are pregnant should not abruptly stop their medication.

Check for swallowing or dexterity issues

Patients with post-stroke epilepsy or epilepsy following a head injury may have potential issues with dexterity or swallowing. Discussion with or referral to a Speech Language Therapist may be necessary for some patients with dysphagia. Patients who have trouble handling medicine containers or pills may benefit from input from a pharmacist, or involving family members or carers in their epilepsy management.

✔ Use the NZF Interactions Checker when initiating new medicines in people taking anti-epileptic medicines: www.nzf.org.nz

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