

Clozapine

Information for patients, family members and carers

This information is intended for people who are being treated with clozapine or are considering clozapine treatment. The brochure also serves to provide information for family members, carers and anyone else involved.

This brochure is a publication of the Clozapine Plus Werkgroep (Clozapine Plus Collaboration Group):

Johan Arends

Bert Bakker

Jan Bogers

Dan Cohen

Daniël van Dijk

Raphael Schulte

© 2013 Clozapine Plus Werkgroep, Castricum, The Netherlands

The copyright of the text and images in this publication is held by the Clozapine Plus Werkgroep.

Contents

Clozapine treatment

1. When is clozapine treatment given?
2. What does the treatment involve?
3. How long is clozapine treatment needed?

Side effects

1. Side effects that are common and often unpleasant, but do not pose a direct threat to health
 - 1.1 Side effects that occur in more than 10% of users
 - 1.2 Side effects that occur in 1-10% of users
2. Side effects that are rare, but can pose a threat to health
 - 2.1 Side effects that occur occasionally (0.1 - 1% of users)
 - 2.2 Side effects that are rare (0.0 - 0.1% of users), but require immediate treatment
 - 2.3 Side effects that occur very rarely (< 0.001% of users)

Safety

1. Is clozapine dangerous?
2. Safe use of clozapine
3. What to do if you have forgotten a dose
4. How should clozapine be distributed throughout the day?
5. Are all clozapine tablets the same?
6. Concentration of clozapine in the blood
7. How can I tell if there is too much clozapine in my blood?
8. Contraceptives, pregnancy and breastfeeding
9. Surgery
10. Alcohol and drugs
11. Driving and operating machinery

Important addresses

Summary of the most important information

Clozapine treatment

1. When is clozapine treatment given?

Your doctor has suggested you take clozapine because other drugs have not been very effective or because their side effects bothered you too much. Clozapine is prescribed mainly for psychosis when other medicines have not helped enough. A psychosis is a mental condition in which a person suffers from delusions and hallucinations. Delusions are beliefs which do not correspond with reality according to other people, such as the belief that you are being followed by the secret service or that you are Napoleon. Hallucinations are sensory perceptions that are false, such as hearing voices that nobody else hears.

Antipsychotics (such as risperidone, olanzapine, haloperidol etc.) are prescribed for a psychosis. These medicines often work well, but not for everybody. For about forty per cent of people these antipsychotics are not effective enough. If a person has not recovered sufficiently after two treatments with different antipsychotics, often clozapine is prescribed, because it appears to work well precisely in that situation. That is the special feature of this medication.

Other symptoms, such as mania, can also be relieved by clozapine. Mania is associated with a lack of restraint; manic people are very busy and hyperactive, excessively cheerful and enthusiastic, become annoyed or angry very easily (to a degree out of proportion with the direct cause), overestimate their own capacities (delusions of grandeur), need less sleep, are more talkative than usual, are easily distracted and have lots of energy.

There is also evidence that clozapine has a beneficial effect on suicidality (suicidal thoughts), substance abuse or dependency (such as cannabis or alcohol), aggression and self-harm.

2. What does the treatment involve?

For clozapine to be effective you must take it every day. Stopping clozapine treatment suddenly can even be harmful to your health. You will have regular appointments with your doctor or with a nurse. Your doctor will arrange the tests you will need.

You will have the most tests and checks during the first month: blood pressure, weight, pulse rate and blood levels. Sometimes an ECG is performed. The reason for all of this is to keep you physically healthy.

Over the first 18 weeks you will have a blood test every week. One reason is to check there is no drop in the number of white blood cells in your blood. After that, these blood tests are usually done once a month. Once a year you will have more extensive tests and checks.

3. How long is clozapine treatment needed?

The first clozapine treatment, to see if it helps you, lasts no longer than a few months. If clozapine is no more effective for you than previous medications, you can taper it off again (slowly). If it is more effective, then in most cases clozapine treatment is needed for a long time. This is not always easy to accept. On the other hand, it is not as strange as it seems; after all, many medications have to be taken for life.

Side effects

What are the side effects of clozapine?

Like most medications, clozapine has side effects. We divide the side effects into two categories:

- Side effects that are common and often unpleasant, but do not pose a threat – or not a direct threat – to health.
- Side effects that are rare, but may pose a threat to health.

