## Introduction & Background

Epilepsy is not one condition, but is a diverse family of disorders, having in common an abnormally increased predisposition to seizures. At least one seizure is required to establish the presence of epilepsy. The definition does not include a requirement that the seizure be "unprovoked", a feature of several prior definitions of epilepsy. Instead, the definition requires, in addition to at least one seizure, the presence of an enduring alteration in the brain, capable of giving rise to other seizures. An epileptic seizure is a brief disturbance of consciousness, behaviour, emotion, motor function, or sensation that is due to abnormal electrical discharge in the brain. “Seizures” and “epilepsy” are often used synonymously; this is not correct.

Seizures are a symptom of epilepsy. While all seizures are characterised by seizures, not all seizures are epileptic (for example febrile convulsions).

### How are epileptic seizures classified?

The classification of epilepsy is undergoing considerable change. In 1981 the International League Against Epilepsy (ILAE) classified epileptic seizures by clinical type and by epileptic syndrome (See Table ONE). Although the ILAE classification remains in common use, it is now considered to be insufficiently flexible to take into account the changing aspects of epilepsy diagnosis. The ILAE now recommends use of a classification across five axes that consider seizure types, focal or generalised seizure onset, the syndrome, causation, and associated deficits. The proposed new diagnostic scheme is divided into five parts or “axes” to describe ictal events, seizure type, syndrome, aetiology and impairment. Detailed discussion of the new classification is outside the remit of this paper but further information can be found on the ILAE website (www.ilae-epilepsy.org).

### What are the causes of epilepsy?

There are a multitude of underlying causes of epilepsy. Advances in neuroimaging mean that a cause is now found in over two-thirds of people with epilepsy. Of defined causes, the most common are: cerebrovascular disease; cerebral tumours; genetic, congenital, or hereditary conditions; head trauma (including neurosurgery); and post-infective causes (encephalitis and meningitis). Disease outcomes are also heterogeneous. Most people who develop epilepsy during their life have a relatively short-lasting susceptibility to seizures and enter remission shortly after starting treatment with antiepileptic drugs (AEDs). However, at least 20-30% of people who develop epilepsy will have incomplete seizure control and will have ongoing seizures for many years, if not lifelong, despite AED treatment.

### How common is epilepsy?

Epilepsy affects over 300,000 people in the UK and over 50 million people worldwide. In the UK a typical GP will: Be treating ten people with epilepsy. See one or two new cases per year. Care for about 15-25 people who have had seizures in the past, but who have either not been treated or who have stopped treatment.

### Diagnosing Epilepsy and Starting Treatment

**Who should make a diagnosis of epilepsy?** It is thought that more than 90,000 people in England and Wales are wrongly given a diagnosis of epilepsy each year. Thus, it is recommended that all individuals with a suspected seizure should be seen urgently (ideally within two weeks) by a 

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### Table ONE: Classification of epileptic seizures according to clinical type

<table>
<thead>
<tr>
<th>Partial (focal, local) seizures</th>
<th>Generalised seizures (convulsive or non-convulsive)</th>
<th>Unclassified seizures</th>
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</thead>
<tbody>
<tr>
<td>Simple partial seizures (consciousness not impaired).</td>
<td>Absence seizures (impairment of consciousness alone or with; mild clonic, atonic or tonic components; automatisms; and/or autonomic symptoms/signs).</td>
<td>Myoclonic seizures</td>
</tr>
<tr>
<td>With motor signs</td>
<td>Atypical absence</td>
<td>Clonic seizures</td>
</tr>
<tr>
<td>With somatosensory or special sensory symptoms (tingling, light flashes, buzzing).</td>
<td></td>
<td>Tonic seizures</td>
</tr>
<tr>
<td>With autonomic symptoms or signs (e.g. epigastric sensation, pallor, sweating, flushing, piloerection, and papillary dilatation).</td>
<td></td>
<td>Tonic-clonic seizures</td>
</tr>
<tr>
<td>With psychic symptoms, e.g. déjà vu, distortion of time sense, fear.</td>
<td></td>
<td>Atonic seizures</td>
</tr>
<tr>
<td>Complex partial seizures (with impairment of consciousness).</td>
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<td></td>
</tr>
<tr>
<td>With simple partial onset followed by impairment of consciousness.</td>
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<td></td>
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<tr>
<td>Partial seizures evolving to secondarily generalised seizures (may be tonic-clonic, tonic or clonic).</td>
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<td></td>
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<tr>
<td>With impairment of consciousness at onset.</td>
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specialist. A person diagnosed as having epilepsy would usually be managed by a specialist until their condition is stable. Adults are often discharged back to the care of their GP, if this is felt to be appropriate, but they should have the option of review by a specialist.

After a first seizure, how likely is it that further seizures will occur?

Recurrence risk after a first seizure varies greatly. The risk is lowest (13-40%) for provoked seizures, or in people with a normal EEG and no identifiable cause. The risk is highest (up to 90%) in people with epileptic discharges on EEG, or with congenital neurological defects. The overall risk is 30-40%. Recurrence is most likely in the first 12 months, and falls to less than 10% after 2 years. Treatment with AEDs halves the recurrence risk.

When is it appropriate to consider starting an AED?

Treatment with an AED is generally recommended after second seizure, unless these are separated by an extended time period (several years or more). Recent evidence shows no difference in the long-term outlook for deferred versus immediate treatment, which justifies the practice of waiting for further events rather than starting treatment immediately after a single seizure. Patients perceived to be at high risk of recurrence because of a structural abnormality thought to be responsible for their seizure, an abnormal EEG, a pre-existing neurological deficit, or an initial high density of seizures, should, however, still be offered an AED at the first opportunity. The same holds true for those who, on understanding the risks of recurrence and the scope and limitations of AEDs wish to take medication to reduce the risk of a further seizure.

Drug Treatment of Epilepsy in Adults

More than 20 AEDs are licensed worldwide. These drugs suppress the symptom (seizures) rather than modify disease process (epileptogenesis). There is no evidence that the drugs used at present change the longer term prognosis for most people.

Randomised controlled trials (RCTs) in epilepsy provide useful data for guiding drug treatment. However, epilepsy studies are generally short term and usually do not take into account the heterogeneity of patients in terms of epilepsy syndrome, associated comorbidities, and lifestyle factors that direct advice on individual treatment options.

Why are patients given AEDs?

