



M.E./CFS: a guide for pharmacy teams



Supporting patients living with myalgic
encephalomyelitis/chronic fatigue syndrome

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Essential M.E. facts

M.E. is a complex, fluctuating, long-term condition affecting 250,000 men, women and children in the UK. A GP surgery with 10,000 patients will have around 40 people with M.E. – see p 5.

Function levels for people with M.E. can range from being in work (this requires careful energy management) to not being able to wash or feed themselves – see p 5.

M.E. fluctuates in symptoms and severity, so people who seem well one day can be very unwell the next – see p 5.

The key symptom of M.E. is post-exertional malaise, triggered by physical/mental activity, so patients must carefully manage rest and physical/mental activity. General exercise programmes have no evidence-base in M.E. and can cause harm – see p 7.

M.E. is not easily recognisable from prescriptions alone as there's no specific treatment for the condition – see p 8.

Issues associated with multi-morbidity and polypharmacy are common in patients living with M.E. – see p 8.

People with M.E. often have increased susceptibility to side effects, and the similarity of these and the symptoms of M.E., can result in misinterpreting them as new symptoms – see p 8.

People with M.E. have difficulty accessing services, and pharmacy teams may be their only contact with health professionals. Support with ordering repeat prescriptions, deliveries and other pharmacy services can be invaluable – see p 8.

Cognitive difficulties in M.E. can affect concentration and the ability to retain information, so offering a written summary, as per the Accessible Information Standard, is recommended, particularly for patients with severe M.E. – see p 8.

You can refer anyone affected by M.E., including carers, to Action for M.E. for information and support on all aspects of living with the condition, including applying for welfare benefits and accessing peer-support. Call 0117 927 9551 or visit www.actionforme.org.uk

Introduction

Myalgic Encephalomyelitis (M.E.) is a relatively common long-term condition with complex symptoms.

It causes significant and, in some cases, profound disability.

Within the NHS, a diagnosis of chronic fatigue syndrome (CFS) or CFS/M.E. is often given. We will refer to it as M.E. throughout this resource.

A lack of understanding and awareness about M.E. as a debilitating, physical, hidden illness means that patients can experience disbelief, and even discrimination, from friends, family, health and social care professionals and employers. Consequently, their health needs may be going unmet.

Action for M.E. has produced this booklet for community pharmacy teams in the UK to ensure that people with M.E. receive evidence-based pharmaceutical care and that their needs are met when using pharmacy services. We also offer information to people affected M.E. about the pharmacy services that might help them to manage their long-term condition.

We are hugely grateful to pharmacist and Action for M.E. volunteer, Emily Beardall, who wrote this resource and continues to devote considerable time, energy and expertise to engaging with health professionals and improving outcomes for people with M.E.

Pharmacy professionals will be familiar with the guidelines for managing many of the symptoms of M.E. from other patients. For this reason, we have focused on special considerations when applying your existing expertise to patients with M.E., non-pharmacological management, and the ways M.E. could affect delivery of pharmacy services for people with the illness. Our case studies (see p 16), based on real patients, show typical medication used and demonstrate polypharmacy seen in people with M.E.

We hope you find this resource useful, and would welcome your feedback: you'll find our contact details on the back.



What is M.E.?

Although the aetiology of M.E. is unknown, emerging evidence about the cause of M.E. includes autoimmune deficiencies, viral infections, autonomic nervous system dysfunction and genetic factors, among others.

Evidence suggests a population prevalence of at least 0.2–0.4% which means that a general practice with 10,000 patients is likely to have up to 40 patients with M.E.¹ They might be difficult to identify from their prescriptions because there is no specific treatment that is licensed for M.E. At present, there is only symptom management available, so you might see chronic pain, sleep, migraine, nausea, dizziness or depression treatments, among others, on prescriptions.

M.E. patients often have multimorbidity² so even if they are not taking prescribed medication for their M.E. symptoms, you may still come across them. It is important to know how M.E. may affect the safe and effective use of medicines and the services you provide.

As a long-term, fluctuating condition, M.E. is categorised as a disability by the Equality Act 2010.³

Symptoms

There are many symptoms of M.E. affecting many body systems, listed in the [Symptoms and management](#) quick reference table on p 12. Not all patients will experience all of these symptoms all of the time. Any new symptoms should always be checked, even if they may seem related to M.E. (see [Red flags for referral](#) on p 6.)