1. Side effects that are common and often unpleasant, but do not pose a direct threat to health

1.1 Side effects that occur in more than 10% of users

Drowsiness, fatigue and sleepiness. These symptoms are the strongest at the beginning of the treatment. After a few weeks of treatment the drowsiness usually decreases. In many cases it continues to occur for the first few hours after taking the medication. Taking clozapine before going to bed is often a solution. Clozapine also sometimes leads to sleeping longer.

Producing more saliva. This often happens at night in particular, so that your pillow may get wet. Putting a towel over the pillow is often a solution. There are also medications that can help.

Constipation. Clozapine may cause constipation; your bowel movements are less frequent and hard to pass. You should always tell the doctor about this, because the problem can be solved with the right diet and harmless medicines. However, if constipation is not treated it can sometimes lead to severe bowel obstruction.

Dizziness. Dizziness occurs mainly at the beginning of clozapine treatment. After a few weeks it disappears or gets much better. In itself dizziness is harmless, but you must be careful not to stand up or bend over too quickly, because you might fall. As soon as you feel dizzy, sit down and wait until the dizziness passes and then try to stand up more cautiously. Dizziness tends to occur at night in particular, for instance if you get up to go to the toilet. Be extra careful then.

Rapid heart beat. This is an acceleration of the heart rate that is usually harmless. Sometimes people feel anxious and have palpitations. If necessary, medication can be prescribed to calm down the heart rate.

Weight gain. Often taking clozapine lead to weight gain, usually through increased appetite. More exercise and paying attention to your diet can help to keep you at your normal weight. Consulting a dietician may be helpful.

1.2 Side effects that occur in 1 - 10% of users

Urinary incontinence. This means that you pass urine when you do not intend to. It can occur at night when you're lying in bed. This probably happens because you are in such a deep sleep that you don't notice that you're passing urine. Lowering the dose or taking medication that makes it less easy for the bladder to empty may help. Not drinking much in the evening and going to the toilet before you go to bed can also help.

Diabetes. Long-term use of antipsychotics, certainly including clozapine, can increase the risk of diabetes. Major risk factors for this are too little exercise and being overweight. Good lifestyle habits (a healthy diet and regular exercise) can reduce the risk. Clozapine can also increase certain blood fats (lipids) such as cholesterol. They can be brought back down by medication.

Heartburn. Heartburn is a burning sensation behind the breastbone which is usually associated with gastric reflux. This complaint can be treated well by adapting your lifestyle, if necessary following the recommendations of your doctor.

2. Side effects that are rare, but can pose a threat to health

2.1 Side effects that occur occasionally (0.1 - 1% of users)

Drop in the white blood cell count (agranulocytosis). If you have too few white blood cells, your body can no longer defend itself against pathogens such as bacteria or fungi. The risk of agranulocytosis is the highest during the first 18 weeks of treatment. Because of this you must have weekly blood tests during that period. After that you must have monthly blood tests. If you find it hard to cope with blood being drawn from your arm, you can have finger pricks instead. The blood tests make it possible to detect a drop in the white blood cell count at an early stage. You would then stop taking clozapine so that the white blood cells could recover. The blood tests make it safe to take clozapine.

After the first year of treatment this side effect hardly ever occurs. If you were to decide not to have the blood tests any more after the first year, the risk of dying from agranulocytosis would be about the same as the risk of dying in a traffic accident.

If you are taking clozapine, it is important for you and the people around you to watch for signs of infection. If you develop an infection – for example a cold and a sore throat with a temperature above 38°C, you should warn your doctor (your psychiatrist or your GP) and tell them you are taking clozapine. You will have an extra blood test to check that you have enough white blood cells..

2.2 Side effects that are rare (0.01 – 0.1% of users), but require immediate treatment

Inflammation of the heart muscle. In rare cases clozapine can lead to inflammation of the heart muscle during the first four weeks of treatment. Your doctor will watch out for signs of any such inflammation. This is one of the reasons why you must see your doctor once a week at the beginning of the treatment.

2.3 Side effects that occur very rarely (< 0.001% of users)

Bowel obstruction. In rare cases clozapine can cause bowel activity to shut down completely. This is why it is very important that you discuss any bowel movement problems you may have with your doctor immediately. Then bowel obstruction can be prevented (see constipation).

Rapid disruption of blood sugar levels (ketoacidosis). In exceptional cases blood sugar levels can suddenly go off the rails, especially in the first few months. This can be monitored by blood tests.