The aim of drug treatment of epilepsy is to control seizures as quickly as possible without adverse effects. Improved seizure control is likely to reduce the morbidity and premature mortality associated with continuing seizures, especially convulsive attacks. Further, seizure remission is the major determinant of good quality of life.

By taking AEDs, most people with epilepsy can have good control of seizures and this can enable them to lead a normal life. Up to 70% of people with epilepsy can be completely seizure-free on an appropriate drug and dose for their epileptic syndrome. This usually requires careful and rigid adherence to drug regimens, which involve taking medication regularly each day for many years, sometimes for a lifetime.

Old and New AEDs

Conventionally, AEDs are divided into older drugs and new drugs, according to whether or not they were available before the 1990s (See Table TWO). Newer AEDs have often been promoted as having advantages over old drugs. There is, however, no evidence that new drugs are more effective, although they might be better tolerated, than older drugs.

A study known as SANAD (Standard and New Antiepileptic Drugs) comparing new and older AEDs has reported recently. SANAD was a large multi-centre, unblinded RCT in hospital-based outpatients clinics in the UK. Its aim was to help physicians select a first-line drug in light of the number of new AEDs that have become available.

Should the results of the SANAD study change practice?

SANAD concluded that lamotrigine is the drug of first choice for patients with partial epilepsy, and valproate for generalised and unclassifiable epilepsy.

What does NICE recommend with respect to using newer AEDs?

NICE guidance states that the newer AEDs are recommended for the management of epilepsy in people who have not responded to treatment with older AEDs, or for whom the older AEDs are unsuitable because:

- There are contraindications to their use,
- They could interact with other drugs the person is taking (notably oral contraceptives),
- They have been poorly tolerated,
- The patient is a woman of childbearing potential.

However, the NICE guidelines have not been received with overwhelming acceptance by clinicians, many of whom believe that newer AEDs may offer advantages over the older ones. Ultimately, the choice of one AED will be determined by an individual risk-benefit assessment in which the most effective drug for an individual patient is chosen.

Starting an AED

Who should initiate AED therapy?

AED therapy should be initiated on the recommendation of a specialist. If management of the condition is straightforward, continuing AED treatment can be prescribed in primary care if local arrangements and/or licensing allow.

Why is dose titration required when initiating AEDs?

Most AEDs are not well tolerated if treatment is started at the full therapeutic dosage. In particular:

- Benzodiazepines, topiramate, tiagabine and vigabatrin may produce prominent CNS adverse effects when started at levels close to the recommended maintenance dosages.
- Starting lamotrigine or carbamazepine at full dosages may result in an unacceptable high risk of idiosyncratic reactions.

To avoid these adverse effects, most AEDs should be introduced cautiously and the dose stepped up gradually. Titration of the drug is usually symptom-led, and if seizures are still taking place, the drug should be titrated up to the maximum dose. If toxic effects occur at any stage, the dose should be reduced.

Are there any AEDs that can be started at the therapeutic dose?

Phenobarbital, levetiracetam, valproate and gabapentin are probably the drugs that are best tolerated when started at full dosage, and may therefore be used preferentially whenever there is a need to minimise the time to onset of therapeutic action.

Stopping or withdrawing AEDs

Is seizure-remission common?

<table>
<thead>
<tr>
<th>Table TWO: Older &amp; Newer AEDs</th>
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<tbody>
<tr>
<td><strong>“Older” AEDs</strong></td>
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<tr>
<td>Carbamazepine</td>
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<tr>
<td>Ethosuximide</td>
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<tr>
<td>Phenytoin</td>
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<tr>
<td>Sodium valproate</td>
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</table>

Box ONE: NICE guidelines key points

- Diagnosis should be made urgently by a specialist with an interest in epilepsy.
- NICE recommends that an EEG should be performed only to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin. An EEG should not be used in isolation to make a diagnosis of epilepsy.
- Seizure types and epilepsy syndrome, cause, and co-morbidity should be determined.
- Initiation of appropriate treatment recommended by a specialist.
- Treatment should be individualised according to the seizure type, epilepsy syndrome, co-medication and co-morbidity, individual’s lifestyle, and personal preferences.
- Comprehensive care plans should be agreed.
- Regular structured review should be undertaken at least once a year.
- Refer back to secondary/ tertiary care if - epilepsy inadequately controlled, or - pregnancy considered or pregnant, or - AED withdrawal considered.
Stopping or withdrawing AEDs

Is seizure-remission common?
Yes, remission of seizures is common. At 9 years after diagnosis about 70% of people will have been seizure-free for the preceding 3 years and only about 30% will still be on medication.29,30 Predictors of a good outcome include earlier age of onset, fewer early seizures,31,32 and early response to drug treatment.33

When can AEDs be stopped?
Whether to continue or stop AED treatment in patients with prolonged seizure remission is still a controversial issue and the optimal time to consider AED withdrawal is unclear. Most studies in this area involve patients who stop AEDs when they have been seizure free for a minimum of two years. On this basis, the NICE and SIGN guidelines recommend that patients should be seizure-free for at least two years before treatment withdrawal is considered.11,12

Who should decide if it is appropriate to withdraw AEDs?
Whether to continue or withdraw AEDs should be decided following discussion between the individual and their epilepsy specialist.11,12 Although patients may have been in remission for some time, AED withdrawal may lead to seizure recurrence in some.24 The consequences of this on driving, employment and lifestyle should be discussed in detail before deciding to withdraw AEDs. (Further information on epilepsy and driving is given later.)

Which patients are at highest risk of seizure recurrence after AED withdrawal?
The risk of seizure recurrences has been studied in a large RCT35 of continued treatment versus slow withdrawal in individuals who had been seizure free for at least two years. This study found that the risk of seizure recurrence was higher in those:
- Patients over 16 years
- Taking more than one AED
- With seizures after starting medication
- With tonic-clonic or myoclonic seizures
- With an abnormal EEG in the last year

How should AEDs be withdrawn?
Withdrawal features such as recurrent seizures, and rare symptoms such as anxiety, panic, restlessness and sweating, can usually be avoided if the dose is reduced gradually over a period of months rather than stopped abruptly.36 Guidelines suggest when withdrawing carbamazepine, lamotrigine, phenytoin, valproate or vigabatrin, the dose should be reduced by about 10% every two to four weeks.11,12,22 Barbiturates, benzodiazepines and ethosuximide should be tapered more slowly, reducing the dose by about 10% every 4 to 8 weeks.11,12 When patients are taking a combination of AEDs, only one should be withdrawn at a time, with a period of one month between completing withdrawal of one drug and beginning withdrawal of the next.