For recent research findings relating to the multi-system nature of the illness and its symptoms, please see the [Pathophysiology](#) quick reference table on p 11.

Symptoms can fluctuate and women with M.E. often find that symptoms worsen at different times in their menstrual cycle. If a patient appears better or worse at a given moment, this does not indicate a change in their overall condition.

The characteristic symptom of M.E. which differentiates the illness from fatigue experienced in other conditions is post-exertional malaise, sometimes referred to as “payback.”⁴ This is defined as the body’s inability to recover after expending even small amounts of energy on simple physical or mental activity.¹ The onset of post-exertional malaise is delayed for at least 24 hours, with slow recovery over several days. Some patients also experience widespread muscle and neuropathic pain, along with worsening of their other symptoms, as part of post-exertional malaise.

The fatigue experienced by people with M.E. is very different from ordinary tiredness or sleepiness. Simple physical and mental activities can leave patients struggling to function, and pushing through this can trigger post-exertional malaise. For this reason, the National Institute of Health and Care Excellence’s guideline for M.E. (NICE CG53, see p 6) stresses that M.E. patients need to space out their activities and may find that their capacity is typically greater at a specific time of day.

Severity and function levels

NICE CG53 describes three levels of severity of M.E.:¹

- People with **mild M.E.** are mobile, can care for themselves and can do light domestic tasks but with difficulty. Most are still working or in education, but to do this they have probably stopped all leisure and social pursuits.
- People with **moderate M.E.** have reduced mobility and are restricted in all activities of daily living, although they may have peaks and troughs in their level of symptoms and ability to do activities some of the time.
- People with **severe M.E.** are unable to do any activity for themselves, or can only carry out minimal daily tasks (such as face washing, cleaning teeth). They have severe cognitive difficulties and depend on a wheelchair for mobility.

Complications can develop in severe M.E. as a result of being mostly bedbound, such as postural hypotension, deep venous thrombosis, osteoporosis, pressure sores and deconditioning.¹

Diagnosis

There is no specific single test to diagnose M.E., though potential biomarkers are being investigated. Diagnosis is currently made after other possible causes for symptoms have been excluded via blood tests specified by NICE CG53.¹ This should be a positive clinical diagnosis based on well-characterised set of symptoms.

These are post-exertional fatigue or malaise, cognitive difficulties, sleep disturbance and chronic pain, which have persisted for four months in an adult and three months in a child. Early diagnosis and management may aid recovery and prevent further worsening to severe M.E.,⁵ so if you suspect from their symptoms that someone might have undiagnosed M.E., please refer them to their GP.

Red flags for referral

Symptoms that can be caused by other serious conditions should not be attributed to an existing M.E. diagnosis as they may be part of an alternative diagnosis or comorbidity which should be investigated and treated. NICE CG53¹ lists the following red flags for referral:

- any new symptoms, including pain that is new or localised to a specific area
- sudden, unexplained weight loss – people with M.E. may have explained weight loss due to difficulty eating and this should be managed
- spatial disorientation
- localising/focal neurological signs
- signs and symptoms of inflammatory arthritis or connective tissue disease
- signs and symptoms of cardiorespiratory disease
- sleep apnoea
- clinically significant lymphadenopathy.

UK treatment guidelines

- National Institute for Health and Care Excellence (NICE) guideline CG53 and NICE pathway at www.nice.org.uk/guidance/CG53
- *Scottish good practice statement on M.E./CFS*, formally endorsed by RCGP (Scotland) and the Scottish Neurosciences Council at www.scot.nhs.uk/scottish-good-practice-statement-on-me-cfs
- *Therapy and symptom management in CFS/M.E.* published by The British Association for CFS/M.E. (BACME), a professional body for M.E. clinicians and multi-disciplinary teams, at www.bacme.info



Non-pharmacological management

The following are used to manage the overall impact of symptoms (see [Pharmacological management](#) below for individual management of symptoms), as suggested by [Treatment guidelines](#) on p 6.

