

Antipsychotic medication

Our answers to your questions



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The **NIHR CLAHRC Greater Manchester** is part of the National Institute for Health Research and is a partnership between providers and commissioners from the NHS, industry, the third sector and the University of Manchester

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*Illustrations created by **More Than Minutes** based on discussions of service user and carer panel
Illustration of brain – **J E Theriot**.*

What this leaflet is for

We wrote this leaflet to answer questions that people have asked us about antipsychotic medication. Often these are questions that people have found it difficult to get the answers to. Some of the things here only apply to people taking one type of medication and so may not be relevant to you. You don't need to read the whole of the leaflet – you might want to read just the parts that are relevant or interesting to you.

As this leaflet is based on people's concerns, it is not intended to give a balanced view of treatment. The pros and cons of treatment are different for each person. Antipsychotics help many people recover from severe illness and many people see a huge improvement in their quality of life. Some serious side effects we mention are worth watching out for but are very rare. Compared to many drugs for physical illness, the side effects of antipsychotics are no worse. Many people use aspirin even though there's a long list of possible side effects.

This leaflet is designed to be read alongside the information that is given with your medication. There are also some helpful websites that can give you information about the side effects of specific drugs. For example, www.choiceandmedication.org.uk. Your clinical team should also be able to help with any questions. There are ways to help with almost every problem we mention.

There are boxes throughout this leaflet that contain information that could help people understand the topic but do not answer the question directly.

Brains are very complex and so medications are hard to get right. They can cause all sorts of side effects. Many chemicals that work in the brain work in nerves in the rest of the body too. For example, they regulate how the heart or the gut works. So although professionals would like these drugs to work on just the brain, they can affect other parts of the body too.



Two out of three people will relapse in the next year if they stop taking their medication.



About one out of five people will relapse in the next year despite taking this medication.

How do antipsychotic drugs work?

Our brains make a chemical called dopamine [DOH-pa-mein]. Deep inside the brain, in a part called the "striatum" [str-eye-ATE-um], one lot of nerve cells lets out dopamine and another picks it up. When this happens it is a signal to the rest of the brain that something important and unexpected is happening. Sometimes these cells make too much dopamine and let out more than normal. This tells the brain that random things mean something and are important. When this happens someone suffers a psychosis [si-KOH-sis]. They sometimes hear voices when no one is there, they are sometimes sure of things for no obvious reason, or sometimes they can't think straight.

Antipsychotic [anti-SI-ko-tic] drugs all block the effect of dopamine in the brain. They stop the nerve cells in the striatum that pick up dopamine from doing this. When most people take them the psychosis starts to improve. It can take a few weeks to get the full benefit. For some people they do not work very well. We are not yet sure why.

We are not sure why the cells in the striatum start to make too much dopamine either. So even if the antipsychotics work, if you stop taking them it can start all over again. This happens often; maybe four people out of five who get psychosis the first time will relapse eventually.

Sometimes this can be weeks after stopping the drugs, sometimes years. If you keep taking the antipsychotics the psychosis comes back much less often, maybe only for one person in every five.

Antipsychotic drugs are not addictive. People do not crave taking them in the same way they crave cigarettes or heroin or even chocolate. But our bodies and brains get used to almost any drug so it is a good idea to stop them gradually, so our brains have time to adjust.

How well do antipsychotic drugs work?

Changes in brain dopamine may not be the cause of the problem for everyone with psychosis, or the antipsychotics might not work every time when it is. Still, three out of every four people who get psychosis for the first time and take antipsychotics find that things get much better.



Three quarters of people who get psychosis for the first time find that their symptoms improve when they take antipsychotics.

There are very few studies to tell us how many would improve if they just had support and psychological treatments instead, but it seems clear that the medications work better than tablets with no drugs in them (called placebos).

There are more clinical trials comparing antipsychotic medications to placebos for people who have relapses of psychosis. In one study, half of people who took antipsychotics got a lot more benefit than the people taking placebos. This fits with the evidence from people taking antipsychotics long-term. In most studies, long-term antipsychotics stop more than about one person in every four relapsing in the next year or so. In some studies it is even fewer than one in six, while about two in every three people taking a placebo in the same studies relapsed.

Do any work better than the others?