Monitoring therapy with AEDs

Is routine Therapeutic Drug Monitoring (TDM) required for AEDs?
With the exception of phenytoin, routine monitoring of AED concentrations is not indicated.11,12 In most people, seizure control and development of adverse effects determine the dose. Measurement of AED blood levels should only be carried out if clinically indicated in selected situations;11,12
- When doubts exist about compliance,
- Where toxicity is suspected,
- To manage pharmacokinetic interactions,
- When seizures occur in a previously well-controlled patient.

What is known about the desired therapeutic ranges of the AEDs?
For several AEDs, ranges of serum concentrations have been established that are associated with optimal therapeutic effects in most patients. However, these concentrations have statistical value only. Clinical studies have repeatedly showed that large inter-patient variability exists in responses achieved at any given serum drug concentration.25 For the best response, many patients require serum drug concentrations outside these ranges.26 Thus, AED dosages should be individualised to maximise therapeutic benefit and avoid adverse effects.

Why is particular caution required with phenytoin?
In the case of phenytoin, the checking of serum concentrations may be helpful. Phenytoin has a narrow therapeutic range and the relationship between dose and plasma concentration is non-linear. Thus, small dosage increases may produce large rises in plasma concentrations with acute toxic side effects. The therapeutic range is only a rough guide; many patients obtain seizure freedom with concentrations below this range, whereas others tolerate and require concentrations above this range.

What other monitoring is required for someone on an AED?
Minor blood dyscrasias are associated with many AEDs; the majority (for example, mild leucopenia with carbamazepine, or thrombocytopenia with valproate) require no action. Severe blood dyscrasias occur in 6 in 10,000 patients and although there is no evidence to suggest that routine monitoring can reduce this risk,36,41 the NICE guideline recommends that full blood counts are taken every 2-5 years for adults taking enzyme-inducing AEDs.11

Prescribers, other healthcare professionals and patients themselves should be alert for the symptoms of bone marrow failure (anaemia, bruising, infection)

Adverse Effects of AEDs

Adverse drug reactions are common with AEDs and are a major cause of drug withdrawal. Most are mild but a minority can be life threatening. Many adverse effects are dose related and may occur at therapeutic doses. Accurate data on the prevalence of adverse drug reactions with long-term AED therapy are scarce; almost all reports refer to short term clinical trials and, as experience with vigabatrin and visual field defects has shown, long term surveillance is needed to identify all adverse drug reactions.42
- Minor blood dyscrasias (See earlier)
- Acute psychotic reactions are seen occasionally with topiramate ▼, levetiracetam and zonisamide ▼, particularly in those patients with a previous history of psychiatric disease. Withdrawal of the drug usually results in recovery.43 There is a risk of depression related to barbiturates and topiramate ▼, and possibly phenytoin.44 Underlying depression and anxiety symptoms may be exacerbated by levetiracetam.
- Weight gain is seen with many AEDs but significant weight gain (that is more than 10% of body weight) is particularly associated with valproate.45 Weight loss is frequently observed with topiramate ▼.46 The average weight loss is about 4 kilograms, appears to be dose-related and is more common in heavier patients.46
- Sedation and dizziness are common complaints of patients starting AED therapy but usually resolve with time. Sedation may be less with the newer AEDs.
- Many patients on long term AED therapy report cognitive side-effects but studies to confirm this have been contradictory and confounded by the effects of chronic epilepsy and by poor study design.37 Difficulty finding words seems to be a fairly specific problem with topiramate ▼ and is reported as an ADR in up to one third of patients.45
- Effects on Bone – AEDs have been implicated in bone disease since the 1960s.44 While the reported prevalence of bone disease varies, studies have found osteomalacia in as many as 75% of patients on long-term AED treatment (>10 years).49 Epilepsy has been associated with a decreased bone mineral density50 and an increased fracture risk.51 The increased fracture risk may be the result of increased risk of trauma due to seizures.51,52 and/or decreased bone mineral density and thus a more frail skeleton.53,54 The decreased bone mineral density may be the result of AEDs having an influence on bone metabolism.55 Patients using AEDs for more than 2 years, in particular those taking enzyme-inducing AEDs and those older than 40 years, have significantly lower bone mineral density.56 The most recent SIGN guidelines on epilepsy12 indicate that patients taking
AEDs should receive advice on diet and exercise to minimize the risk of bone loss.

- Patients should be advised of the possibility of skin reactions. These may be severe particularly with carbamazepine and lamotrigine. (Allergic skin reactions are the ADR that most frequently requires withdrawal of lamotrigine.) Rashes develop in about 12% of patients, typically within the first eight weeks of lamotrigine administration.57 These necessitate drug withdrawal in about 3% of cases. Rarely, severe cutaneous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been associated with lamotrigine,62 particularly when it is used in combination with valproate. The risk of allergic reaction is related to the initial plasma concentration; low starting doses and titration should always be used.

- Peripheral visual field defects associated with the use of vigabatrin are well documented. This irreversible, typically asymptomatic, bilateral loss of concentric visual fields occurs in 40% of chronically exposed patients.59-61 Patients should undergo systematic screening examination when starting vigabatrin and at regular intervals for detection of visual field defects. Visual field testing should continue at 6-month intervals for the whole duration of treatment.

**Drug Interactions with AEDs**

AEDs exhibit a wide range of drug interactions, which constitute a major concern for the healthcare professional. This applies particularly to AEDs which may induce or inhibit cytochrome P450. (See prescribing point) Drug-drug interactions are reported to give rise to adverse effects in at least 6% of subjects with epilepsy.52 When multiple drug therapy is used, there is a possibility of clinically relevant drug interactions, which in people with epilepsy, are particularly common for a variety of reasons:63,64

1. AEDs are administered for prolonged periods, often for a lifetime, thereby increasing the probability of co-prescription;
2. Most AEDs have a narrow therapeutic index, and even relatively modest alterations in their pharmacokinetics can result in loss of response or toxic effects;
3. Some of the most widely used AEDs have prominent effects on the activity of enzymes which metabolise drugs;
4. Most of the old and new generation AEDs are substrates of the same enzymes.

