

a closer look – questions about anti epileptic drugs

Our 'a closer look' series of factsheets looks at some subjects in greater technical detail. Here we try to answer some of the more common questions about anti-epileptic drugs (AEDs).

Deciding to take anti-epileptic drugs (AEDs) can be a big decision, and you might have lots of questions about how the drugs work before you take that step.

how are drugs developed?

Drug companies research and develop drugs during a very long, complicated, and expensive process. Each step of the process is designed to make sure that the drug is safe for us to use, that it works, and that it can be produced in a way to make sure it is consistent.

Trials and testing

The first stage of developing drugs is to find a possible drug. Researchers look for chemical compounds, which might be similar to a drug that already exists, that they think might work for a particular condition.

Once a compound is found, the next stage is to trial it. This involves testing the compound to see if it does the job the researchers expect it to. The first trials might be computer tests. After this, the compound is tested on animals before it is tested on human volunteers. These trials happen in three phases and can take up to six years to complete. Strict guidelines and ethical standards make sure that drug trials are fair, accurate, thorough, and give enough information about the drug to know whether it works.

Tests include checking that the drug is safe by testing it on people who do not have the condition.

Some drug tests (or trials) are double-blind randomised controlled trials. This means that, from a group of volunteers, half are chosen at random to take the drug and the other half take a placebo (a dummy drug that has no active ingredient in it). Placebos are used as controls in drug trials to compare the effects of the real drug.

Randomly selecting who takes the drug and who takes the placebo means that the researchers cannot choose who they think will respond best to the drug or treat them differently to the volunteers taking the placebo.

In some drug trials, after a certain length of time, the drugs are 'crossed over'. The volunteers are switched from one treatment to the other. So if a volunteer was taking the placebo, they will be swapped on to the 'real' treatment and if they were taking the 'real' treatment, they will be swapped to the placebo.

The idea is to develop a drug that is as effective as possible with the least side effects. Side effects are unexpected or unintended effects of a drug. The benefits of taking the drugs are compared to the risk of side effects and the risks from not treating the condition. A drug will only be licensed if the benefits outweigh the risks.

Licensing drugs

Once a drug is discovered, tested, works, and is safe, the next stage is to license it. Once a drug is licensed it can be prescribed and used. Drugs are licensed either by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK, or the European Medicines Evaluation Agency (EMA) in the European Union. Licensing can take two to three years. Once a drug has been licensed it can be manufactured and appear in shops or pharmacies. Getting to this stage can take up to 12 years.

Sometimes drugs are prescribed off licence or for something they do not have a licence for. For example, some AEDs are licensed for particular seizure types and not others. But the AED may be prescribed to someone who has seizures that it is not licensed for, if it is thought to be helpful.

Ethics

Drug trials have to be ethical (conform to what is morally right). Certain groups of people are not allowed to have drugs tested on them. This includes children, people aged 60 and over, and pregnant women. The way that the body absorbs and removes drugs in children, pregnant women and older people can be different to adults in general.

Once a drug has been licensed for adults, further tests are needed for these groups of people, testing first with older people and then with children.

New drugs will not normally be prescribed to pregnant women until they have been thoroughly tested in other groups. Once a pregnant woman is prescribed a new drug, she will be very closely monitored.

Patents

Like many inventions, new drugs are patented. This patent is the legal right the drug company has to be the only company to make that drug for a certain length of time (usually 20 years). During this time no other drug company can make it. Because developing a new drug costs so much, the company has time 'on patent' to try and recover some of these costs by selling their drug at a price that reflects the cost of development.

When the drug comes 'off-patent' (after the 20 years), other companies can make their own versions of the drug. These versions are called generic (see below). Because other companies have not had the cost of developing the drug from scratch, their versions can be cheaper than the original versions.

types of drugs

There are many different of AEDs. Some are brand versions, some are generic. Some are first-line, and some are second-line (see opposite).

What do brand and generic mean?

AEDs often have two names: a brand (or trade) name and a generic name.

All drugs have an active ingredient – the chemical part of a drug that works on the body to control or treat a condition or disease. The generic name of a drug is the name of that active ingredient, and all drugs with the same active ingredient will have the same generic name. Generic names start with a lower case letter such as sodium valproate and carbamazepine.

