



## Midodrine

Midodrine is a drug that can be used to treat people with disorders of the autonomic nervous system which include low blood pressure, neuro-cardiogenic syncope (fainting) and postural tachycardia syndrome. It is used only after other measures have been ineffective in controlling symptoms (e.g. high fluid intake, additional salt in some patients, counter manoeuvres, small frequent meals, gentle exercise, compression tights as appropriate).

Midodrine hydrochloride is the generic (chemical) name but some manufacturers use their own brand names for the same drug, which include Bramox, Gutron, ProAmatine and Orvaten. It comes in 2.5, 5 or 10mg tablets.

In 2015, Bramox became licenced for use in adults with severe orthostatic hypotension (low blood pressure on standing up) in the UK. It is not yet licenced for use in PoTS or in children. Bramox is available in 2.5 and 5 mg tablets.

### How does midodrine work?

Midodrine is an  $\alpha_1$  adrenergic agonist, and works by stimulating receptors that noradrenaline normally works on. After swallowing, midodrine is rapidly converted into another, more active drug that binds to noradrenaline receptors causing blood vessels to narrow, thereby increasing blood pressure. There have been reports of reduction in heart rate in some PoTS patients following treatment with midodrine.

It reaches peak concentration in the blood about an hour after swallowing a tablet, but the effect is brief, with levels falling to half about 2-3 hours later.

The brain has a protective mechanism that stops some drugs from entering and very little midodrine crosses this blood-brain barrier. It is removed from the body by the kidneys.

### How do I take midodrine?

As its effect is short lived, midodrine needs to be taken frequently throughout the day. It works best if the first dose is taken an hour or so before getting out of bed\*, then at 3 to 4 hourly intervals throughout the day. The last dose should NOT be taken within 4 hours before going to bed. If necessary, your doctor may instruct you to gradually increase the amount to a maximum total dose of 30mg in 24 hours. Midodrine can be taken with or without food.



## What are the risks of taking midodrine?

The main risk of taking midodrine is 'supine hypertension'. This is excessively high blood pressure on lying down. One advantage of midodrine is that it only works for a short time. Not taking it within 4 hours of going to bed reduces the risk of supine hypertension. Supine hypertension does not usually cause symptoms, but rarely people may experience chest pain, unexpected headache or blurred vision. If you develop these symptoms, you should stop midodrine and inform the prescribing doctor. Elevating the head of your bed may reduce the risk of supine hypertension.

In addition, midodrine should not be continued if it causes high or unstable daytime blood pressure.

## Who should not take midodrine?

Midodrine should not be prescribed in patients with the following conditions: severe heart disease, unusually slow heart rate, hypertension, conditions that cause blockage, narrowing or spasm of the arteries, enlarged prostate gland, urinary retention (when the bladder can't empty properly), phaeochromocytoma (noradrenaline producing tumour), acute or severe kidney disease, overactive thyroid, diabetic eye disease, narrow-angle glaucoma, allergy to any component of the product.

Use of Midodrine has not been studied in children and it should only be used in people under the age of 18 following the recommendation of a specialist who is very experienced in its use.

## What are the side effects of midodrine?

**Common** – tingling and itching, increased blood pressure when lying down, headache, nausea (feeling sick), heartburn, inflammation of the lining of the mouth, flushing, rash, chills, difficulty urinating.

**Less common** – sleep disturbances, restlessness, agitation, irritability, slowed heart rate, urge to urinate.

**Rare** – palpitations, rapid heartbeat, abnormal liver blood test.

Possible side effects – abdominal pain, being sick (vomiting), diarrhoea, anxiety, feelings of confusion.

## Interactions with other medicines

Midodrine should be used with caution in combination with the following drugs:

digoxin, beta blockers (eg bisoprolol, atenolol, propranolol), other drugs that reduce the heart rate, steroids (prednisolone, fludrocortisone), alpha adrenergic receptors stimulators (phenylephrine, methoxamine), tricyclic antidepressants, antihistamines, thyroid hormones, MAO inhibitors, dihydroergotamine, rauwolfia alkaloid medicines (eg reserpine), other drugs that narrow blood vessels or stimulate the central nervous system. Midodrine should not be given to people taking alpha blockers (phentolamine, prazosin).

## Is midodrine safe to take in pregnancy?

The effects of midodrine in the unborn baby are unknown as there have been no studies investigating the use of midodrine in pregnancy. Midodrine is not generally recommended in pregnancy but is occasionally used with extreme caution and only upon the advice of a specialist during pregnancy and breastfeeding.



## Monitoring midodrine treatment

Blood pressure and a kidney function blood test should be checked before midodrine is started. Blood pressure and heart rate should be monitored during treatment with midodrine. It is especially important to have your blood pressure checked after lying down.

## What does 'unlicensed' mean?

Midodrine has marketing authorisation in the UK, USA and some other European countries for the treatment of symptomatic postural hypotension due to disorders of the autonomic nervous system only. It is not licensed for any other condition and is therefore unlicensed (or 'off licence') for use in PoTS.

## How do I obtain midodrine?

As midodrine is unlicensed in the UK for PoTS, it is usually recommended by a hospital doctor with experience in using this drug. Midodrine may be obtained in the following ways:

- ♥ Now that it has a license in the UK for postural hypotension, some GPs may also be willing to prescribe it in PoTS. This is more likely to happen if the patient's hospital consultant provides a 'Shared care Agreement' (a document which provides advice to the GP about how to prescribe, side effects, monitoring and how to contact the hospital team if there are problems).
- ♥ Some hospital consultants will prescribe the midodrine and it is dispensed by the hospital pharmacy. Other hospital consultants will issue an FP10, which is the green NHS prescription that can be dispensed by your local community pharmacy.

- ♥ Midodrine is usually obtained on an NHS prescription. If it is prescribed during a private consultation with a consultant, they will issue a private prescription (and the patient will have to pay the full cost of the drug, which can be hundreds of pounds)
- ♥ A private consultant may write to an NHS doctor asking if they would be willing to issue an NHS prescription (in which case the patient will pay only the cost of an NHS prescription, or nothing if they are entitled to free prescriptions).

To obtain the version of midodrine that holds a license in the UK it should be prescribed by its brand name Bramox, rather than by its generic (chemical) name midodrine.

## How to store midodrine

Midodrine should be stored out of reach of children and used before its expiry date.

It should be kept in its original packaging to protect it from light, and stored below 25oC

If your doctor prescribes Midodrine / Bramox for you, you should read the patient information leaflet that is issued with the medication for more detailed information.

## NICE Evidence Summary Oct 2015

<https://www.nice.org.uk/advice/esnm61/chapter/Key-points-from-the-evidence>



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Details regarding the sources of evidence used in the production of this leaflet are available on the PoTS UK website.

See [www.potsuk.org/sources\\_of\\_evidence](http://www.potsuk.org/sources_of_evidence)