**Which AEDs will interact with each other when used together?**

When two or more AEDs are combined, interactions may occur at a pharmacokinetic level (involving a change in the absorption, distribution or elimination of the affected drug) and/or at a pharmacodynamic level (resulting in additive, antagonistic or synergistic effects at the site of action).28

**Table THREE** summarises the important interactions amongst the AEDs when they are used concomitantly.55-68

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**What other drugs will interact with AEDs?**

**Table FOUR** summarises the clinically significant drug interactions of the AEDs.

**Epilepsy and Alcohol**

**Can a person on AED(s) consume alcohol?**

Alcohol consumption of 1-2 units per day is usually safe for most people taking AEDs, but excessive alcohol intake and binge drinking should be avoided. Those who drink heavily may not respond to standard doses of some AEDs, and in particular may need to be prescribed higher doses of phenytoin and possibly carbamazepine to maintain adequate serum levels. Alcohol withdrawal may trigger epileptic seizures in some people.12

There are however, some individuals for whom polytherapy cannot be avoided. **When would combination therapy be considered?**

In people whose epilepsy is refractory to two or three AEDs at maximally tolerated dosages given as monotherapy, combination therapy may be tried. The therapeutic gain from adjunctive therapy is often marginal and may be complicated by the increased risk of adverse effects and drug interactions.65 Some evidence indicates that not all types of combination therapy are equal and that specific drug combinations exist which provide improved therapeutic benefit with a lower risk of adverse effects. For example,

- A combination of valproate and lamotrigine exhibits a favourable outcome in some patients with complex partial seizures resistant to other AEDs.71
- Refractory absence seizures may respond to dual therapy with valproate and ethosuximide.69

If combination therapy does not bring about worthwhile benefits, treatment should revert to the regimen (monotherapy or combination therapy) that has proved most acceptable to the individual, in terms of providing the best balance between effectiveness in reducing seizure frequency and tolerability of side effects.11,71

**What are the potential side effects of polytherapy?**

Drug-drug interactions may result in loss of response or toxic effects; alteration in their pharmacokinetics can be avoided by the increased risk of adverse effects and drug interactions.70 When multiple drug therapy is used, there is a possibility of clinically relevant drug interactions, which in people with epilepsy, are particularly common for a variety of reasons:63,64

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### Epilepsy and Mortality

People with epilepsy have an increased risk of premature death.73 Symptomatic epilepsy can reduce life expectancy by up to 18 years.73 Sudden death, trauma, suicide, pneumonia, and status epilepticus are more common in people who have epilepsy than those without the disorder.75 The most common epilepsy-specific cause of death is sudden unexpected death in epilepsy (SUDEP).76,77

#### What is SUDEP?

Sudden unexpected death in epilepsy (SUDEP) has been defined as “a sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy, with or without evidence of seizure and excluding documented status epilepticus, in which post-mortem examination does not reveal a toxicological or anatomical cause of death”.78

#### How common is SUDEP?

The risk of SUDEP is small for most people with epilepsy. Of the 1,000 epilepsy-related deaths each year in the UK, around half are thought to be due to SUDEP.78 In people with refractory epilepsy attending specialist clinics, the yearly rate is 1 per 200. The highest risk is in male teenagers and young adults with convulsive seizures.30

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### Table FOUR: Clinically significant drug interactions of the AEDS

<table>
<thead>
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<th>Drug</th>
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<tr>
<td>Combined oral contraceptives (COCs)</td>
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<td>Significant reduction in levels of circulating hormones. Give at least 50 micrograms of oestrogen.</td>
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<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
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<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Primidone</td>
<td></td>
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<tr>
<td>Topiramate ▼ (at doses ≥ 200mg/day)</td>
<td>Lamotrigine</td>
<td>Seizure frequency can increase and lamotrigine serum concentration can decrease when a COC is initiated. While there is no evidence that lamotrigine reduces the effectiveness of hormonal contraceptives, the possibility of reduced contraceptive effectiveness cannot be ruled out.</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Phenyoitin</td>
<td>Topiramate can reduce plasma concentrations of digoxin. The clinical relevance of this observation has not been established. When topiramate is added or withdrawn in patients on digoxin therapy, careful attention should be given to the routine monitoring of serum digoxin.</td>
</tr>
<tr>
<td>Macrolide antibiotics (erythromycin, clarithromycin)</td>
<td>Carbamazepine</td>
<td>Plasma levels of carbamazepine are markedly and rapidly increased by erythromycin and to a lesser extent by clarithromycin. Toxicity can develop within 1-3 days. Concurrent use of carbamazepine with either erythromycin or clarithromycin should be avoided. Azithromycin appears not to interact with carbamazepine.</td>
</tr>
<tr>
<td>Omeprazole, esomeprazole</td>
<td>Phenytoin</td>
<td>Esomeprazole (and possibly omeprazole) enhances effects of phenytoin. Phenytoin dosage may require adjustment.</td>
</tr>
<tr>
<td>SSRIs</td>
<td>Carbamazepine</td>
<td>Consideration should be given to the fact that SSRIs have been known to cause seizures. Carbamazepine levels can be increased by fluoxetine and fluvoxamine. The interaction appears to be rare and reports are inconsistent. However, it would be prudent to monitor concurrent use of carbamazepine and SSRIs. Be alert for the need to reduce the carbamazepine dosage.</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Carbamazepine</td>
<td>Plasma levels of theophylline and carbamazepine can fall when the two are given concurrently. Reports of this interaction are limited so concurrent use need not be avoided but careful monitoring would be prudent.</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Carbamazepine</td>
<td>Metabolism of warfarin accelerated by carbamazepine. Anticoagulant effects of warfarin can be reduced. Careful INR monitoring is advised.</td>
</tr>
<tr>
<td></td>
<td>Phenobarbital</td>
<td>Phenobarbital accelerates the metabolism of theophylline (reduced theophylline effect).</td>
</tr>
<tr>
<td></td>
<td>Phenytoin</td>
<td>Plasma concentrations of both theophylline and phenytoin are reduced when both are given together. This interaction is well established and clinically important. Monitor the effects of both drugs carefully.</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
<td>The effects of warfarin are reduced by phenobarbital. Full anticoagulation may only be achieved by raising the warfarin dose by about 30-60%.</td>
</tr>
<tr>
<td></td>
<td>Phenobarbital</td>
<td>The effects of warfarin are reduced by phenobarbital. Full anticoagulation may only be achieved by raising the warfarin dose by about 30-60%.</td>
</tr>
<tr>
<td></td>
<td>Phenytoin</td>
<td>Metabolism of warfarin accelerated by phenytoin or primidone. Anticoagulant effects of warfarin can be reduced. Careful INR monitoring is advised.</td>
</tr>
</tbody>
</table>

*Note: This is not meant to be exhaustive but highlights those interactions most commonly encountered.*

---

### What are thought to be the causes of SUDEP?

Studies have identified possible risk factors but no mechanism for SUDEP.81 When it occurs, SUDEP usually follows a generalised tonic-clonic seizure. Although not fully understood, three mechanisms have been proposed for SUDEP:

1. **Cardiac arrhythmia** caused either by AEDs or by seizures themselves.
2. **Neurogenic pulmonary oedema** caused by increases in pulmonary vascular permeability that occurs during a seizure.
3. **Postictal suppression of brainstem respiratory centres** leading to central apnoea.