Safety

1. Is clozapine dangerous?

In spite of the side effects described above, there is evidence that patients who take clozapine live longer than patients who take other antipsychotics or no antipsychotics at all. In short: clozapine is an effective antipsychotic which often works better than other antipsychotics, but both doctors and patients must be careful when using it.

2. Safe use of clozapine

To use clozapine safely it is important for you and your doctor to cooperate well. There are also some important rules, which are set out below; we recommend that you read them carefully:

- If you observe any side effect that is new to you, always tell your doctor about it.
- If you have flu-like symptoms with a temperature above 38°C or a sore throat and you are still in the first 18 weeks of clozapine treatment, you should tell your doctor or the locum within 24 hours. (You can also tell your GP or the GP on duty). You must have a blood test the same day to check for a drop in your white blood cell count. It is also sometimes necessary to reduce the dose of clozapine temporarily. After the first 18 weeks you can wait until the next working day to report these symptoms.
- If you develop an infection, let your doctor know quickly, because your dose may need to be adjusted or you may need a blood test.
- If there is any change in your bowel habits (particularly constipation), always tell your doctor.
- If you notice that you've suddenly started to drink a lot more fluid and also to urinate more often than usual, tell your doctor as soon as possible.
- If you stop smoking cigarettes, start to smoke much less or start smoking, you must tell your doctor quickly.

In the final pages of this brochure you will find a card with 10 main rules you must remember with regard to taking clozapine.

3. What to do if you forget to take a dose

If you forget to take a dose one day, never take a double dose the next day. The rule is: if you forget to take a dose, just skip it. If you have forgotten the morning or noon dose, you can still take this dose within four hours. Try to establish why you forgot to take your medicine, so that you can avoid doing so in future. If you have not taken the clozapine for more than two days, you will have to start with a low dose again and build it up. Talk to your doctor about this.

4. How should clozapine be distributed throughout the day?

How clozapine should be taken throughout the day is different for each individual. Most people prefer to take the whole dose for a day before going to bed, because clozapine can make you feel sluggish and drowsy in the first few hours after taking it, which helps people to sleep well. However, some people prefer to distribute the clozapine evenly throughout the day, because they feel best when they do that.

5. Are all clozapine tablets the same?

Clozapine tablets are made by different manufacturers, so that at some point you may be given tablets that look different from those you are used to. All these tablets contain the same active ingredient, clozapine. The effect is the same in spite of differences in the shape or size of the tablet.

6. Concentration of clozapine in the blood

It is not the number of tablets or the dose that determines the effect of clozapine, but the concentration of the medicine in the blood (blood level). This is why your doctor may check the concentration of clozapine in your blood if the effect is not satisfactory or if there are side effects; for instance, it may not be effective enough (the concentration may be too low) or there may be too many side effects (the concentration may be too high).

Some factors that may influence the concentration of clozapine in your blood:

- If you are taking other medications, always tell your doctor, preferably before you start taking those other medications.
- If you smoke, clozapine is removed from your body more quickly. If you stop smoking, the clozapine blood level can rise considerably. You should therefore tell your doctor if you stop smoking, and also if you start smoking.
- Certain drinks (coffee is the main one, but also cola) and foods may affect the clozapine blood level. This does not mean that you may not drink coffee, but you should not suddenly switch from drinking a lot of coffee to drinking very little coffee.
- Illnesses with fever (such as flu) and inflammations can also make the concentration of clozapine in your blood rise. If you develop an illness like this, always see your doctor.

7. How can I tell if there is too much clozapine in my blood?

It is important to know what the symptoms are, because then you can go to see your doctor in good time:

- Lethargy, drowsiness, sleepiness, dizziness and loss of concentration
- Muscle weakness, heaviness in arms and legs
- Uncertain gait, difficulty talking
- Muscle twitching, muscle cramps, epileptic seizure

If you have one or more of these symptoms, you should warn your GP or psychiatrist immediately.

8. Contraceptives, pregnancy and breastfeeding

- Contraceptives. If you don't want to become pregnant, you should choose a reliable contraceptive. Clozapine does not affect the contraceptive pill.
- Pregnancy. If you are taking clozapine and you want to become pregnant, you should talk to your doctor about it first. Most medications should be avoided during pregnancy if possible, because of the adverse effects they may have on the unborn child.
- Breastfeeding. If a woman taking clozapine were to breastfeed, there would be clozapine in the breast milk. This is why women are strongly advised not to breastfeed while taking clozapine.

9. Surgery

If you are going to have surgery, when you speak to the anaesthetist before surgery you must tell them you are taking clozapine.

