

AMITRIPTYLINE AND ME/CFS

*Why low-dose Amitriptyline might be helpful
in ME/CFS*



Including:
About Amitriptyline
Why Amitriptyline might
be helpful in ME/CFS
Guideline
recommendations

Patient evidence
How and when to take
Amitriptyline
Possible side-effects
Amitriptyline and
children



AMITRIPTYLINE AND ME/CFS was written by **Dr Charles Shepherd**, Trustee and Hon. Medical Adviser to The ME Association.

DISCLAIMER

We recommend that the medical information in this leaflet is discussed with your doctor. It is not intended to be a substitute for personalised medical advice or treatment. You should consult your doctor whenever a new symptom arises, or an existing symptom worsens. It is important to obtain medical advice that considers other causes and possible treatments. Do not assume that new or worsened symptoms are solely because of ME/CFS or Long Covid.



AMITRIPTYLINE AND ME/CFS

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WHAT IS AMITRIPTYLINE?

Amitriptyline is the generic (non-trade) name for one of the oldest members of a group of antidepressants 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, this use has diminished in recent years – mainly because new types of antidepressants such as 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 antidepressant for someone who needs treatment for depression.

KEY POINTS:

- Amitriptyline is an older type of antidepressant that is now prescribed far less frequently for treating depression - as the newer antidepressants are safer to use and have less side-effects.
- At lower doses than are used for treating depression, amitriptyline can sometimes be helpful for treating pain – including irritable bowel syndrome pain, sleep disturbance, and preventing migraine type headaches.
- Feedback from people with ME/CFS indicates that a significant minority find amitriptyline helpful for pain relief or sleep disturbance.
- The remainder report no benefit and/or find that the side-effects outweigh any possible benefits.
- Side-effects tend to be more prominent at the start of treatment and then tend to decline, whereas it may take several weeks for the benefits to take place.
- So it's normally worth trying amitriptyline for at least 4 weeks before deciding whether it is going to be a useful form of treatment.

Amitriptyline can provide effective pain relief in migraine-type headaches, which appear to be more common in ME/CFS – as well as what is called atypical facial pain.

WHY LOW-DOSE AMITRIPTYLINE MIGHT BE HELPFUL IN ME/CFS

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.

Amitriptyline may therefore be recommended for pain relief when first-line analgesics such as paracetamol or ibuprofen/Brufen are not effective.

Amitriptyline can also help to relieve abdominal pain associated with irritable bowel syndrome, especially when this is combined with diarrhoea – but not when this includes constipation because amitriptyline can cause constipation as a side-effect. This pain-relieving action may be due to amitriptyline dampening down nervous messages that are controlling gut muscle contractions.

Sleep disturbance:

One of the common 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.

Prevention of migraine:

Migraine-type headaches 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.



GUIDELINE RECOMMENDATIONS

The first (2007) NICE guideline on ME/CFS stated that prescribing of low-dose tricyclic antidepressants, specifically amitriptyline, should be considered for people with ME/CFS who have poor sleep or pain. However, the new NICE guideline on ME/CFS does not make any specific recommendations and refers doctors to the NICE guideline on the management of neuropathic pain:

<https://www.nice.org.uk/guidance/cg173>

...which does refer to the use of Amitriptyline.



The Chief Medical Officer's Working Group Report on ME/CFS also recommended that: low dose tricyclics can be especially useful for pain with neuropathic quality (and the related paraesthesiae) and that ... if medication needs to be used, low doses of tricyclic agents, if tolerated, are often effective in restoring sleep quality and rhythm, and are preferable to hypnotic agents.

...Tricyclic agents, if tolerated, are often effective in restoring sleep quality and rhythm, and are preferable to hypnotic agents.

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 (see page 13) 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).



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

Feedback to a more recent, but smaller, survey on the MEA Facebook page in November 2018 indicated that 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 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



One of the most common side-effects was adverse effects on mental functioning – feeling groggy or zombie-like reactions.



Depression is the only condition for which Amitriptyline has a product license. So doctors may be cautious or uncertain about using even a low dose for unlicensed purposes.

HOW AND WHEN IS LOW-DOSE 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 even a low-dose 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, possibly up to six weeks for pain relief.

HOW AND WHEN 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. To reduce morning drowsiness, it can therefore be helpful to take it 12 hours before the time you normally get up.

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 amitriptyline 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 these three strengths and can be prescribed in a 5ml spoonful. The liquid form can therefore be used to provide a 5mg dose if needed.