### Which patients are at particular risk of SUDEP?

Reported risk factors for SUDEP are thought to include:

- Frequently generalised tonic-clonic seizures. As few as one to three tonic-clonic seizures per year increases the risk of SUDEP.84
- Simultaneous treatment with two or more AEDs. The association between SUDEP and AED polytherapy is a further reason to use only as many AEDs as are needed.
- Age 20-40 years.
- Acquired epilepsy (primarily from traumatic brain injury orencephalitis/meningitis).
- Intractable epilepsy.
- Frequent changes of AEDs.
- Early onset epilepsy.

In the past there have been questions asked about the possible role of carbamazepine in SUDEP.85 Currently it is agreed that frequent changes of carbamazepine dose with concentrations outside the therapeutic range are more likely to constitute a risk factor than use of carbamazepine itself.82

### What can be done to minimise deaths from SUDEP?

Following the publication of the clinical audit by the charity Epilepsy Bereaved that looked at epilepsy-related deaths in the UK,75 the following recommendations were made:86

- Patients at risk of SUDEP should be identified, and they and their families educated about this possibility.
- Treatment of continuing seizures should be early and aggressive.
- Compliance with AEDs should be promoted.
- Seizure precipitants should be identified.

The National Epilepsy Association recommends several precautions that may reduce the risk of harm during seizures; for further information see www.epilepsynse.org.uk.
Epilepsy in women – Special Considerations

What particular issues should be considered in women of childbearing age?
In order to enable informed decisions and choice, and to reduce misunderstandings, women with epilepsy and their partners, as appropriate, must be given accurate information and counselling about contraception, conception, pregnancy, breastfeeding, and the menopause.

Contraception
Women with epilepsy who are treated with AEDs face unique challenges in contraception. Advice on contraception should be given before women are sexually active.11,12 Women who take AEDs have a high oral contraceptive failure rate.95 In women and girls of childbearing potential, and girls who are likely to need treatment into their childbearing years, the possibility of an interaction between AEDs and oral contraceptives should be discussed and an assessment made of the risks and benefits of treatment with individuals.5

Can the combined oral contraceptive (COC) pill have an effect on seizure control?
In general COCs do not aggravate epileptic seizures,90,91 and may improve seizure control in some patients. The proconvulsant effects of oestrogens have been demonstrated,92 but tend to be balanced by the anticonvulsant properties of progestogens.93

Can oral contraceptives have an effect on AED serum levels?
In 2005, physicians were warned that levels of lamotrigine may drop when the oral contraceptive is prescribed. Studies confirm that administration of a COC causes a decrease in serum lamotrigine levels by about 50%,94 which may lead to loss of seizure control in some women.96

Conversely, a rebound increase in serum lamotrigine levels with possible signs of toxicity may be observed when the COC is discontinued. This interaction follows a cyclical pattern, with a marked decrease in serum lamotrigine levels during the 21 days of intake of the COC, and an increase in lamotrigine concentration during the pill-free week.96 In women taking lamotrigine, a hormonal contraceptive should only be used if there is no other alternative. If the COC is chosen as the sole method of contraception, women should be advised to promptly notify their physician if they experience changes in menstrual pattern (e.g. breakthrough bleeding) while taking lamotrigine as this may be an indication of decreased contraceptive efficacy. Women taking lamotrigine should notify their physician if they plan to start or stop use of COC.

Can AEDs affect the efficacy of the COC?
The interactions between enzyme-inducing AEDs (See Table FOUR) and the COC have been recognised for many years.97,98 Enzyme induction by AEDs can substantially decrease the concentration of circulating oestrogen and reduce unbound progestogene. In the general population, the COC has a failure rate of 0.1%.99 However, when used in concurrently with an enzyme-inducing AED, this rate may increase to 2.5%.100

A COC regimen containing a minimum dose of 50micrograms of ethinylestradiol should be tried first by taking two low-dose COCs providing a total daily dose of 50-60micrograms ethinylestradiol. If breakthrough bleeding occurs with 50micrograms of ethinylestradiol the dose may be increased to 80-100 micrograms101 and “tricycling” of the COC considered [this involves taking three packs of high dose COC without interruption followed by a reduced pill-free interval of four days102].

Are other forms of hormonal contraception suitable for women taking AEDs?
The progestogen-only contraceptive pill is likely to be unreliable in women taking enzyme-inducing AEDs.11,103

Progestogen-only contraceptive injections (Depo-Provera8, Noristerate 6) will theoretically interact with enzyme-inducing AEDs. While the recent NICE guidelines recommend increasing the frequency of injection for women taking such drugs to every 10 weeks from the usual 12 weeks,11 the Faculty of Family Planning and Reproductive Healthcare (FFPRHC) have advised that every 12 weeks is sufficient.104

Progestogen-only implants (Implanon®) are not reliable if used concomitantly with enzyme-inducing AEDs.105

Intra-uterine devices containing progestogen (Mirena®) can be used along with any AED. This is because levonorgestrel is released directly into the uterine cavity, contraceptive effects are mainly local and therefore not thought to be affected by AEDs.106-108 In view of this, they are a good choice of contraception in women taking enzyme-inducing AEDs.2

Combined contraceptive patches (Evra®) are unreliable in women on an enzyme-inducing AED. Other methods of contraception are advised.2

Can women on AEDs use Emergency Hormonal Contraception?
For women who wish to use progestogen-only emergency contraception (Levonelle®) and are taking enzyme-inducing AEDs, the FFPRHC advise that a dose of 3milligrams (two of the 1.5mg Levonelle® tablets) are taken soon as possible and within 72 hours of unprotected intercourse.109 There are no published studies on compliance or side-effects with this regimen and it is outside the product licence.

