



MANAGEMENT FILE

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MEA membership costs £18 a year for people living in the UK/BFPO.

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the ME association



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AMITRIPTYLINE EXPLAINED

WHAT IS AMITRIPTYLINE?

Amitriptyline is the generic (non-trade) name for one of the oldest members of a group of antidepressant drugs known as tricyclics.

Drugs in this group can help some people with depression because they alter levels of brain chemicals – in particular, noradrenaline and serotonin – that transmit messages between brain cells and which may be reduced in depression.

Although amitriptyline was developed for treating depression, its use has diminished in recent years – mainly because new types of antidepressants (drugs like Prozac and Lustral) are just as effective, or more effective, and tend to cause fewer problems with side effects. Newer antidepressants also tend to be safer if an overdose is taken.

So amitriptyline is not usually a first choice drug for someone who needs treatment for depression.

SO WHY MIGHT AMITRIPTYLINE BE USED IN ME/CFS?

Firstly, for pain:

At low doses, amitriptyline can provide effective pain relief in the muscles, joints or nerves (= neuropathic pain or neuralgia). Neuropathic pain is often described as a searing or burning pain.

So amitriptyline may be recommended for pain relief when first-line analgesics such as aspirin, paracetamol or

ibuprofen/Brufen are not effective.

Amitriptyline can also help to relieve abdominal pain associated with irritable bowel syndrome – but not when this includes constipation because amitriptyline can cause constipation as a side effect.

Secondly, for sleep disturbance:

One of the side effects of amitriptyline is sedation. So a low dose can be helpful for people who are waking during the night and not sleeping solidly for at least five hours.

Thirdly, for the prevention of migraine

These appear to be more common in ME/CFS – as well as what is called atypical facial pain. Amitriptyline is also sometimes used to treat what are called cluster headaches.

Section 1.6.3.2 in the NICE guideline on ME/CFS states that prescribing of low-dose tricyclic antidepressants, specifically amitriptyline, should be considered for people with CFS/ME who have poor sleep or pain.

PATIENT EVIDENCE FROM THE MEA ON THE USE OF AMITRIPTYLINE IN ME/CFS

Feedback from people with ME/CFS in our 2010 *Illness Management Report** indicated that, while a significant proportion found amitriptyline helpful for pain and sleep disturbance, others gained no benefit or found it made them feel worse – mainly as a result of the side effects.

Key findings from the MEA Management Report

For pain relief:

11% reported a good response; 31% a moderate response; 9% a poor response; 19% no change. 31% said amitriptyline made them feel worse (1196 respondents).

For sleep disturbance:

13% reported a good response; 30% a moderate response; 11% a poor response; 18% no change. 27% said amitriptyline made them worse (1122 respondents)

Feedback to a more recent but smaller survey on the MEA Facebook page in November 2018 indicated that only around a third of people found amitriptyline to be helpful (in some instances very helpful) for pain, sleep disturbance or preventing migraine type headaches.

However, around two-thirds reported no benefit, or a significant problem with side-effects which outweighed any possible benefits. The most common side-effects reported were:

- adverse effects on mental functioning – feeling groggy or zombie-like reactions were quite frequently mentioned
- dry mouth
- dizziness
- nausea and gastric upsets
- weight gain

Lessons to be learnt from our extensive patient evidence are:

- Some people find amitriptyline helpful but many do not and have significant problems with side effects
- Amitriptyline is a drug that may be worth trying but only with caution
- Treatment should start with a very low dose and any increase in dose should be done gradually
- It may take several weeks for any benefits to occur whereas side effects may be more prominent on starting treatment and then diminish over time.

HOW AND WHEN IS AMITRIPTYLINE PRESCRIBED BY DOCTORS?

Prescribing amitriptyline for migraine, pain and sleep disturbance are all unlicensed uses of this drug. Depression is the only condition for which amitriptyline has a product license. So doctors may be cautious or uncertain about using it for unlicensed purposes.