Some antipsychotics seem to work a bit better than others, but the difference is too small to make a difference in practice. Drugs like olanzapine [oh-LANZ-a-peen], amisulpride [am-ee-sul-pride] or risperidone [ri-SPAIR-i-dohn] seem to work slightly better than some of the others in clinical trials (studies run by drug companies to see how well their drugs work). Only a minority of patients would ever be able to take part in most clinical trials though; they would be ruled out because they have physical illnesses or they use other medications or illegal drugs. Or they might just not want to take part. When doctors do studies comparing all these drugs in the real world,

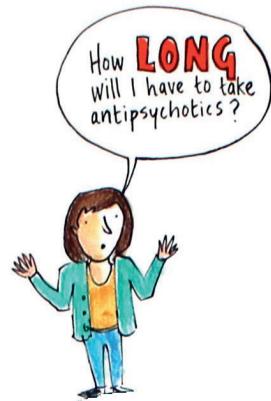
giving them to all sorts of people, patients seem to do equally well on any of the antipsychotics. The most important thing is to get the right drug for you at the right dose. Even the best drugs do not suit some people.

Clozapine

The one antipsychotic that is different to the others is clozapine [CLOZ-a-peen]. This reduces symptoms quite a lot better than other antipsychotics and this difference is big enough to be important in practice. We are not sure why. It has many side effects (we discuss them later) so health professionals only give it to people when other antipsychotics have not worked. In one study of people who had only been ill a few months it helped about three people in every four who took it. It may only help about half the people who have been ill longer. If clozapine does not work well doctors sometimes give people a second antipsychotic as well as the clozapine. This seems to help about half the people who take the two drugs.

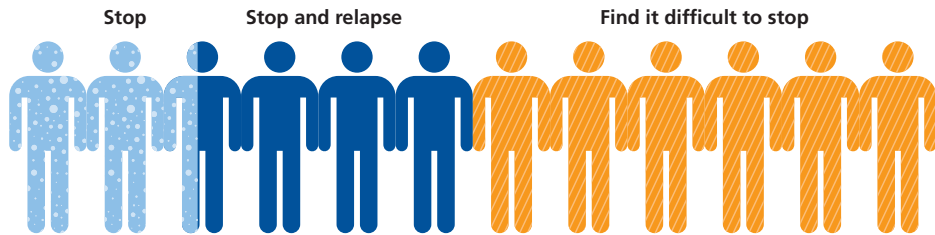
Depot antipsychotics

Some people take antipsychotic injections instead of antipsychotic tablets. These are called depot [de-POH] or long acting injections. This means that they do not have to remember to take the tablets every day and the health service staff and their families can remind them if they forget to go. Most people have injections every two or four weeks. The medication is injected into a big muscle. Usually this muscle is in the bottom but for some drugs a muscle in the shoulder can be used. The depot drug moves slowly out from the muscle over the next few weeks. Once it is in your blood it goes round to the rest of the body and to the brain.



How soon can I stop medication?

Studies tell us that many people will benefit by avoiding relapse for at least a couple of years after they first get ill, maybe even five years. On the other hand, antipsychotics have many side effects. Doctors do not agree how safe it is to stop antipsychotic drugs in the first two years, or even how safe it is after that. In one recent study, psychiatrists tried to help half the people in the study stop medication as early as possible after they had a psychosis for the first time. They compared them to people who carried on the medication.



In the group who tried to stop, about half managed it. Most people who stopped relapsed within 18 months and took medication again. One fifth of the group trying to stop medication managed to stay off medication for 18 months.

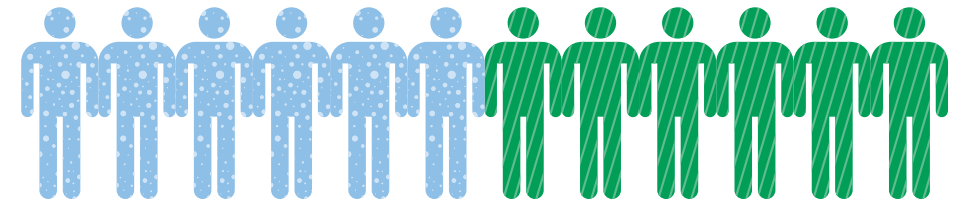
After 18 months, twice as many relapsed in the group trying to stop as in the group carrying on.



After 7 years, a quarter of the group who were trying to come off medication had managed and were well. Another one in six was on a very low dose. Most still took medication at a normal dose.