Any women on an enzyme-inducing AED who requests an “over-the-counter” sale of Levonelle® from her community pharmacist should be referred to her GP.

Epilepsy and pregnancy

What is the effect of the menopause on seizure frequency?
Information about the effects of the menopause on epilepsy is limited but seizure frequency is thought to increase in about 40% of women around menopause.110

If, during her reproductive years, a woman with epilepsy experienced seizures triggered by hormonal changes during her menstrual cycle, she is at particular risk for an increase in seizure frequency during peri-menopause but may experience a seizure reduction after becoming menopausal.111 These women appear to represent a subgroup of patients with epilepsy who have heightened sensitivity to endogenous reproductive hormone levels.111 110

Can Hormone Replacement Therapy (HRT) be prescribed for women with epilepsy?
Some studies show that HRT can increase seizure frequency.112 whilst others demonstrate that HRT has no effect on seizure frequency.112 HRT can be offered to postmenopausal women with epilepsy if it is clinically indicated for the management of menopausal symptoms.112 In women who are taking enzyme-inducing AEDs standard doses of HRT may not be effective.12 Some dosage adjustment may be necessary.
Managing Depression in Someone with Epilepsy

Depression is the most common co-morbid condition affecting patients with epilepsy. It affects up to 55% of patients with refractory epilepsy and up to 9% of those with well-controlled seizures, while anxiety is estimated to occur in 3-50% of individuals with epilepsy.\textsuperscript{113}

**Can AEDs have negative psychotropic effects?**

With the exception of the barbiturates, the evidence for any negative psychotropic effects is largely anecdotal or based on small case series. Vigabatrin is thought to be associated with depressive episodes\textsuperscript{114} and these appear to be dose related.\textsuperscript{115} Tiagabine and topiramate are also associated with an increased rate of depressive disorders,\textsuperscript{116} however, titrating these drugs slowly is likely to minimize these symptoms.\textsuperscript{115}

AEDs that do not carry an increased risk of depression include lamotrigine, gabapentin, and levetiracetam.\textsuperscript{117}

**Which antidepressants can exacerbate epilepsy?**

The risk of antidepressant-induced seizures is well known, particularly in people with epilepsy.\textsuperscript{118} In general, use of tricyclic antidepressants (TCAs) is not advisable in patients with epilepsy.\textsuperscript{119} Amongst the TCAs, clomipramine carries a relatively high risk of provoking seizures.\textsuperscript{117} Amitriptyline and imipramine can induce seizures at high daily doses.\textsuperscript{115} Seizures have been reported in 0.26% of patients treated with venlafaxine.\textsuperscript{120}

**Which antidepressants are safer in epilepsy?**

The BNF advises that SSRIs should be used with caution in patients with epilepsy; however SSRIs are associated with a lower incidence of seizures at therapeutic doses compared to TCAs. Citalopram,\textsuperscript{121} fluvoxamine,\textsuperscript{122} and paroxetine have not been reported to have a proconvulsive effect. Fluoxetine also has a favourable seizure profile.\textsuperscript{123} Unless a large scale trial is carried out, the safest antidepressant in epilepsy will remain unknown. All patients require an individual assessment of their risk factors and recognition that there is a dose-dependent relationship between antidepressants and seizures. A slow rate of introduction of the antidepressant reduces the risk.\textsuperscript{120}

**What clinically important interactions occur between AEDs and antidepressants?**

Higher doses of SSRIs may be needed to achieve the desired clinical effect when given in conjunction with enzyme-inducing AEDs.\textsuperscript{115} Antidepressants should be started at a low dosage and the dose slowly titrated.\textsuperscript{115} It is known that:

- Carbamazepine, phenytoin and primidone reduce paroxetine levels.\textsuperscript{124}
- Fluoxetine and fluvoxamine can increase carbamazepine or phenytoin levels.\textsuperscript{124}
- Carbamazepine or phenytoin can reduce levels of TCAs.\textsuperscript{124}
- Co-administration of sertraline with lamotrigine can lead to lamotrigine toxicity.\textsuperscript{125}

**Complementary Medicine and Epilepsy**

**Are complementary therapies useful in the management of epilepsy?**

There is no evidence to support the use of acupuncture, herbal medicines, homeopathy, osteopathy or yoga instead of AEDs and no evidence that these improve seizure control when used along with AEDs.\textsuperscript{125-127}

**Should people suffering from epilepsy avoid any complementary therapies?**

Patients should be asked about their use of complementary medicines and warned about the possibility of adverse effects. Problems may arise because of interactions between complementary therapies and prescribed medication. The potential reduction in plasma concentrations of carbamazepine, phenobarbital and phenytoin should be noted if St John’s Wort is used concomitantly.\textsuperscript{122} Case reports in the literature indicate that Ginkgo biloba may have precipitated seizures in patients with previously well-controlled epilepsy.\textsuperscript{129} Caution is also advised in the use of Evening Primrose Oil but the evidence for this is less robust.\textsuperscript{130} Some aromatherapy preparations (hyssop, rosemary, sweet fennel, sage and wormwood) may exacerbate seizures.\textsuperscript{132}

**Epilepsy and Driving**

The following are the recommendations of the Driver and Vehicle Agency (DVA) with regard to epilepsy and driving either cars or motorcycles:

- A person who has suffered an epileptic attack whilst awake must refrain from driving for one year from the date of the attack.
- A person who has suffered an attack whilst asleep must also refrain from driving for one year from the date of the attack. However, if they had an attack whilst asleep more than three years previously and have not had any awake attacks since that original sleep attack then they may drive even though asleep attacks may continue to occur. If an awake attack subsequently occurs then the formal epilepsy regulations apply requiring one year off driving.
- In anyone undertaking withdrawal from AEDs, driving should cease from the commencement of the period of withdrawal and for six months after withdrawal is complete.

In any of the above situations, the licence holder must notify the Driver and Vehicle Agency.

**Standards of care and Medicines Management for someone with epilepsy.**

All people with epilepsy should have:

- An accessible point of contact with specialist services,
- A comprehensive care plan that is agreed between the individual, family and/or other carers where appropriate, and primary care and secondary care providers. This should include lifestyle as well as medical issues,
- Access to an epilepsy specialist nurse.