- Rest periods are a core component of all management approaches for M.E.; they can also be part of management of pain, sleep problems and comorbid stress or anxiety, especially for those who cannot tolerate medication.
- Pacing is a structured approach to managing activity and rest that people with M.E. repeatedly report that they find helpful.⁶
- Research into the efficacy of individual dietary regimens has been inconclusive,⁷ so there is no specific dietary advice for people with M.E., though some report finding exclusion diets helpful, in which case a dietician should be referred to for advice on preventing malnutrition.¹
- Graded exercise therapy (GET) may be helpful for a specific sub-group of patients, though some patients report adverse effects on symptoms and functioning.^{1,6} CG53 says GET should be completely avoided in people with severe M.E. and, for those with mild/moderate M.E., only be delivered by appropriately trained professionals. General exercise programmes are not evidence based for M.E. patients and can cause harm.¹
- Cognitive behavioural therapy (CBT) is used to support people through long-term conditions, including M.E. Its use does not imply that the cause of the illness is psychological but it can help some cope with the challenges of living with M.E.
- There is insufficient evidence regarding the use of complementary and alternative medicines (CAMs) to treat M.E. However, some patients report using complementary approaches to help them manage their symptoms,⁶ so being aware of this is important for checking interactions and reviewing medication.

The most frequently self-prescribed approaches in Action for M.E.'s 2014 survey of more than 2,000 people with M.E. were pacing, rest (including bed-rest), vitamin and mineral supplements, and dietary changes.⁶ Other symptoms are managed as in usual clinical practice, using the standard guidelines for each symptom.

Pharmacological management

There is very little evidence of the safety of pharmacological treatments in people with M.E. for symptoms or comorbid conditions, so the response may be unpredictable and should be monitored, for example with [New medicines](#) (see p 9), if applicable.

Important medication considerations in people with M.E. are listed in the [Common medication issues](#) quick reference table on p 15.

There are no treatments for the symptoms of post-exertional malaise, fatigue, cognitive dysfunction, or recurrent flu-like symptoms, but the approaches in the [Non-pharmacological management](#) section (above) may be helpful.

See the [Symptoms and management](#) quick reference table on p 12 for specific advice.

It is recommended that sleep disturbances are treated if possible, as a priority. Low-dose tricyclics (eg. amitriptyline up to 75mg) and/or anti-epileptics are used for their sedating and pain-relieving effects but guidelines state they should only be initiated after referral to specialist M.E. care, as these are unlicensed indications.¹ Tricyclics are not effective as an antidepressant at this low dose.¹ If sleep management strategies do not improve sleep, the possibility of an underlying sleep disorder such as sleep apnoea should be considered (see [Red flags for referral](#) on p 6).

Any vitamin deficiencies should be treated. For example, vitamin D deficiency, which may contribute to fatigue and pain, is common due to lack of sunlight, and the lack of weight-bearing exercise and possible dietary restrictions due to food intolerances.¹

Drug treatment in children and young people with M.E. should be initiated by a paediatrician but may be continued in primary care. Drug treatments sometimes prescribed for children include melatonin, amitriptyline, gabapentin, NSAIDs and analgesia.¹

There are a number of drugs in clinical trials for M.E., including the disease-modifying antirheumatic drugs (DMARDs) cyclophosphamide and rituximab, currently in phase III. Other trials include CNS stimulants, low-dose naltrexone, antibacterials, antivirals, and antihypertensives. More information can be found on NHS Choices (www.nhs.uk/conditions/chronic-fatigue-syndrome), which queries the WHO International Clinical Trials Registry Platform; see also the 2016 systematic review in *Clinical Therapeutics* (<http://linkinghub.elsevier.com/retrieve/pii/S014929181630306X>).

Issues with polypharmacy

A significant number of people with M.E. take medication for individual symptoms. One patient interviewed had 20 different regular prescription items (see [Case studies](#) on p 16) to manage severe M.E. and co-morbid conditions.

Organising and taking medication, along with coping with side effects, may add to the burden of living with M.E. Although sometimes appropriate, polypharmacy could occur due to the following factors in someone with M.E. Please also refer to your region's relevant polypharmacy guidance.

- Managing numerous symptoms individually can result in many medicines being prescribed over time.
- People with M.E. can attend many different specialists, especially during investigations at the start of the illness to establish a diagnosis, and each may prescribe medication.
- Increased susceptibility to side effects (see [Common medication issues](#) on p 15), and the similarity of these and the symptoms of M.E., can result in misinterpreting them as new symptoms and medication being prescribed to alleviate them, resulting in a prescribing cascade.
- A high occurrence of multimorbidity can contribute to the number of medicines prescribed.²
- Some symptoms may fluctuate over time, so it is possible that the indication for which medication has been prescribed is no longer current.

