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Peripheral Neuropathy

A guide for those with myeloma



towards a world
without myeloma

MY Foundation – Myeloma Foundation of Australia

The Myeloma Foundation of Australia is a national not-for-profit organisation dedicated to providing information and support for those affected by myeloma. Founded in Victoria in 1998 by three families personally touched by myeloma, MY Foundation has grown to become a significant provider of services and comfort for the myeloma community. MY Foundation raises awareness of the disease in the community, promotes research and advocates to governments for more generous support for the myeloma community. MY Foundation also provides education, information and support to patients and carers through its specialist Myeloma Support Nurses.

Peripheral Neuropathy – A guide for those with myeloma

This guide is written specifically for patients who have been diagnosed with myeloma and who are at risk of, or are experiencing the troubling side effect of peripheral neuropathy. It will also be helpful for their families and friends. Peripheral neuropathy is a common side effect of some therapies for myeloma.

If you would like to talk to someone about the information in this guide, or about other aspects of myeloma including its treatment and management, call the Myeloma Foundation of Australia on the Myeloma Support Line: free-call 1800 MYELOMA (1800 693 566). The support line is available 9 am to 5 pm, Monday to Friday. A Myeloma Support Nurse will answer your call in confidence.

Acknowledgements

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Disclaimer

The information in this guide is not meant to replace the professional advice of your doctors and other members of your healthcare team. They are the best people to ask if you have questions about your individual clinical situation.

Introduction

Peripheral neuropathy is a relatively common side effect associated with myeloma and several of its treatments. This booklet has been written to help you understand more about peripheral neuropathy. It will firstly explain what peripheral neuropathy is, what may cause it in those with myeloma, and then finally explain how it may be managed.

The information in this guide is not meant to replace the professional advice of your doctors and other members of your healthcare team. They are the best people to ask if you have questions about your individual clinical situation.

What is peripheral neuropathy?

Neuropathy describes damage to nerves causing impaired function and leading to symptoms that relate to the type of nerves affected. Nerves that can be affected by peripheral neuropathy are the motor, sensory or autonomic nerve fibres.

What is the peripheral nervous system?

Your nervous system is made up of:

- **The central nervous system (CNS)**, which consists of the brain and the spinal cord.
- **The peripheral nervous system (PNS)**, which consists of all the nerves outside the brain and spinal cord. The peripheral nervous system includes nerves in your arms, hands, fingers; legs, feet, toes; chest; face, and some nerves in your skull. It also includes the nerves that regulate the function of organs you do not have conscious control over, called the **autonomic nervous system**. The autonomic nervous system is made up of nerves that connect your spinal cord to your lungs, heart, stomach, intestines, bladder and sex organs.

There are different peripheral nerve pathways:

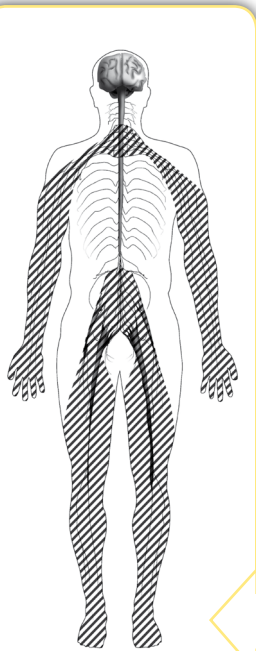
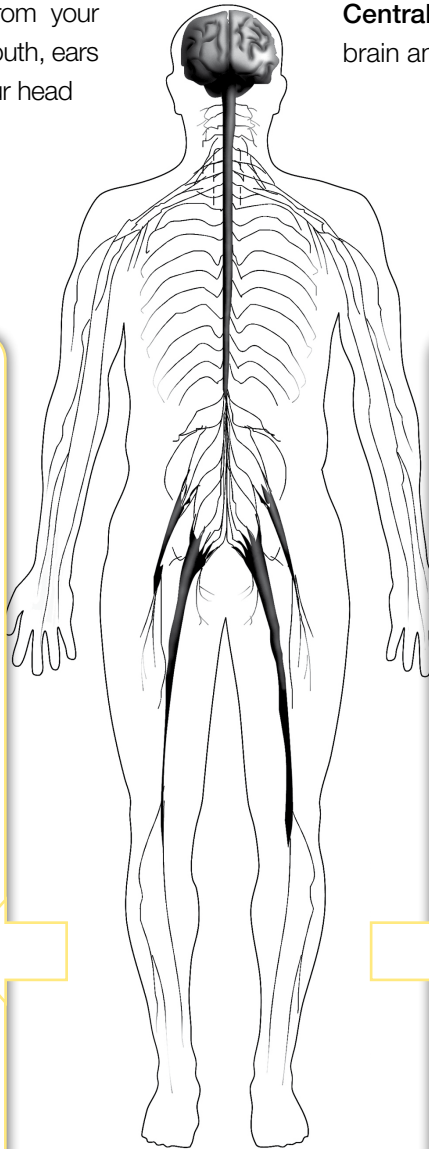
- **Motor** nerve cells carry messages from the brain to the muscles along the motor nerves, to cause movement.
- **Sensory** nerve cells carry messages from sensory receptors all around the body to the brain along sensory nerves. These messages enable you to feel physical sensations such as pain, and touch, and also sense where your body is in relation to your surroundings.