**How can adherence to treatment be optimised?**

- Educate individuals and their families and/or carers in the understanding of their condition and the rationale of treatment,
- Use simple medication regimens,
- Reduce the stigma associated with the condition.
• Strive for a positive relationship between healthcare professionals, the person with epilepsy, and their family and/or carers.

Strive for a positive relationship between healthcare professionals, the person with epilepsy, and their family and/or carers.

**Review of someone with epilepsy**

People with epilepsy should have regular, structured reviews. Treatment should be reviewed to ensure that individuals with epilepsy are not maintained for long periods on treatment that is ineffective or poorly tolerated, and that concordance with prescribed medication is maintained. The frequency of review will be determined by the individual’s epilepsy and their wishes.

**GMS Contract**

Epilepsy is one of the specific disease areas for which quality-standard indicators have been introduced in the new General Medical Services (GMS) contract quality and outcomes framework (See Table FIVE). The recognition of epilepsy in the contract is a reflection of the considerable efforts of the major epilepsy patient organisations to raise the profile of this distressing and debilitating illness. The GMS contract quality indicators encourage the development of registers of people with epilepsies in each practice. These are to be used to ensure that people diagnosed with epilepsy are regularly assessed.

Within integrated care, primary care services have a vital role in the management of epilepsy, especially in the coordination of care with particular emphasis on social, psychological and emotional support.

It should be recognised that the evidence base for many aspects of the care of patients with epilepsy is limited. There is currently a lack of evidence to suggest that meeting the quality standard indicators will lead to important outcomes, such as reduced seizure frequency and severity, or reduced mortality for patients with epilepsy.

<table>
<thead>
<tr>
<th>Table FIVE: QOF2 Clinical Indicators: Epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indicator</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>EPILEPSY 5</td>
</tr>
<tr>
<td>The practice can produce register of patients aged 18 and over receiving drug treatment for epilepsy.</td>
</tr>
<tr>
<td>EPILEPSY 6</td>
</tr>
<tr>
<td>The percentage of patients aged 18 and over on drug treatment for epilepsy who have a record of seizure frequency in the previous 15 months.</td>
</tr>
<tr>
<td>EPILEPSY 7</td>
</tr>
<tr>
<td>The percentage of patients aged 18 and over on drug treatment for epilepsy who have a record of medication review involving the patient and/or carer in the previous 15 months.</td>
</tr>
<tr>
<td>EPILEPSY 8</td>
</tr>
<tr>
<td>The percentage of patients aged 18 and over on drug treatment for epilepsy who have been seizure-free for the past 12 months recorded in the previous 15 months.</td>
</tr>
<tr>
<td><strong>Total points</strong></td>
</tr>
</tbody>
</table>

**Information Sources and Web sites**

- The Expert Patients Programme (www.expertpatients.nhs.uk)
- Joint Epilepsy Council of UK & Ireland (www.jointepilepsycouncil.org.uk)
- Epilepsy and Pregnancy Register (www.epilepsyandpregnancy.co.uk)
- Epilepsy Action (www.epilepsy.org.uk)
- National Society for Epilepsy (www.epilepsynse.org.uk)
- Website for Epilepsy Bereaved (www.sudep.org)
- International League Against Epilepsy (www.ilae-epilepsy.org)
- Driver and Vehicle Agency Northern Ireland (www.dvani.gov.uk)
**Table SIX: Summary for the AEDs**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Important points to remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Carbamazepine is a liver enzyme-inducing AED. It increases the metabolism of oestrogens and progestogens, and can reduce the effect of the oral contraceptive. Carbamazepine can even increase its own metabolism. St John’s Wort may reduce the plasma concentration of carbamazepine if used concomitantly. Rare idiosyncratic but serious adverse effects include Stevens-Johnson syndrome, exfoliative dermatitis, and hepatitis. Hypersensitivity occurs in 20% of people taking carbamazepine but is usually mild. If the hypersensitivity is clinically significant, restriction of fluid intake or a slight reduction in the dose of carbamazepine usually resolves the issue. Introduction slowly &amp; titrate dose upwards until seizures are controlled or until unsteadiness or drowsiness limit dose. At higher doses patients may complain of double or blurred vision. The incidence of dose-related adverse effects may be reduced by: • Altering the timing of the medication. • Use of modified-release tablets (to maintain peak plasma levels). Abrupt withdrawal of carbamazepine may precipitate seizures.</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Oxcarbazepine is an enzyme-inducing AED and is an analogue of carbamazepine. Common adverse effects include diplopia, headache, andnausea. Serious but rare dermatological reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme, have been reported. The median time to onset was 19 days. Patients or their carers should be told how to recognise the signs of blood, liver, or skin disorders, and advised to seek immediate medical attention if symptoms such as lethargy, confusion, muscular twitching, fever, sore throat, rash blistersing, mouth ulcers, bruising or bleeding develop.</td>
</tr>
<tr>
<td>Valproate</td>
<td>Use in pregnancy is not advised. Common adverse effects include: • Drowsiness, lethargy, and mental depression, as well as allergic skin reactions and hypokinesia. The most troublesome side effects are psychological or cognitive changes and weight loss. Acute myopia with secondary angle-closure glaucoma has been reported in 1 in 3 people taking vigabatrin. The CSM advises that onset of visual symptoms ranges from 1 month to several years after starting treatment. In most cases, visual field defects have persisted despite vigabatrin discontinuation. Product literature advises visual field testing before treatment and at 6-month intervals. Individuals taking vigabatrin should be warned to report any new visual symptoms that develop and those with symptoms should be referred for an urgent ophthalmological opinion and gradual withdrawal of vigabatrin considered. For s eizures.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Causes little cognitive impairment or overt sedation compared with other treatments. Common adverse effects include headache, tiredness, rash, nausea, dizziness, drowsiness, and insomnia. Can cause a maculopapular rash which necessitates drug withdrawal in about 3% of people. The incidence can be reduced by starting with a low dose and avoiding rapid increases in dose. Rare but serious skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been found to develop mainly within the first 8 weeks. Factors associated with the risk of serious skin reactions include: • Initial dosing higher than recommended, • More rapid dose escalation than recommended, • Concomitant use of sodium valproate. Lamotrigine can interact with the COC, although it is not an enzyme inducer. • The effect of COCs may be reduced, • Seizure control may be reduced in women who are stable on a lamotrigine dose and then start taking a COC. Adverse effects of lamotrigine may occur during withdrawal of a COC.</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Levetiracetam is licensed as both monotherapy and as adjunctive treatment. Drug interactions are unlikely. Well tolerated. Good efficacy. The most common adverse effects include dizziness and drowsiness. Other less common adverse effects include irritability, insomnia, emotional lability, ataxia, tremor, headache, andnausea. Adverse effects generally appear in the first month of treatment. Levetiracetam is an antiepileptic drug (AED) that is used to treat epilepsy. It is available as an oral preparation. Levetiracetam has a favourable profile with regard to cognitive dysfunction. Minimal adverse effects and interactions. Limited efficacy for s eizures.</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Dizziness may be a problem but can be eased with taking the drug with food. Other common adverse effects include tiredness, nervousness, tremor, concentration difficulties, and depressed mood. Rare cases of visual field defects have been reported with tiagabine. If visual symptoms develop, the patient should be referred to an ophthalmologist for further evaluation including perimetry. Short elimination half-life requires thrice daily administration in some patients.</td>
</tr>
<tr>
<td>Tiagabine</td>
<td>Treatment may only be initiated by a specialist. Follow-up should be arranged under supervision of a specialist. Common adverse effects include drowsiness (very common), nausea, agitation, aggression, irritability and depression. Visual field defects have been reported in 1 in 3 people taking vigabatrin. The CSM advises that onset of visual symptoms ranges from 1 month to several years after starting treatment. In most cases, visual field defects have persisted despite vigabatrin discontinuation. Product literature advises visual field testing before treatment and at 6-month intervals. Individuals taking vigabatrin should be warned to report any new visual symptoms that develop and those with symptoms should be referred for an urgent ophthalmological opinion and gradual withdrawal of vigabatrin considered. For s eizures.</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Topiramate is largely converted to oxcarbazepine. Both topiramate and oxcarbazepine are enzyme-inducing AEDs. Common adverse effects include drowsiness, lethargy, and mental depression, as well as allergic skin reactions and hypokinesia.thumb</td>
</tr>
</tbody>
</table>
Successful completion of this MCQ form equates with **3 hours** Continuing Professional Development / Continuing Medical Education. Circle your answer TRUE (T) or FALSE (F) for each question. When completed please post this form to the relevant address shown overleaf.