Some AEDs also have a brand name given by the drug company that developed it, and this starts with a capital letter. For example, a brand name for sodium valproate is Epilim, and carbamazepine is Tegretol.

Some drugs have many brand names or are sold by different companies under the generic name. For example, sodium valproate may be sold as generic sodium valproate or as branded Epilim, and the drug carbamazepine as generic carbamazepine or as branded Tegretol.

why do my AEDs look different to normal?

If your drugs look different to normal, there could be several reasons for this. The drug company itself could have changed how the drug looks.

Or you could have a parallel import version of your drug. This is when the drug is made outside the UK and brought back into the country. Often this is not a problem, but the company may not be able to guarantee how the drug has been stored and this could affect how it works. Some parallel imports have different packaging to UK versions and the patient information leaflet (PIL) may not be in English.

Or, you may have been given a different form of the drug. For example, if you usually take a branded form and have been given a generic form, or have been given a different generic form to usual. This may affect how well the drug works for you.

 [See our factsheet – generic and branded.](#)

what are 'first-line' and 'second-line' AEDs?

AEDs are licensed for controlling particular types of seizures. 'First-line' and 'second-line' refers to how AEDs are selected and used.

First-line AEDs are usually considered first when starting epilepsy treatment. They tend to be used on their own (monotherapy). They include sodium valproate and carbamazepine. Which one is chosen depends on the type of seizures the person has.

Second-line AEDs are usually taken alongside first-line therapy as polytherapy (also called adjunctive therapy). They include topiramate and gabapentin. Second-line AEDs also include AEDs that were used as first-line treatments but that are no longer generally considered as a first treatment option when treatment is started.

However, treatment with AEDs is always individualised, and sometimes the neurologist may use their specialist knowledge and decide to put an individual on a second-line rather than first-line drug.

Neurologists often use monotherapy at the start of epilepsy treatment. This is because taking just one AED means there are no interactions with other drugs, it reduces the chance of getting side effects, and it is clear to see if the drug works or not. If a single AED does not stop your seizures, the options are to try a different first-line drug, or to add on a second drug.

Taking more than one drug (polytherapy) means that there may be different side effects from each of the different drugs.

Your neurologist will have to consider which side effects may be from which drug. They will also need to be aware of possible interactions between the drugs, and, if your seizures become better controlled, they may find it hard to see which drug is working best.

old and new AEDs

AEDs can be divided into two groups according to when they were developed and how long they have been around for. Newer drugs (licensed after 1989) include lamotrigine and topiramate. Older drugs (licensed before 1989) include phenytoin and sodium valproate. There are positives and negatives to each. The positives and negatives about older drugs include:

- they have been used over many years so the long term benefits and side effects are better known;
- we know more about how they work and what seizures they are likely to work for;
- they are known to be very effective for some people (through years of experience using them); and
- some have serious side effects or interactions with other drugs.

The positives and negatives about newer drugs include:

- they are less likely to interact with other drugs;
- they are more expensive (see section on licensing);
- they often have fewer side effects; and
- we don't have the years of experience to know what types of seizures they work best for.

So the decision about which AEDs to choose is more complicated than their age alone. Choosing AEDs depends on:

- the type of seizures you have;
- the AED that is known to work best for that type of seizure; and
- your lifestyle. Some side effects are more important to some people than others. For example a student may avoid an AED that affects their concentration.

Today many doctors recognise that people know a lot about their medical condition and want to play a part in any decisions about treating it. Weighing up the risks and benefits of taking or not taking treatment includes the following:

- the possible risks of taking AEDs, including side effects;
- the possible benefits of taking AEDs, including stopping seizures;
- the possible risks of not taking AEDs, including continuing to have seizures (and accidents and injuries because of them); and
- the possible benefits of not taking AEDs, including not having side effects.

How important these risks and benefits are will vary from one person to another and will depend on individual circumstances.

Ultimately the decision is yours, but having the input and support from your doctor can help you to weigh up these points and come to a decision that you are happy with. Taking part in making this choice may also help you to feel more in control.

how often should AEDs be taken?

How often you take an AED (once, twice or possibly three times each day) depends on its half-life. The half-life of a drug is the length of time it takes for the original amount of the drug to reduce by half. The half-life is used to measure the concentration of the drug in the blood, which is not exactly the same as the dose of drug you take.

