Clopidogrel for 'mini-stroke' (transient ischaemic attack or TIA)

Information for the public
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About this information

This information explains the evidence summary about the off-label use of clopidogrel for 'mini-stroke' (also known as a transient ischaemic attack or a TIA). The evidence summary is an overview of the available information about this medicine. It aims to help prescribers and patients when they are considering whether or not to use an unlicensed or off-label treatment. The summary does not contain recommendations from NICE on whether the medicine should be used.

Licensing medicines

In the UK, medicines need to have a licence before they can be marketed. To get a licence, the manufacturer of the medicine has to provide evidence that shows that the medicine works well enough and is safe enough to be used for a specific condition and for a specific group of patients, and that they can manufacture the medicine to the required quality. Medicines can be prescribed without a licence (an 'unlicensed medicine') if there is no suitable licensed alternative and it is likely to benefit the patient.

A medicine can also be prescribed 'off-label'. This means the prescriber wants to use it in a different way than is set out in the terms of its licence. This could mean using the medicine for a different condition or a different group of patients, or it could mean a change in the dose or that the medicine is taken in a different way. There is more information about licensing medicines on NHS Choices.
What is a transient ischaemic attack or TIA?

A transient ischaemic attack (or TIA) is a mini-stroke that happens when the blood supply to part of the brain is interrupted for a short time. The symptoms are the same as for a stroke, but usually last for only a few minutes or hours and disappear altogether within 24 hours. If symptoms last longer than 24 hours it is considered a stroke. A TIA should always be treated as an emergency because it might indicate a greater risk of a major stroke in the near future.

About clopidogrel

Clopidogrel is a drug that helps prevent blood clots from forming in blood vessels. It does this by affecting blood cells (called platelets) that are involved in clotting.

Blood clots can block the blood supply to parts of the brain, causing a stroke or mini-stroke (also known as a transient ischaemic attack or TIA). They can also block blood supply to heart muscle, causing a heart attack. Clopidogrel has a licence for preventing blood clots in people who have already had a heart attack or a stroke caused by a blood clot (called an ischaemic stroke). However, clopidogrel does not have a licence for use in people who have had a TIA, so use in these people is off-label. Clopidogrel is not used in people who have a stroke caused by a burst blood vessel (called a haemorrhagic stroke). Clopidogrel is given by mouth, usually as a tablet.

The NICE guideline on diagnosis and early treatment for stroke and TIA (NICE clinical guideline 68) recommends that people with a suspected TIA should be started on a daily dose of aspirin straight away to reduce their risk of stroke. Once the diagnosis is confirmed, patients and healthcare professionals should discuss and agree the most appropriate drug treatment to prevent blood clots in the future. Drugs licensed for people who have had a TIA include the anti-clotting drugs aspirin and modified-release dipyridamole (which is usually given with aspirin unless the person cannot take aspirin). The NICE Technology Appraisal on clopidogrel and dipyridamole for vascular disease (NICE Technology Appraisal 210) recommends aspirin plus modified-release dipyridamole to prevent bloods clots in people who have had a TIA.

Healthcare professionals will also talk to the patient about making lifestyle changes to reduce the risk of clots. These might include stopping smoking.
Summary of possible benefits and harms

How well does clopidogrel work?

No studies were identified that looked at how well clopidogrel works when given on its own, compared with another treatment such as aspirin in people who have had a mini-stroke (also known as a transient ischaemic attack or TIA).

Two studies looked at how well clopidogrel works when given with aspirin to people who in the past 24 hours had either a suspected TIA or a suspected minor ischaemic stroke with mild symptoms. In both studies, people received clopidogrel for 90 days, and also received aspirin for at least the first 21 days.

The larger study of 5170 people in China found that clopidogrel with aspirin reduced the chance of another stroke in the 90 days after a TIA or minor stroke compared with aspirin alone. About 8 in every 100 people receiving clopidogrel with aspirin had a stroke, compared with about 12 in every 100 people receiving aspirin on its own.

The smaller study of 392 people in the USA and Canada found no difference between clopidogrel with aspirin and aspirin alone in the risk of having another stroke in the 90 days after a TIA or minor stroke. However because of the smaller numbers it was not possible to be sure that there was no difference between clopidogrel with aspirin and aspirin alone in the risk of having a stroke.

Although the Chinese study suggested a benefit of adding clopidogrel to aspirin for preventing stroke, the effect might be different in people from western countries. A similar large study is being carried out to find out the effects of clopidogrel plus aspirin in a western population who have had a TIA or minor stroke. The results from this trial are expected in 2016. The Chinese study also only included people who had a suspected TIA with signs that they were at high risk of a stroke in the future.

What are the possible harms or side effects?

Because clopidogrel stops blood clots forming, it is not suitable for people who have any serious bleeding or who have severe problems with their liver, or who are taking an anticoagulant (a different type of drug to stop clotting). It should be used with caution in people who have a higher than normal chance of bleeding, or who are using other medicines that may affect clotting. Other anti-clotting drugs such as aspirin and modified-release dipyridamole that are licensed for people who have had a TIA can also cause bleeding.
The 2 studies included in this evidence summary compared clopidogrel plus aspirin with aspirin alone.

The large Chinese study found no difference between clopidogrel plus aspirin and aspirin alone in the number of people who had moderate or severe bleeding. Moderate bleeding was defined as bleeding needing a transfusion but not more intensive treatment; severe bleeding was bleeding that was life-threatening or bleeding needing intensive emergency treatment.

Out of the 198 people taking clopidogrel plus aspirin in the USA and Canadian study 6 people had bleeding that caused symptoms. Five of these people had moderate or severe bleeding. No-one out of the 194 people who took aspirin alone had bleeding that caused symptoms.

As these 2 studies only lasted for 90 days they do not provide any information on the long-term safety of clopidogrel plus aspirin compared with aspirin alone in people who have had a TIA. Also in the large Chinese study aspirin was taken with clopidogrel for the first 21 days of the study only.

Please note that the results of the research studies only indicate the benefits and harms for the population in the studies. It is not possible to predict what the benefits and harms will be for an individual patient being treated with clopidogrel.

Prescribing clopidogrel

If a prescriber wants to use an unlicensed or off-label medicine, they must follow their professional guide, for example for doctors the General Medical Council's good practice guidelines. These include giving information about the treatment and discussing the possible benefits and harms so that the patient has enough information to decide whether or not to have the treatment. This is called giving informed consent.

A full version of the summary aimed at healthcare professionals is available on the NICE website. The summary for healthcare professionals does not contain recommendations from NICE on whether the medicine should be used.

Questions to ask

- Why am I being offered an off-label medicine?
- What does the treatment involve?
- What are the benefits I might get?
• How good are my chances of getting those benefits?

• Could having the treatment make me feel worse?

• Are there alternative treatments?

• What are the risks of the treatment?

• Are the risks minor or serious? How likely are they to happen?

• What may happen if I don't have the treatment?

More information

The evidence summary and this information for the public were produced for NICE by Bazian Ltd.

NICE has published information about how evidence summaries for unlicensed and off-label medicines are developed.

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