Delivering pharmacy services

People with M.E. have difficulty accessing health services, and pharmacy teams may be the only contact they have with health professionals. Bear in mind, especially with new patients, that it's not possible to identify some with M.E. by their prescription alone. Even if they do not take medication for M.E. symptoms, you may come across them taking medication for comorbidities, presenting for over-the-counter (OTC) medicines, or using one of your pharmacy's services.

The following points and [Common medication issues](#) quick reference table on p 15 should be considered in the delivery of pharmacy services to people with M.E. We know that policies and procedures for pharmacy services may differ across pharmacy sectors and/or in England, Wales, Scotland and Northern Ireland. We have used general terms here, while acknowledging that your region may use alternatives.

Ordering repeat prescriptions

The cognitive difficulties that come with M.E. can make it difficult to be organised and remember when to re-order medication, so assistance with ordering medication may be helpful, if this service is available. The patient could also be referred to their GP to organise NHS Repeat Dispensing.

Prescription deliveries

A number of people with M.E. find prescription deliveries an invaluable service.⁸ Approximately a quarter of people with M.E. are housebound⁹ and those with mild or moderate M.E. may look well when they pick up their prescription, but can also have periods of being housebound. Driving can be hazardous and draining for people with M.E., and reaction times may be affected by medication, so they may have difficulty picking up their repeat prescriptions, especially if there is not a carer available.

Accessible information and communication

NHS England's Accessible Information Standard (www.england.nhs.uk/ourwork/accessibleinfo) may apply to someone with M.E., depending on individual need. Cognitive difficulties can affect concentration and the ability to retain verbal information, so offering a written list of points covered is recommended, particularly for patients with severe M.E.¹

Communication may be impaired by speech, concentration and word-finding difficulties, so people with M.E. may need to take their time and have longer consultations. Use of the consultation room, including for OTC consultations may be helpful, both for seating due to weight-bearing difficulties, and because many people with M.E. have light and sound intolerance so find it more difficult to concentrate in a busy environment.

M.E. patients need to space out their activities to avoid exacerbating their symptoms and may find that their functioning is greater at a specific time of day, so consultations could be arranged to fit this.

Medicines Use Reviews

People with M.E. may benefit from a Medicines Use Review (MUR) in England to discuss any problems with their medication, such as side effects, remembering to take medication, polypharmacy, and other **Common medication issues** (see quick reference table on p 15).

New medicines

With the increased susceptibility to side effects mentioned previously, giving advice on what side effects to expect with any new medication, how to cope with them, and what to do if they cannot be tolerated, will likely improve adherence. Explaining that a low-dose antidepressant has not been prescribed for depression, but rather pain or sleep difficulties, is also likely to improve adherence. Patients would be eligible for the New Medicine Service (NMS) in England if the medicine is on the NMS medicines list.

Domiciliary visits

Severely affected house- or bedbound patients with M.E. are unlikely to be able to come into the pharmacy for a MUR but might have complex medication problems, such as managing polypharmacy. NICE identified concerns that patients made housebound by severe M.E. received little or no care or support because they are unable to access potentially effective care. The guideline states these patients would benefit from domiciliary healthcare visits,¹ so where possible a visit by a domiciliary medicines optimisation pharmacist could be helpful, especially for those with polypharmacy. Action for M.E.'s 2014 survey found that 63% of people with severe M.E. said home visits would make a real difference to their healthcare.⁶

Common or minor ailments and OTC prescribing

People with M.E. often take a range of supplements and herbal medicines, which may cause side-effects or interact with prescribed medication. OTC preparations containing caffeine and other substances may not be well tolerated, so patients should be advised to purchase "plain" preparations with a single active ingredient to avoid potential side effects. **Red flags for referral** on p 6 details the circumstances in which a person with M.E. should be referred to their GP.