If you experience 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.

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 both weight loss and weight gain as some people feel more hungry whereas others feel less hungry
- **Low sodium** leading to headaches and confusion

Less common and more severe side-effects include:

- **A serious 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.



WHAT ARE THE POSSIBLE SIDE-EFFECTS?

- Liver function abnormalities and jaundice
- Muscle tremors and twitching
- Gynaecological problems including occasional vaginal bleeding and breast swelling
- Tinnitus – ringing noises in the ears

If side-effects occur, or you think that you might have acquired a new ME/CFS symptom, 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 often diminish over a period of weeks.

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

More prolonged use could possibly increase the risk of dementia – due to the way in which Amitriptyline affects a brain chemical transmitter called acetylcholine.

There is now some research evidence to indicate that more prolonged use of this type of antidepressant medication could affect a part of the nervous system that is involved with memory and cognition. More prolonged use could possibly increase the risk of dementia – due to the way in which amitriptyline affects a brain chemical transmitter called acetylcholine.

More information here:

<https://tinyurl.com/2a6599ud>

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.



Amitriptyline must only be used with caution, or not at all, if you have certain medical conditions in addition to ME/CFS. Check the list below.

WHAT ARE THE POSSIBLE SIDE-EFFECTS?

It is far too early to say whether these research findings create a 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 in more elderly people and/or 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 – important to check blood-sugar levels more frequently 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





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



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.

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) such as 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.

Caution is also required with:

- Cold and flu remedies that contain a decongestant called pseudoephedrine
- Anti-hypertensive drugs (for high blood pressure)
- Baclofen – as this can increase muscle weakness
- Cimetidine - for stomach problems
- Sleeping tablets and antihistamines – can increase drowsiness
- Thyroid treatments
- Tramadol, codeine and other opioid-type drugs for pain – as this can cause drowsiness
- Warfarin – may interfere with blood-clotting control

IS THERE ANYTHING ELSE I SHOULD DO WHILST TAKING AMITRIPTYLINE?



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.

If a low dose of amitriptyline for pain or sleep disturbance has not produced any benefits after a few weeks, 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 (e.g. trimipramine) before concluding that this approach isn't going to be helpful.

Don't combine amitriptyline with alcohol – this will enhance the sedative effects.

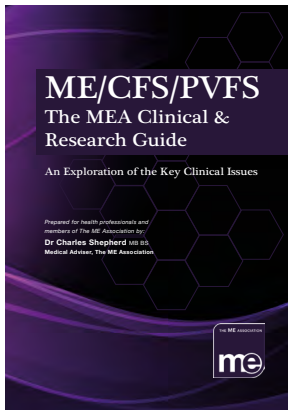
Take care when driving or operating machinery because of the sedative effect.

If you are going to have an operation or a dental anaesthetic, let the doctor or dentist know you are taking amitriptyline as it can interfere with some anaesthetic drugs.

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.

Finally, when used at a low dose, amitriptyline is not normally addictive.



Use this QR code to link to the MEA's Clinical and Research Guide ME/CFS/PVFS: An Exploration of the Key Clinical Issues (The Purple Book).



FURTHER INFORMATION

There is more information on depression and all the different types of antidepressant medication in an MEA information leaflet:

Depression and Antidepressants:

<https://meassociation.org.uk/i5bx>

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 'Purple Book':

The Clinical and Research Guide ME/CFS/PVFS: An Exploration of the Key Clinical Issues:

<https://meassociation.org.uk/pbme>

Also available on Kindle:

<https://meassociation.org.uk/4nop>

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

Headaches & Migraines and ME/CFS:

<https://meassociation.org.uk/qhed>

Our **Illness Management Report** can be ordered by phone (as a paper copy) or downloaded free from the MEA website:

<https://meassociation.org.uk/eocu>



“Thank you for producing such a helpful magazine. The standard is consistently high and each edition is interesting and varied. I need all the help I can get and this magazine is consistently encouraging, realistic, and helpful.”



HOW WE CAN HELP

■ **COMMUNITY:** We provide a safe and welcoming community for people affected by ME/CFS and Long Covid who come together and benefit from sharing their experiences. We provide membership, an essential support service, excellent website resources and we host engaging discussions on the most popular social media channels. Knowing that you are not alone can be a great comfort and we are happy to answer your questions and share helpful tips.

