Intravenous iloprost for chronic, severe restriction of blood flow to the limbs (critical limb ischaemia)

Information for the public
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About this information

This information explains the evidence summary about the unlicensed use of intravenous iloprost for treating severe restriction of blood flow to the limbs (critical limb ischaemia). 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 critical limb ischaemia?

Critical limb ischaemia (severe restriction of blood flow to the limbs) occurs when the blood vessels (arteries) that carry blood to the limbs (usually the legs and feet) are hardened and narrowed or blocked by a build up of fatty deposits (this is known as peripheral arterial disease). The severe restriction of blood flow causes pain in the toes, feet and legs even when resting. Sometimes in severe cases, foot ulcers or gangrene develops. In these cases, amputation (removal of part of the foot or leg) may be needed. Critical limb ischaemia is a serious condition that can be life threatening.

About iloprost

Iloprost is a drug that mimics the effects of a natural substance in the body called prostacyclin. Iloprost works by causing the smaller blood vessels to widen, allowing more blood to flow through them.

In the UK, an inhaled form of iloprost is licensed for treating primary pulmonary hypertension, a condition in which the blood pressure is too high in the blood vessels between the heart and the lungs. This summary does not cover the inhaled form of iloprost.

When iloprost is used for treating critical limb ischaemia, it is injected into a vein. The injection takes place over a 6-hour period and is called an intravenous infusion. The infusion is given once a day, usually for 4 weeks. Iloprost is licensed for use in this way for various conditions in some countries, but not in the UK. Therefore intravenous infusion of iloprost for critical limb ischaemia is unlicensed in the UK.

The main treatment for critical limb ischaemia is surgery to restore the blood flow in the leg (called revascularisation). There are various ways to do this including:

- Redirecting the blood so that it bypasses the blocked section of artery (called bypass surgery). This is done with a vein taken from another part of the body or a synthetic tube.

- Inserting a small balloon into the narrowed artery and inflating it to widen the artery (called balloon angioplasty). A mesh tube called a stent may then sometimes be used to hold open the artery.

However, some people with critical limb ischaemia cannot have these surgical procedures because of other medical conditions. For these people drug treatments that increase blood flow are the only options. These treatments include iloprost and similar drugs such as prostaglandin E1 (also
unlicensed for critical limb ischaemia) as well as drugs licensed for use in peripheral arterial disease in the UK, such as naftidrofuryl oxalate and pentoxifylline.

Summary of possible benefits and harms

How well does intravenous iloprost work?

Seven studies were identified that looked at using intravenous iloprost to treat critical limb ischaemia in people who could not have surgery. Five of these studies compared intravenous iloprost with a 'dummy' infusion (containing no drug and known as placebo).

Intravenous infusion of iloprost each day for 2 to 4 weeks:

- increased the number of people who had relief from limb pain when resting from about 37 in 100 to about 56 in 100
- increased the number of people with healing of leg ulcers from about 28 in 100 to about 51 in 100
- reduced the number of people who needed a major amputation (removal of the foot and leg from above or below the knee) from about 44 in 100 to about 31 in 100.

The number of people needing any kind of amputation – that is both major (removal of the foot and leg from above or below the knee) or minor (removal of part of the foot or fingers) – was less in those receiving iloprost than in those receiving the dummy infusion but this could have occurred by chance.

The studies had some weaknesses that mean it was not possible to be certain how well iloprost works. It is also not clear how well iloprost works over a longer period.

One study looked at whether intravenous iloprost improved how well bypass surgery worked for critical limb ischaemia compared with a dummy infusion. People had intravenous iloprost for 3 days around the time of surgery and an iloprost injection directly into the bypass graft. In the 12 months after surgery, there was no difference in how well the bypass grafts worked between those receiving iloprost and those receiving a dummy infusion. There was also no difference in the number of people whose symptoms improved or who needed amputation.
What are the possible harms or side effects?

The most common side effects of intravenous iloprost are headache, flushing of the skin, nausea (feeling sick), vomiting (being sick) and sweating. These usually happen at the start of treatment while the doctors are working out the best dose. The side effects usually get better quickly if the dose of iloprost is reduced.

Serious side effects of intravenous iloprost are less common, but may include low blood pressure, faster than normal heartbeat, chest pain, shortness of breath, stroke, heart attack, blood clot in the artery supplying the lungs, heart failure, convulsions, asthma and fluid in the lungs.

In the studies comparing intravenous iloprost with dummy infusion about twice as many people had side effects with iloprost as those receiving the dummy infusion – about 83 in 100 compared with 41 in 100 people. These side effects were mainly headache, flushing, nausea and vomiting.

The study in people having bypass surgery for critical limb ischaemia also found that people having iloprost were more likely to have side effects than those having dummy infusions. These side effects included low blood pressure, headache, flushing, nausea and vomiting. The number of people who died or had serious side effects in the 2 weeks after surgery, such as heart attacks or strokes was similar in people receiving iloprost and those receiving dummy infusions.

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 intravenous iloprost.

Prescribing intravenous iloprost

If a prescriber wants to use an unlicensed 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 unlicensed 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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