After 7 years the same number of people had relapses in the group who tried to come off medication as the group who were supposed to stay on it. But at least a quarter of the group who were supposed to stay on had stopped them or started taking a very low dose. The group who tried to carry on coped less well in their day-to-day lives after 7 years but, by chance, they had coped less well at the start too. So the results of this study are not clear.

For people who have been well for years while they take the drugs, stopping them means about half will get the psychosis again within the next six months.



About half of people who suddenly stop antipsychotics will relapse within the next six months.

Studies comparing stopping suddenly to stopping gradually find that people relapse twice as fast after stopping suddenly.

It is clear that some people can stop their drugs and that they do well but many relapse and end up taking more drugs as a result. People who relapse more often in the early years of psychosis are more likely to kill themselves, so psychiatrists are cautious about advising people to stop their medication, even though stopping can avoid side effects. If you plan to do it talk to your healthcare staff first.

Side effects

Some people's side effects are worse than others. It is also true that some people find it easier to deal with side effects than others. So different drugs suit different people better.

Many side effects get better after a few weeks on the drug. Often sleepiness, dizziness when you stand up, and movement side effects can improve.

There are many different antipsychotic drugs. They all work in a similar way but their side effects are often different. The different companies who make these drugs all tried to come up with drugs that worked better than the others or had fewer side effects. Some drugs work a bit better than others but for most people the differences are too small to notice, except for clozapine.

The drug companies had more luck with changing side effects but usually when they avoided one lot of side effects they ended up with different side effects instead. Although all the drugs block dopamine, they have effects on other brain chemicals too. The main way the drug companies made each drug different from the last was to change the way new drugs worked on these other brain chemicals. So each drug blocks different brain chemicals as well as dopamine and blocking each brain chemical causes different side effects.

Movement side effects

Some drugs often make people's muscles go stiff. They make them move more slowly and sometimes the muscles in the face that change our expressions do not work very well. It may be a sign the dose is too high. Drugs like procyclidine [PROH-s-eye-kli-deen] can reduce these side effects, but these other drugs have their own side effects.

Movement side effects happen because at high doses the drugs affect dopamine in the parts of the brain that are not involved in psychosis. Dopamine works in a different way in different parts of the brain, even though it is the same chemical. It all depends on the job of the nerve cells in that part of the brain. Dopamine can be involved in making the muscles move, so blocking its effect in the wrong part of the brain affects a person's movements.

Blocking dopamine with antipsychotics can also make people feel restless and make them move around a lot. Some people find this very upsetting but others do not mind. This is called akathisia (AY-ka-this-EE-a). Several drugs seem to help with this but again each has its own side effects. These drugs are medicines like procyclidine, drugs called beta blockers, Valium-type drugs (benzodiazepines [BENZO-diaz-e-peens]) and a drug called mirtazapine [mur-TAZ-a-peen]). This is usually used to treat depression.

Other very common side effects



Feeling sleepy or tired is very common with some antipsychotics. Difficulty sleeping is less common but happens with some drugs. Psychosis itself can interfere with the normal rhythm of your day and leave people sleeping at odd times.

Mostly these drugs make people feel calm, or just less interested in things going on in front of them. A few drugs can make some people anxious. Mostly antipsychotics stop people feeling sick but an uncommon side effect is feeling sick. This is more common in one or two (aripiprazole [AIR-i-PIP-re-zohl]), for example).

Feeling hungry is a big problem with some antipsychotics. Some people eat a lot and gain several stone in weight, yet others might gain very little despite taking the same medication. It is not clear how much the symptoms of psychosis, such as lack of motivation, reduce the amount of exercise people take and influence weight gain. Some drugs cause high levels of cholesterol or other fats in the blood.

Constipation is more common with some medications than others. It is less common at low doses of medication. Often eating lots of fruit and vegetables will help. Sometimes people take tablets or sachets of fibre.

Some drugs also cause dry mouth, make things look blurry and (uncommonly) make it difficult to wee. These drugs can also slow people's reactions down even if they are not too tired, so they need to drive carefully and leave more time to stop, if they drive at all.

Antipsychotics can reduce people's blood pressure and make people feel dizzy when they stand suddenly. One drug (quetiapine [kwi-TY-e-peen]) can occasionally increase blood pressure.

Certain drugs can cause sunburn, sometimes quite quickly and severely.