When amitriptyline is being taken for either pain relief or sleep disturbance, a dose of 5mg, 10mg or 25mg may be all that is required. At this level – much lower than the normal antidepressant dose – side effects are less likely.

One important practical point to remember is that amitriptyline does not usually start to produce beneficial effects immediately – these may take several weeks to achieve.

HOW TO TAKE AMITRIPTYLINE

Amitriptyline is normally taken as a once daily dose at or around bedtime because it makes you feel sleepy. It can be taken earlier in the evening if sedating side effects are still prominent in the morning.

Amitriptyline does not normally cause stomach upsets – so it can be taken with or without food. The tablets should be swallowed with a drink of water. Do not chew the tablets – as they have an unpleasant bitter taste.

Try to take the drug at the same time

each day to avoid missing a dose. If you forget, take it as soon as you can unless it is nearing the time for the next dose. Do not take two doses together to make up for a forgotten dose.

Store in a cool dry place away from direct heat and light.

Amitriptyline is normally prescribed in tablet form which comes in three different strengths: 10mg, 25mg and 50mg. Liquid amitriptyline also comes in three strengths and can be prescribed in a 5ml spoonful. The liquid form can be used to provide a 5mg dose if needed.

WHAT ARE THE POSSIBLE SIDE-EFFECTS?

Relatively common side effects, some of which overlap with ME/CFS symptoms and may obviously exacerbate them, include:

- Blurred vision - but if you experience eye pain do check with your doctor as soon as possible
- Constipation – try to avoid this by eating a well balanced diet with fruit and vegetables and drinking plenty of water
- Dry mouth – this can increase the risk of tooth decay with long-term use, so take good care of your teeth and have a regular dental check up. Chewing sugar-free gum or sweets can also help.
- Gastric upsets
- Postural hypotension and dizziness (= a fall in blood pressure on standing) – try to avoid this by moving from lying to standing more slowly. If you feel dizzy, sit or lie down until the symptoms pass.
- Palpitations – speak to your doctor if these occur
- Increased sweating
- Taste problems
- Difficulty passing urine – speak to your doctor if this occurs
- Weight change – including weight gain
- Low sodium leading to headaches and confusion

Less common and more severe side-effects:

Serious reactions are rare but amitriptyline can cause an allergic reaction involving wheezing, breathlessness and swelling of the face and mouth.

- Allergic skin rashes and sensitivity to the sun – amitriptyline can cause the skin to become more sensitive to sunlight. So avoid strong sunlight until you know how your skin reacts.
- Blood sugar changes – if you already have diabetes you may need to have your blood sugar checked more regularly.
- Confusion
- Heart rhythm disturbances – speak to your doctor if your heart is racing or you are having palpitations.
- Liver function abnormalities and jaundice.
- Muscle tremors and twitching
- Sexual problems
- Tinnitus – ringing noises in the ears

If side effects occur, or you think that you might have acquired a new ME/CFS symptom, then do talk to your doctor or pharmacist – who can decide if it is safe for you to continue.

Three important points about side-effects:

First – side effects are less likely to occur at the lower doses used for pain relief and sleep disturbances.

Second – they tend to be worse when the drug is first started and then they often diminish over a period of weeks.

Third – side effects are more likely to occur in the elderly.

It should also be noted that some new research evidence indicates that this type of antidepressant medication could increase the risk of dementia – possibly due to the way in which amitriptyline affects brain chemical transmitter systems.

Amitriptyline has also been reported to cause mitochondrial dysfunction (mitochondria are energy-producing components of cells and mitochondrial

dysfunction occurs in ME/CFS) and deficiency of a substance called co-enzyme Q10, which plays an important role in energy production at a cellular level.

It is far too early to say that these research findings create a strict contra-indication to the use of amitriptyline in ME/CFS. But they do need to be taken into consideration when weighing up the pros and cons of using amitriptyline, especially for a prolonged period of time.