Flu vaccinations

People with M.E. may be eligible for the free flu vaccination service if they have comorbidities (eg. asthma). Anecdotally, some people with M.E. don't want to have the vaccine because they are worried it might make them relapse. However, the vaccine has been shown to be both safe and effective in people with M.E.¹⁰ Research shows that many more patients who had never been vaccinated against flu reported fears of a relapse than those who had.¹¹ Carers of people with M.E. will be eligible if they are in receipt of Carers Allowance, or if the welfare of the person they care for would be put at risk if the carer becomes ill.¹²

Supporting carers

Family and partners are the most frequent carers of people with severe M.E. and community pharmacy teams can help make life a little easier for them. Advice on giving medicines might be helpful, such as when and how to give them, and what to do if the person they care for has difficulty taking medicines or using devices; it may also be helpful to invite a carer to attend an MUR with the patient. NICE CG53 (see p 6) recommends that people with M.E. should be offered information about local and national self-help groups and support for people with M.E. and their carers.¹

Signposting patients and carers

Action for M.E.'s Online M.E. Centre (www.actionforme.org.uk) offers information, advice and support on most aspects of living with or caring for someone with M.E., including a searchable directory of local M.E. support groups and specialist healthcare services. The charity also offers printed information resources, specialist welfare benefits advice, and peer-support forums for children and adults affected by M.E.

Promotion of healthy lifestyles to people with M.E.

Although people with M.E. inherently live a relatively sedentary lifestyle due to their physical limitations, a study has shown that people with M.E. tend to live healthier lifestyles than the general population, possibly to manage symptoms, and that an unhealthy lifestyle does not influence the severity or duration of M.E.¹³ There are several factors to be considered when promoting healthy lifestyles to someone with M.E.

Diet

The effort required to buy food and prepare nutritious meals can mean that people with M.E. find it difficult to maintain a healthy diet. It can be made more difficult by loss of appetite or intolerance to some foods. If they are experiencing significant problems with their diet or struggling to maintain an adequate food intake, your patient with M.E. could ask their GP for a referral to a dietician.

Exercise

NICE CG53 states that advice to undertake unsupervised, or unstructured, vigorous exercise (such as simply “go to the gym” or “exercise more”) should not be given, as it may worsen their symptoms.¹ People with M.E. have to pace themselves and stay within a safe baseline of physical, mental and emotional activity to manage their illness, and the patient is the most knowledgeable about their own limits.

Smoking

As nicotine is a central nervous system stimulant, someone with M.E. who smokes may have inadvertently self-medicated with nicotine to treat cognitive difficulties and symptoms related to the autonomic nervous system, such as gastrointestinal symptoms. Being aware of these issues may help health professionals support people with M.E. to quit and allow the patient to be more prepared so that they can manage any changes in symptoms.

Alcohol

Some with M.E. report intolerance to alcohol, with consumption exacerbating their symptoms. Research has found that 38% reduce their alcohol intake and around a quarter stop drinking alcohol altogether.¹⁴ Tolerance may improve as symptoms improve and it would be advisable for people with M.E. to be aware of the depressant effect of alcohol, considering depression is a common comorbidity.



Quick reference tables

Pathophysiology

NB. This list is not exhaustive, but includes a selection of recent findings to demonstrate the multi-system nature of the illness and its symptoms.

System affected	Pathophysiology
Immunological	<ul style="list-style-type: none"> • Chronic lymphocyte activation, with altered immune response to exercise¹⁵ • Reduced cytokine and heat shock protein responses correlating with lengthened and accentuated oxidative stress with incremental exercise¹⁶ • Elevated levels of mast cells¹⁷ • Autoimmunity, including elevated antibodies to β-adrenergic and muscarinic cholinergic receptors¹⁸
Neurological	<ul style="list-style-type: none"> • Widespread neuroinflammation¹⁹ • Bilateral white matter atrophy and right anterior arcuate fasciculus abnormality²⁰ • Autonomic dysfunction²¹ and abnormalities in pH handling in peripheral muscle related to autonomic dysfunction²²
Cardiovascular	<ul style="list-style-type: none"> • Reduced cardiac volumes and blood volume²³ • Down-regulation of renin-aldosterone and antidiuretic hormone systems²⁴
Gastrointestinal	<ul style="list-style-type: none"> • Altered composition of the gut microbiome²⁵
Energy metabolism	<ul style="list-style-type: none"> • 20 metabolic pathways showing a hypometabolic dauer state²⁶ • Impaired pyruvate dehydrogenase function²⁷ • Disturbed fatty acid and lipid metabolism²⁸
Musculoskeletal	<ul style="list-style-type: none"> • Loss of capacity to recover from acidosis on repeat exercise²⁹ • Increased oxidative stress and altered muscle excitability in response to incremental exercise³⁰ • Abnormalities of AMPK activation and glucose uptake in cultured skeletal muscle cells³¹

Symptoms and management

This table shows management options for adults recommended by the [Treatment guidelines](#) on p 6. Considering the [Common medication issues](#) on p 15, it is advisable to try non-pharmacological management from the guidelines before resorting to pharmaceuticals. As symptoms are managed as in usual clinical practice with the standard guidelines for each symptom, these have been listed, along with any deviations and adapted advice recommended by the BACME guide (see p 6). The equivalent NICE guidelines for children for these symptom groups should be referred to.