When you take a drug it takes time to be absorbed into your blood. When it is in your blood the amount can be measured. This is expressed as the drug's concentration or level, which relates to how much of the active ingredient of the drug is available to work.

Once the drug has done what it is meant to do, it becomes metabolised (broken down) and eliminated (removed) from the body. In simple terms, when the drug reaches its half-life, half of it is still in the blood and half of it has been metabolised and eliminated.

what is the average dose range of an AED?

When considering how much medication someone takes the doctor will look at two different things. Firstly, their average dose. This is a measure of the number of tablets they take and how much active ingredient each tablet contains. For example, for an adult an average dose range for carbamazepine is 600–2000mg per day.

These figures are a very general guide. Some people may have their seizures controlled on a dose lower than the lowest dose or higher than the highest.

The second way of monitoring medication is to look at the amount of an AED in the blood and compare this to a reference range. The reference range is a range of concentrations of an AED within which most people will get a benefit from the drug.

Below the reference range the drug is unlikely to work, whereas above the reference range toxic effects are likely to happen. Again, this is a general guide and not specific to an individual.

By monitoring drug levels in an individual and seeing what amount of an AED gives them the best seizure control, it is possible to work out an individualised therapeutic range for them. This range will vary from one person to another but will often fall within the general reference range for that AED.

what is blood level testing?

Blood-level testing, or therapeutic drug monitoring (TDM), is a system of monitoring the AED levels in an individual to help manage their epilepsy treatment. TDM involves taking blood or saliva samples to measure the amount of the drug that is available to work (its bioavailability). So this is a good way of measuring how much of the drug your body is getting.

 See our factsheet – *Monitoring epilepsy*

when you increase a dose, how long does it take to work?

This varies from one AED to another and depends on the half-life of the drug. Generally, you can see the effect of an increase in five half-lives' time, so if the half-life of the AED is 24 hours, you will see the effect five days (that is, 5 x 24 hours) later. If the half-life is 12 hours, you will see the effect two-and-a-half days (that is, 5 x 12 hours) later.

side effects

One of the biggest concerns people have when taking medication is the possible risk of side effects.

Generally, these are not the effects you want to happen. Some side effects, such as feeling tired or drowsy may be unwelcome, but some can have a beneficial effect, such as lowering cholesterol.

When you take a prescribed drug you are obviously taking it for a reason, which is to make something happen, such as preventing a condition or treating a symptom. The aim of AEDs is to stop seizures happening. But when you take any drug, there is also the possibility of side effects.

 See our booklet – *Medication for epilepsy*

A patient information leaflet (PIL) comes with every drug and uses terms like common and rare. These terms refer to the likelihood that a side effect will happen. This likelihood is shown by how many people will get it:

- Very common means more than one-in-10.
- Common means one-in-100 to one-in-10.
- Occasional means one-in-1,000 to one-in-100.
- Rare means less than one-in-1,000.
- Very rare means less than one-in-10,000.
- Extremely rare means less than one-in-100,000.

These terms tell you how many people are likely to get the side effect, but they cannot tell you how likely you are to get it. Knowing what these terms actually mean may help you to put side effects into perspective. This can be helpful when you are making decisions about taking, or not taking, medication.


are side effects the same for all AEDs?

No, they vary from one drug to another. When drugs are developed they are tested on many people and the common side effects are listed on the PIL for that drug. If the side effects are very serious, the drug may not continue to be developed.

Although the tests are done on many people, once a drug is licensed and prescribed it may be used by thousands of people over long periods of time. Some side effects, particularly those that are extremely rare may not have been seen during the trials.

what should I do if I have a side effect that is not listed in the PIL?

If you have a side effect that is not listed in the drug's PIL you can report it to the Medicines and Healthcare products Regulatory Agency (MHRA) through their yellow Card Scheme.

 See our factsheet – *The yellow card scheme.*

further information

Epilepsy Society information

generic and branded medication for epilepsy
monitoring epilepsy
the yellow card scheme

epilepsysociety.org.uk



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Epilepsy Society, Chesham Lane
Chalfont St Peter, Bucks SL9 0RJ

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