ARE THERE ANY CAUTIONS OR CONTRA-INDICATIONS?

If you have any of the following medical conditions in addition to ME/CFS, this will mean that amitriptyline must only be used with caution or not at all:

- Allergic reaction to amitriptyline in the past
- Chronic constipation
- Diabetes – it's important to check blood sugar levels more frequently

DOES AMITRIPTYLINE REACT WITH OTHER DRUGS?

The effects of amitriptyline can be altered or exacerbated if you are taking some other types of prescribed or over-the-counter medication. Examples include:

- Other types of antidepressants, including SSRIs (selective serotonin reuptake inhibitors) like Prozac or Lustral. Amitriptyline should not normally be used in combination with an SSRI and should not be used with the herbal remedy St John's Wort
- Cold and flu remedies that contain a decongestant called pseudoephedrine
- Anti-hypertensive drugs (for high blood pressure)
- Baclofen – as can increase muscle weakness
- Cimetidine - for stomach problems
- Sleeping tablets and antihistamines – can increase drowsiness
- Thyroid treatments
- Tramadol and codeine for pain – as can cause drowsiness

if you have diabetes

- Epilepsy – as it can trigger seizures
- Glaucoma – as it can increase pressure in the eye
- Heart disease and low blood pressure
- Liver or kidney disease
- Mania, psychosis or schizophrenia
- Pregnancy or breast-feeding
- Prostate enlargement/hypertrophy – causing a poor urinary stream
- Thyroid disease

CAN AMITRIPTYLINE BE GIVEN TO CHILDREN?

All drugs have to be used with care when given to children, especially in the case of ME/CFS.

Amitriptyline is sometimes prescribed by paediatricians for pain relief and sleep disturbance in children and adolescents – provided there are no specific contra-indications.

- Warfarin – may interfere with blood-clotting control

Your doctor and pharmacist will be aware of all the possible interactions. So do check if in doubt. And always check with your doctor or pharmacist if you are going to start taking any other drugs, including over-the-counter medicines or supplements, at the same time as amitriptyline.

IS THERE ANYTHING ELSE I SHOULD DO WHILE TAKING AMITRIPTYLINE?

If a low dose of amitriptyline for pain or sleep disturbance has not produced any benefits after a few weeks, then go back and see your doctor.

It may be worth trying a cautious

increase in dose or switching to another type of sedating tricyclic drug (eg, trimipramine) before concluding that this approach isn't going to be helpful.

- Don't combine amitriptyline with alcohol – this will enhance the sedative effects.
- Take care when driving or operating machinery because of the sedative effect.
- If the dose is going to be increased, this should be done slowly because people with ME/CFS tend to be very sensitive to drugs that affect brain chemical transmitters.
- If amitriptyline is going to be discontinued, this should be done by gradually reducing the dose. This will help to reduce the chances of any withdrawal symptoms. These can include flu-like symptoms, chills, muscle pain/myalgia, sweating, headaches and nausea.

FURTHER INFORMATION

There is more information on depression and all the different types of antidepressant medication in an MEA information leaflet: called *Depression and Antidepressants*: <https://tinyurl.com/yx9q42dj>

Similar information can be found on pages 231-242 of *Living with ME* and in the sections on depression, pain relief and sleep disturbance in our clinical and research guide *ME/CFS/PVFS: An Exploration of the Key Clinical Issues*.

Detailed information on the management of migraine-type headaches, irritable bowel symptoms, pain and sleep disturbance can be found in other MEA information leaflets.

Our *Illness Management Report* can be ordered by phone (as a paper copy) or downloaded free from the MEA website at <http://tinyurl.com/c6fp19p>

Medical information contained in this leaflet is not intended to be a substitute for medical advice or treatment from your doctor. We say that you always consult your doctor or healthcare professional about any specific problem. We also recommend that any medical information provided by The MEA is, where appropriate, shown to and discussed with your doctor.