Symptom group	Specific symptoms	Pharmacological management	Non-pharmacological management
Fatigue	Persistent overwhelming physical and mental exhaustion not improved with rest	None available ⁴	See Non-pharmacological management on p 7
Post-exertional malaise	Flu-like symptoms (eg. general malaise, painful glands with/without swelling, sore throat)		
Cognitive impairment (or "brain fog")	Short-term memory problems Reduced attention span Inability to multi-task Word-finding difficulties Difficulty planning Loss of concentration		
Pain	Neuropathic pain Aching muscles or joints Twitching muscles, cramps or spasms	CG173: Neuropathic pain in adults (www.nice.org.uk/guidance/cg173) with the following adaptations (see above) to pharmacological treatments:	Anecdotally, some people with M.E. experiencing pain report some benefit from heated wheat bags, heat packs and hot water bottles.
		<p>Low-dose Tricyclic anti-depressants (TCAs) at night, commonly amitriptyline (unlicensed use), initially 10mg or less if not tolerated due to daytime drowsiness or antimuscarinic effects, up to 75mg. Imipramine and nortriptyline are less sedating if daytime drowsiness affects function.⁴</p> <p>Antiepileptics for moderate/ severe pain not responding to low-dose TCAs (unlicensed use): gabapentin (initially 100mg at night) or pregabalin (initially 25mg TDS or simplified to BD)⁴</p> <p>Duloxetine or mirtazapine may be helpful in neuropathic pain with comorbid depression (mirtazapine initially 15mg in the evening increasing gradually to 45mg)⁴</p> <p>Non-steroidal anti-inflammatory drugs (NSAIDs) may be helpful for musculo-skeletal pain⁴</p> <p>Opioids have limited efficacy as tolerance is quickly gained⁴ and they are known for triggering prescribing cascades³²</p>	
<i>continued on next page...</i>			

Symptom group	Specific symptoms	Pharmacological management	Non-pharmacological management
Sleep disturbance	Insomnia Hypersomnia Sleep reversal (eg. sleeping from 4am to noon) Non-refreshing sleep	Low-dose TCAs, commonly amitriptyline (unlicensed use), initially 10mg or less if not tolerated due to daytime drowsiness or antimuscarinic effects, up to 75mg 2-4hrs before bed or 12hrs prior to desired waking time ⁴ Sedating antihistamines ⁴ Melatonin may be considered for children, ¹ or for over 55s for 13 weeks max ⁴	Sleep hygiene advice ¹ Changes to sleep patterns should only be introduced gradually so as not to exacerbate symptoms ¹ Avoidance of caffeine ⁴
Headache	Headache Migraine	CG150: Headaches in over 12s (www.nice.org.uk/guidance/cg150)	
Neurological/ Autonomic nervous system	Dizziness on standing, orthostatic intolerance, or autonomic dysfunction Hyper-sensitivity to light and sound Poor temperature control Excess sweating Loss of balance Paraesthesia	Betahistine or cinnarizine may relieve dizziness or balance problems if intrusive, or for travel and other likely triggers, for short-term use only ³³	Increase fluid intake to at least 2.5 litres of water a day ⁴ Patients with low blood pressure are advised to increase their salt intake to maintain blood volume ⁴
Respiratory	Recurrent URTIs Breathing difficulties	Antibiotics should only be given where there is convincing evidence of an acute bacterial infection ⁴ Breathing difficulties may be due to autonomic dysfunction ³⁴ or comorbid asthma and should be treated accordingly	
Gastro-intestinal	Nausea and pallor Loss of appetite Swallowing difficulties or dysphagia GERD Gastroparesis Abdominal pain IBS-like symptoms	CG61: Gastro-oesophageal reflux disease and dyspepsia in adults (www.nice.org.uk/guidance/cg184) CG61: Irritable bowel syndrome in adults (www.nice.org.uk/guidance/cg61)	Eating little and often, snacking on dry starchy foods and sipping fluids ⁴ Supplements and thickeners may be advised by a speech and language therapist to aid swallowing medication and to prevent malnutrition in dysphagia ³⁵ Some patients with severe M.E. may need to be tube-fed ¹
<i>continued on next page...</i>		Antihistamines may be helpful for nausea ⁴ but anti-emetic drugs should only be considered if severe ¹	