10. Alcohol and drugs

As with all medication, you must be careful with alcohol and drugs. Excessive use of alcohol or drugs is not good for anyone and we therefore advise against it.

11. Driving and operating machinery

Clozapine can cause drowsiness, sleepiness, dizziness and blurred vision and can therefore affect your driving skills. Because of these side effects, during the first week of taking clozapine its effect on your driving skills is greater than that of drinking two standard alcoholic drinks, and those two standard alcoholic drinks are often regarded as the limit for driving.

After taking clozapine for a week, most people become accustomed to the medication and the side effects abate, so that they are able to drive again. However, during the first week of taking this medication you should not drive a car, motorbike or motor scooter. After the first week, assess for yourself how much the side effects affect you and discuss it, preferably also with your psychiatrist. Your reaction time and whether or not you are clear-headed are particularly important. Don't drive a car, motorbike or motor scooter if the side effects are still affecting you. If possible, take the medication before you go to bed, so that the side effects will not affect you so much in the daytime..

For more detailed information we refer you to the official website of the Dutch Ministry of Transport. Like most antipsychotics, clozapine is in Category II, for which the recommendation is not to drive during the first few days.

Tips in case you want to drive after one week:

- If you think you can drive, ask someone to sit beside you the first few times and assess your driving skills. It is often difficult for you yourself to see that your driving is not so good. The person who goes with you can see if you keep changing speed, are lurching or getting annoyed at normal behaviour of other drivers.
- Don't drive if your vision is blurred.
- Don't drive if you're drowsy, sleepy or dizzy, have trouble concentrating or staying awake, or if you don't know what route you took to a destination.
- Don't drive if you've had alcohol. Alcohol significantly strengthens clozapine's side effect of making you drowsy.
- Also be careful about driving if you have taken other medications which affect your reaction time (yellow sticker).

Important addresses

Anoiksis

Anoiksis is an association of and for people with schizophrenia or related psychoses. This association serves and defends their interests.

For more information visit www.anoiksis.nl

Clozapine Plus Werkgroep (Dutch Clozapine Collaboration Group)

Research has shown that psychiatrists are reluctant to prescribe clozapine. This may be justifiable, but in some cases it means that patients are deprived of an effective treatment which would really help them to recover. Sometimes patients also deprive themselves of an effective treatment with clozapine, because they are afraid of rare side effects. Although in some cases the remedy is worse than the disease, as a rule this does not apply to clozapine. One third of people with long-term psychotic disorders have severe forms of these disorders which fail to respond or respond sufficiently to ordinary antipsychotics. These people often are helped by clozapine. To increase knowledge about clozapine and the expertise required to prescribe this medication, the Clozapine Plus Werkgroep was set up in 2004.

The Clozapine Plus Werkgroep (CPW) provides information for anyone interested, gives presentations about clozapine and advises or coaches psychiatrists who prescribe the medication or intend to prescribe it. For more information and a detailed guideline, see the website:

www.clozapinepluswerkgroep.nl

Summary of the most important information

Below is a summary of the most important information about taking clozapine.

Tip: cut this list out, laminate it and keep the card in your purse or wallet!

Front:

10 main rules for taking clozapine

1. If you stop taking clozapine, the dose should usually be tapered off slowly.
2. If you have not taken clozapine for more than two days, see your doctor and talk about how to build up the dose of clozapine again.
3. If you have flu-like symptoms, a sore throat and a temperature above 38 degrees Celsius, and you are still in the first 18 weeks of clozapine treatment, you must tell your doctor or the locum within 24 hours.
4. Always tell your doctors that you are taking clozapine.
5. Talk to your doctor first before you stop or start smoking or start smoking less.
6. If doctors prescribe extra or different medication, tell the doctor who prescribes clozapine for you.
7. If you have physical complaints, tell not only your GP, but also the doctor who prescribes clozapine for you.
8. Make sure you know the symptoms of a possible overdose of clozapine.
9. Make sure your bowel habits are regular.
10. Take enough exercise and watch your weight.

Back:

Symptoms of an excessively high clozapine blood level

- Previously non-existent and rapidly worsening drowsiness, lethargy and listlessness
- Increased dizziness
- Muscle weakness, heaviness in arms and legs
- Uncertain 'drunken' gait
- 'Drunken' speech
- Muscle twitching or muscle cramps.

If you have any of these symptoms, contact your doctor immediately!

In most cases the doctor will have the concentration of clozapine in your blood tested urgently.