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1 Antiepileptic drugs:</strong></td>
<td></td>
</tr>
<tr>
<td>a. Should be initiated after a first seizure.</td>
<td>T F</td>
</tr>
<tr>
<td>b. Affect the prognosis of someone with epilepsy.</td>
<td>T F</td>
</tr>
<tr>
<td>c. Can help the majority of people with epilepsy to attain seizure-freedom</td>
<td>T F</td>
</tr>
<tr>
<td>d. Should not be stopped abruptly</td>
<td>T F</td>
</tr>
<tr>
<td><strong>2 Adverse effects associated with the use of AEDs:</strong></td>
<td></td>
</tr>
<tr>
<td>a. Can be dose-related and can occur at therapeutic doses.</td>
<td>T F</td>
</tr>
<tr>
<td>b. All patients on AED therapy need 6-monthly blood counts.</td>
<td>T F</td>
</tr>
<tr>
<td>c. Long-term AED use is associated with adverse effects on bone.</td>
<td>T F</td>
</tr>
<tr>
<td>d. The development of a skin rash is particularly associated with lamotrigine.</td>
<td>T F</td>
</tr>
<tr>
<td><strong>3 Epilepsy in women – special considerations:</strong></td>
<td></td>
</tr>
<tr>
<td>a. The combined oral contraceptive pill is epileptogenic.</td>
<td>T F</td>
</tr>
<tr>
<td>b. Intra-uterine devices containing progestogen (e.g. Mirena) can be used along with any AED.</td>
<td>T F</td>
</tr>
<tr>
<td>c. Women on an enzyme-inducing AED cannot be given the emergency hormonal contraceptive pill.</td>
<td>T F</td>
</tr>
<tr>
<td>d. Menopausal women taking AEDs cannot use HRT.</td>
<td>T F</td>
</tr>
<tr>
<td><strong>4 The following are enzyme-inducing AEDs:</strong></td>
<td></td>
</tr>
<tr>
<td>a. Carbamazepine</td>
<td>T F</td>
</tr>
<tr>
<td>b. Lamotrigine</td>
<td>T F</td>
</tr>
<tr>
<td>c. Phenytoin</td>
<td>T F</td>
</tr>
<tr>
<td>d. Tiagabine</td>
<td>T F</td>
</tr>
<tr>
<td><strong>5 Standards of care and medicines management in epilepsy:</strong></td>
<td></td>
</tr>
<tr>
<td>a. Each person with epilepsy should have a comprehensive care plan agreed between the individual, family and/or other carers, and primary care and secondary care providers.</td>
<td>T F</td>
</tr>
<tr>
<td>b. Anyone with epilepsy should have regular structured reviews of their condition</td>
<td>T F</td>
</tr>
<tr>
<td>c. Reviews should take place every 2 years</td>
<td>T F</td>
</tr>
<tr>
<td>d. Should address issues such as seizure control, adverse drug effects, and compliance.</td>
<td>T F</td>
</tr>
</tbody>
</table>
COMPASS Therapeutic Notes are circulated to GPs, nurses, pharmacists and others in Northern Ireland. Each issue is compiled following the review of approximately 250 papers, journal articles, guidelines and standards documents. They are written in question and answer format, with summary points and recommendations on each topic. They reflect local, national and international guidelines and standards on current best clinical practice. Each issue is reviewed and updated every three years.

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Are you a

Pharmacist? □ Community □ Hospital □ Other (please specify) __________

GP? □ Enter your cipher number: __________

Nurse? □ Enter your PIN number: __________

Title: Mr/Mrs/Miss/Ms/Dr

Surname: ___________________ First name: ___________________

Address: ____________________________

__________________________

Postcode: __________________________

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GPs and Nurses:
Complete the form overleaf and return to:
COMPASS Unit
General Pharmaceutical Services
Central Services Agency
2 Franklin Street
Belfast
BT2 8DQ

Pharmacists:
Complete the form overleaf and return to:
Northern Ireland Centre for Postgraduate Pharmaceutical Education and Training
FREEPOST BEL 3149
Belfast BT9 7BR