Symptom group	Specific symptoms	Pharmacological management	Non-pharmacological management
Urinary	Increased frequency and urgency Urinary retention	Antibiotics should only be prescribed when there is evidence of bacterial infection ⁴	None available
Allergies/ Intolerances	Intolerance to certain odours, foods (eg. dairy or wheat), some medication, alcohol and other substances	Standard treatments for allergies ⁴	If patients have a restricted diet advice should be sought from a dietician as there is a risk of malnutrition ¹

Common medication issues

Issue	Comment
Increased susceptibility to side effects with greater severity	People with M.E. and specialists anecdotally report non-specific drug intolerance and increased susceptibility to side effects. ⁴ Treatment guidelines (see p 6) recommend all drugs should be used with caution, at lower doses than usual, and that effects should be monitored closely.
Withdrawal effects	Specialists report that patients with M.E. experience significant withdrawal symptoms when ceasing antidepressant treatment. ⁴
Switching	Avoid frequent changes of medication because of the above effects, particularly between drugs in the same class. ³³
Drugs to be avoided or used with caution	<p>The “Do not do” recommendations in CG53 state that monoamine oxidase inhibitors, glucocorticoids, mineralocorticoids and CNS stimulants should not be used for the treatment of M.E. because of insufficient evidence of their safety and efficacy.¹</p> <p>A high number of patients withdrew from trials of galanthamine, phenelzine, fludrocortisone and fluoxetine due to adverse effects.¹</p> <p>Anaesthesia involving histamine-releasing anaesthetic agents (such as pentothal) and muscle relaxants (curare, Tracrium, and Mevacurium) are best avoided if possible. Propofol, midazolam, and fentanyl are generally well-tolerated.³⁶</p> <p>Patients with severe M.E. have difficulty sitting up for any length of time, so this, along with dysphagia, would have an impact on the safe use of drugs such as bisphosphonates.³⁷</p>
Comorbidities	Interactions with treatments prescribed for comorbid conditions, for example using low-dose TCAs for pain and sleep disturbance in a patient already taking SSRIs for depression.
Swallowing difficulties/dysphagia	May affect ability to take solid dosage forms. Thickeners are sometimes advised by speech and language therapists to aid taking medicines in dysphagia. ³⁵ The RPS guidance document <i>Pharmaceutical issues when crushing, opening or splitting oral dosage forms</i> ³⁸ provides professional guidance if patients have been instructed to do this or are using this method of overcoming difficulties swallowing solid dosage forms.
Interactions	People with M.E. may be taking a range of supplements, herbal medicines or privately prescribed medication which may cause side-effects or interactions.
Polypharmacy	See Issues with polypharmacy on p 8.
Problems remembering medication	Cognitive dysfunction affects memory and concentration, and can cause confusion, so tips for organising and remembering to take medication may be helpful.
Non-adherence	Medication issues such as side effects, dysphagia, previous experiences with medication, and the burden of polypharmacy are potential contributing factors to non-adherence in M.E. patients. Shared decision-making and an open dialogue about treatment preferences, concerns and previous experiences should take place throughout care ¹ and could avoid non-adherence.

Case studies

These case studies use a combination of information from people with M.E. who kindly volunteered their medication histories, with their names changed.

Case study: Mark

Mark, 30, lives alone. His M.E. began three years ago with severe symptoms following a viral infection, which very gradually improved to mild. Although Mark has been able to return to part-time work, his spare time mainly consists of resting and his social life is still very restricted. He has difficulty remembering to use his inhalers and take his tablets, and finds his medication an extra difficulty to live with. In addition to those prescribed by his GP, he occasionally uses herbal medicines and medicines he buys from the supermarket.

Mark's M.E. symptoms managed by medication are:

- GERD (omeprazole)
- widespread pain and sleep difficulties (low-dose amitriptyline)
- back pain (naproxen)
- dizziness and nausea (cinnarizine).