Some drugs can increase the level of a hormone called prolactin [pro-LAK-tin] in the blood. With most drugs, at the right dose, the rise can be small and have little effect. High prolactin levels in women can stop periods, cause breast tenderness and milk to leak from the nipples. High prolactin in men can cause problems with erections and cause swelling around the nipples. In both men and women it can reduce sexual desire and maybe thin the bones over the years. Sometimes this is only picked up with a blood test, which everyone should have once a year (though at low doses of most antipsychotics this is less important).

All sorts of sexual side effects can happen even if prolactin is normal. They are less common in some medications.

Uncommon and rare side effects

Most medications have rare side effects that can be serious when they happen. Some are so rare that most psychiatrists will never treat someone who has them. Some of these problems might happen anyway even without drugs but antipsychotics can make them happen a little more often.

Diabetes can happen even without the medication but a few drugs definitely make it more likely to start. This is most often near the time when people start the drug and you do not need to gain weight for it to happen.

Antipsychotics cause problems with the rhythm of the heart, which can be very serious in rare cases and even kill. A few, like clozapine, commonly cause a mild increase in heart rate that you might never notice.

Uncommonly, antipsychotics cause fits. This is rare for some types of antipsychotic and rare at low doses of the drug.

A few people get another sort of movement side effect called tardive dyskinesia [TAR-div DIS-k-eye-nee-sia]. This often takes years to start and is more common in people who have taken very high doses of antipsychotics for many years and who got other movement side effects first. It is more common in women and people who have a lot of mood symptoms as well as psychosis. It is more common if there is already some

damage to the brain. It used to be quite common when many people spent years on very high doses of the oldest drugs.

This side effect gives people extra movements that happen without thinking about them. These movements are often like chewing, or tongue movements, or sometimes movements of the hands or feet or the body. They can be hard to spot at first and they can look like akathisia (restlessness). They sometimes just go away. They usually stop if the antipsychotic is stopped, or changed, or the dose reduced. Sometimes, though, they carry on or even get worse without the antipsychotic drugs. There are special drugs to treat this uncommon problem too. Of course, they have side effects too, and they do not always work.

Another very rare side effect of the antipsychotics is neuroleptic malignant syndrome [NEURO-lep-tic mal-IG-nant sin-DROME]. People can go very stiff and can become drowsy or unconscious. Their heart rate and blood pressure can go up and down. So can their temperature. There can be changes in certain blood tests. Sometimes this just settles down if the antipsychotic is stopped and then changed, sometimes people need hospital treatment. Very rarely this can cause death.

Different drugs and different side effects

Older drugs that were invented in the 1950s, 1960s, and 1970s more often cause movement side effects. There are different sorts of movement side effects. Newer ones that were invented in the 1990s or later do not make people stiff or slow to move very often but some cause akathisia (restlessness) quite often. More of the newer drugs cause problems like high cholesterol and diabetes and a couple of them cause hunger and weight gain. The older antipsychotics used to be used at much higher doses than they would usually be used now and some of their bad reputation for side effects is because of this. Some of the newer drugs rarely raise prolactin levels (quetiapine, clozapine) but one (amisulpride) does. One drug, clozapine, has more side effects than the others.

Clozapine side effects

Clozapine works quite a lot better than other antipsychotics and this difference is big enough to be important in practice. Clozapine has more of the common side effects like making people hungry and sleepy and causing diabetes and high cholesterol. It has almost no movement side effects. Some of the very rare side effects of other drugs are just uncommon or quite rare with clozapine.

The white blood cells that fight infection by bacteria (infections that cause some sore throats, some chest infections, bladder infections and so on) are made in the bone marrow. Less than one person in every hundred who takes clozapine in the UK finds that their bone marrow stops making this type of white blood cells. If health professionals pick this up they stop the drug and it usually settles down in a few days. Health professionals use blood tests every week, two weeks or month (depending how long people have taken the medication) to check that the levels of white cells in the blood are not going down. If a small infection is not noticed it might turn into a serious or even fatal one. With these checks now in place this is rare, but people taking clozapine should tell staff if they get an infection, just in case.

Uncommonly, clozapine can cause damage to the muscle in the heart and stop it pumping blood well. This can come on quickly or slowly. This makes people feel tired and breathless and, rarely, can kill.

Also uncommonly, clozapine can cause constipation which is so bad that it leads to severe illness and even, rarely, death. It is important to tell staff about any constipation if you are on this drug.