■ **MEMBERSHIP:** We put the interests of members at the heart of everything we do. Your subscription means that we can support more people, campaign more effectively and fund more medical research. Members receive the exclusive ME Essential magazine which carries the latest news, medical information, personal stories, and feature articles. **Join us today.**

■ **SUPPORT:** ME Connect is the charity's support and information service. We listen and we understand. All our staff and volunteers have knowledge and understanding of these medical conditions. We provide a personalised service and we're here when you need us most. You can contact us via our telephone support line (Freephone) or by email. Please see back page for more details. To view the ME Connect telephone support line opening hours, please visit: <https://www.meassociation.org.uk/me-connect>

■ **INFORMATION:** We produce reliable and timely information written by topic experts and have the **largest range of free literature covering all aspects of life with ME/CFS and Long Covid**. We can show you how to recognise and manage symptoms, get an accurate diagnosis, a referral to specialists, and to obtain the healthcare that you deserve. We also provide an **e-newsletter** and free access on the website to **Medical Matters** and other relevant information.

■ **RESEARCH:** We fund medical research via the **Ramsay Research Fund** and are especially interested in research that can find diagnostic markers, causes, and treatments. We support the UK ME/CFS Biobank and the Manchester Brain Bank, and have invested over £1m in medical research in the last 10 years.

■ **MEDICAL EDUCATION:** We arrange training for healthcare professionals, offer a medical magazine, ME Medical, and are working with the Government, NHS, Royal Colleges of Medicine, and Local Authorities to implement the recommendations of the 2021 NICE Clinical Guideline on ME/CFS – the successful result of 14 years lobbying and hard work.

“The MEA is doing exactly what it said it would by providing support, actively lobbying for recognition, improvements to health and social care, and funding biomedical research.”



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Registered Charity
Number 801279



HOW WE CAN HELP

■ **LOBBYING:** We campaign to raise awareness and bring about positive change. We believe in collaboration and work with the NHS and social care services, the Department of Health and Social Care, the British Association of Clinicians in ME/CFS (BACME), Forward-ME, the ME Research Collaborative (MERC), DecodeME, the All-Party Parliamentary Group (APPG) on ME, Physios4ME, the Chronic Illness Inclusion project (CII), Hidden Disabilities Sunflower, and Long Covid initiatives.

■ **HEALTH & SOCIAL CARE:** The charity works with healthcare providers to successfully implement the NICE Guideline recommendations on ME/CFS and Long Covid to ensure that everyone receives the very best healthcare, wherever they live in the UK. We want well-trained healthcare professionals providing excellent services because timely intervention can lead to better health outcomes and improved quality of life.

■ **DONATIONS:** In order to help more people and invest in medical research we depend on your generosity. If you feel able to make a donation or want to raise funds in other ways, please get in touch with the fundraising team: fundraising@meassociation.org.uk or you can **make a direct donation via the website.**

WHAT ARE ME/CFS AND LONG COVID?

We answer key questions about these medical conditions and compare similarities and differences. You'll also find the NICE Guideline reproduced in full in an easy-to-use database.

MEDICAL MATTERS

Medical Matters is an easy to use online supplement to the more detailed literature. The same topic experts provide answers to commonly asked questions.

NHS REFERRAL SERVICES

If you need to locate an ME/CFS specialist service or Long Covid Clinic then we can help. We have listed all secondary care referral services in an easy-to-use database.



THE ME ASSOCIATION



ME CONNECT

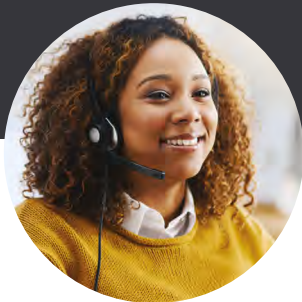
The Support and Information Service
for people affected by ME/CFS/PVFS
and Long Covid

HOW TO GET IN TOUCH:
by phone or email



Freephone
0808 801 0484

For opening hours visit:
meassociation.org.uk/mec



HERE TO LISTEN

We are here to listen,
validate and empathise
with any issues you might
be facing.



VITAL SUPPORT

We are here to help
you reach an informed
decision.



SAFE ENVIRONMENT

We provide a safe,
confidential and
understanding
environment where you
can be heard
and understood.

We're here for you!



meconnect@meassociation.org.uk

For all information relating to ME Connect visit: <https://meassociation.org.uk/mec>

meassociation.org.uk