Mark is also being treated for:

- asthma using an inhaled SABA (salbutamol) and LABA/ICS (Seretide), along with a LTRA (montelukast) as add-on therapy
- vitamin D deficiency (Calceos), which can be common in patients with M.E. due to lack of sunlight; it is a treatable cause of additional pain and fatigue.¹

Mark's problematic polypharmacy and unintentional adherence may mean Mark would benefit from a MUR, particularly regarding his asthma. Advice on improving adherence to inhaled and oral medication would also be helpful, perhaps suggesting a prompt sheet or other reminder techniques, along with a discussion about potential interactions with herbal, P and GSL medication. Any new treatments for his asthma would qualify Mark for the New Medicines Service in England.

Case study: Elizabeth

Elizabeth, 58, has had M.E. for more than 20 years. Living alone, she struggles with daily tasks such as showering and preparing food, and can only leave the house once or twice a week with the aid of a stick or motorised scooter. Elizabeth finds her medication a problem to organise and has difficulty removing tablets from packaging. She takes D-ribose energy supplement, and the herbal remedies "slippery elm" and "digestive tea," which she says help with her side effects.

Elizabeth's M.E. symptoms managed by medication are:

- neuropathic pain (low-dose amitriptyline, gabapentin)
- muscle and back pain (naproxen, co-codomol and diazepam)
- GERD (lansoprazole).

Elizabeth is also being treated for:

- depression and anxiety (sertraline)
- allergic rhinitis (beclametasone spray)
- vitamin D deficiency (Calcichew D3 Forte).

Elizabeth may benefit from a MUR to investigate the side effects she says she is treating with herbal medicines, including a discussion around potential interactions between prescribed and herbal medicines. Popping her tablets out for her or providing them in a dosette tray may help, if this is deemed a safe option. There is possibly a prescribing cascade in that she's taking macrogol for constipation, possibly caused by her opioid pain relief. A clinical review of Elizabeth's pain medication may help to establish whether the opioid, and therefore the Macrogol, is essential. Elizabeth might also need to have her medication delivered when she is too unwell to pick them up herself.

Case study: Sarah

Sarah, 36, lives with very severe M.E. and is bedbound and catheterised. District nurses visit her for bed-sore prevention. Sarah is unable to speak and communicates via computer or tablet. She has seen many specialists who have prescribed medication, such as gastroenterologists, respiratory consultants, endocrinologists, a dietician, and a speech and language therapist.

Sarah's M.E. symptoms managed by medication are:

- pain (MST, Oramorph, paracetamol, naproxen)
- nausea (cyclizine, prochlorperazine)
- constipation (prucalopride, macrogol)
- abdominal cramps (buscopan)
- GERD (lansoprazole)
- allergies (chlorphenamine)
- urinary incontinence (darifenacin)
- malnourishment (Prosource, Maxijul, thiamine, vitamin B complex)
- swallowing difficulties (Resource thickener).

Sarah is also being treated for:

- severe asthma (theophylline)
- dysmenorrhoea (mefenamic acid)
- growth hormone deficiency (Omnitrope).

Sarah may benefit from either a domiciliary MUR or medicines optimisation, to check that all her medication is still helpful and to establish whether there are prescribing cascades adding to her polypharmacy, as it is difficult to tell if the side effects of some of items are being treated as additional symptoms. As Sarah cannot speak, her communication preferences should be used and recorded, as per the NHS England Accessible Information Standard. Sarah needs to have her medication delivered.

Acknowledgements

We are enormously grateful to the following people for their expert input in reviewing this resource:

- Action for M.E. medical advisors Dr Gregor Purdie and Prof Julia Newton
- Members of Action for M.E.'s Patient and Carer Reference Group
- People with M.E. who contributed their medication history for the case studies
- Alison Hemsworth, Head of Primary Care Policy (Pharmacy and Dispensing Doctors), Medical Directorate (Central Team), NHS England
- Dr Mahendra Patel, Fellow of NICE and Principal Enterprise Fellow in Pharmacy Practice, Reader Level
- Stephanie Przepiorka, Branch Pharmacist, Weldricks Pharmacy
- Mike Valentine, Health and Lifestyle Pharmacist, Leger ME Group (Doncaster) lead.

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Action for M.E. takes action to end the ignorance, injustice and neglect experienced by people with M.E. We provide information, support and advice to people affected by M.E. to help improve their health and well-being. We work with professionals to enhance the care and support that people with M.E. receive, and invest in and drive research to advance knowledge of the illness.



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