Drop in blood pressure can be a big problem with clozapine and when the drug is started it is built up day-by-day. Taking nothing for even a few days and then taking a full dose, even if it was fine before, can cause a huge drop in blood pressure because the system is not used to the drug any more. This can make people collapse and, rarely, die.

Dose of drug, and taking more than one antipsychotic

For most drugs, the higher the dose of the drug the more side effects people get. On the other hand if the dose drops too low then the drug does not work because it does not block enough of the extra dopamine being made by brain cells during the psychosis. Some side effects can be avoided in many people by getting the dose just right. This means low enough to avoid the side effect (movement problems or high prolactin, for example) but high enough to work. Adjusting doses like this can be tricky and does not always work.

For most people, taking two antipsychotics means they get two lots of side effects but no more benefit than they would from taking the right dose of one drug. They are also more likely to end up taking high doses of antipsychotic when you take into account the dose of the two drugs added together. Although there are situations where two drugs work better, psychiatrists usually try to avoid prescribing people two. If you are taking two or more and this worries you, talk it over with your team. Do not stop drugs suddenly. It is a bad idea in case your brain has got used to one of the drugs. They are usually cut down in steps to avoid problems like poor sleep or even triggering a relapse.

Antipsychotics and the brain

Many people with psychosis note difficulties remembering appointments or lists, doing two things at once, concentrating or planning complicated things. Guessing how other people are feeling or how they will react can be difficult. This does not happen to everyone in the same way – John Nash, who won a Nobel Prize for economics, had schizophrenia. Many people go back to their jobs, to school, and to family life after psychosis and seem to do fine. It may well be that for most people they stay the same even after years of psychosis or taking medication.

These difficulties are not all due to medication because they can affect people before they ever get psychosis, even as children. Different antipsychotics have different effects on concentration, memory and so on. Some drugs are better for concentration or multi-tasking than memory, for example. Some studies make us think that, compared to not taking medication, antipsychotics tend to improve how people do but some drugs may have more benefit than others. It may be true for some sorts of difficulty more than others. It is not clear how long any benefits last.

After our 20s our brains shrink with age. After having a psychosis for the first time, on average, brains shrink a bit faster than we would expect. It is not clear why. It could be due to losing nerve cells, or the nerve cells might just shrink and lose some of their connections. It could be loss of other cells in the brain that support the nerve cells. Anyway, after a few years of psychosis someone might end up at 30 with a brain the size that many 50 year olds have. It is important to remember that most 50 year olds get along fine so this may not mean much. Again, there is no good evidence that after psychosis most people get worse at doing psychological tests quicker than everyone else.

Experiments in animals make us think that antipsychotic drugs can speed up this shrinkage, perhaps some drugs more than others. It may be that the effect is small at lower doses. Some studies tell us that the loss is due to nerve cell connections that come back when drugs are stopped but it is still not clear what is going on, especially in humans. Maybe some of the older drugs cause more of a problem. On the other hand there is no good evidence that being on an old drug makes any difference to how well your brain works compared to newer drugs. In fact, in some studies people who missed getting treated with antipsychotics in the early years of their illness did worse on all sorts of psychological tests than people who got the older drugs. So the picture is complicated. Also, stopping medication, getting ill and needing more medication probably causes more brain cell loss than taking it all the time.


What is physical health like for people with psychosis?

People with psychosis on average die 15 or 20 years younger than we would expect. This is rarely because of the psychosis itself. Only a small minority deliberately kill themselves. Most people die of heart attacks, strokes, lung disease or other common physical illnesses. The main reason for this is that the physical health of many people with psychosis is poor. People with psychosis very often smoke, get too little exercise, use drugs like cannabis, amphetamine or cocaine, and have poor diets. All these things make their health worse.

Even before taking medication people with schizophrenia often smoke and can show early signs of diabetes. The symptoms of psychosis can affect motivation and make it difficult to look after yourself or cope well with tasks like shopping for healthy food. Sometimes the problem is medication side effects. Antipsychotics can also make people eat too much, get high cholesterol or diabetes and feel slow or lethargic.

Even so, some people are very healthy. Even if a person gets side effects, some people get them worse than others and some cope with them better than others. There are ways to improve almost every physical problem mentioned here. Your clinical team should also be able to help with any questions or concerns that you may have.

It is well worth saying that many people benefit from taking medications. However, it is important to get the right drug for you, at a dose that is high enough to work but low enough to minimise the side effects.



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