Peripheral neuropathy may damage both motor and sensory peripheral nerves.

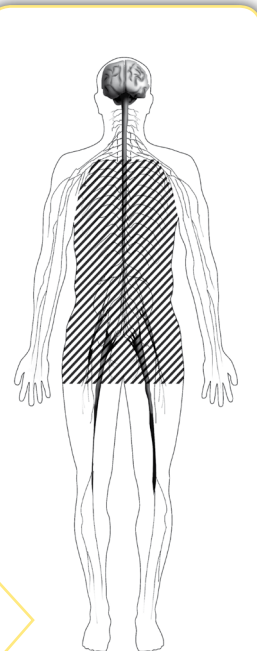
‘Peripheral’ means ‘situated away from the centre’ and refers to the outer areas of the body. ‘Neuropathy’ means ‘disease or malfunction of the nerves’.

Cranial nerves go from your brain to your eyes, mouth, ears and other parts of your head

Central nerves are in your brain and spinal cord

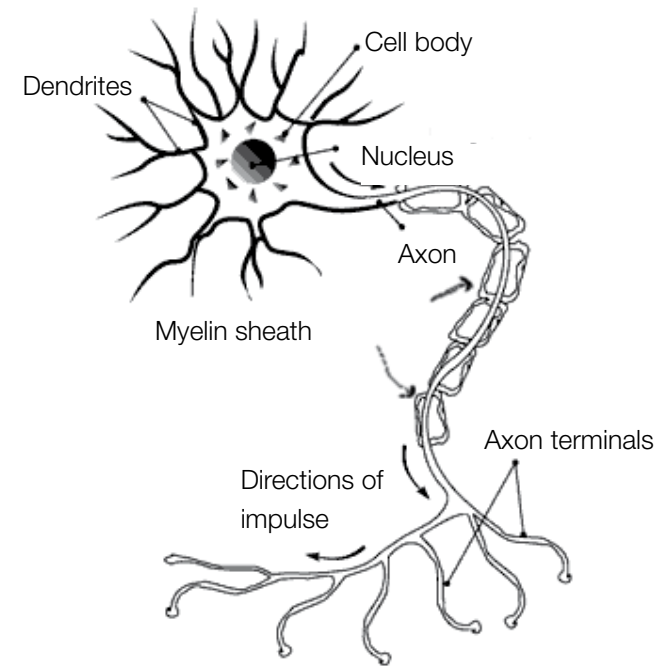


Peripheral nerves go from your spinal cord to your arms, hands, legs and feet



Autonomic nerves go from your spinal cord to your lungs, heart, stomach, intestines, bladder and sex organs

How do peripheral nerves work?



Nerves are the body's communication system. Information about the body's functions, sensation and movement are carried by electrical impulses passed from one nerve cell (neuron) to the next nerve cell along the pathway they form (nerve). When nerves in the peripheral nervous system are damaged, the messages they carry can get mixed up, or perhaps don't get through properly.

What are the symptoms of peripheral neuropathy?

Peripheral neuropathy can cause symptoms ranging from tingling, burning or electric type pains in the hands or feet, through to loss of sensation or numbness, likened to wearing a thin stocking or glove. Peripheral neuropathy caused by myeloma and its treatment usually affects both sensory and motor nerves with similar symptoms on the right and left side (symmetrical). Symptoms usually begin in the toes and fingertips and progress up towards the knees and elbows. Some treatments may also damage the autonomic nerves causing symptoms such as dizziness, digestive problems and impotence. Listed below are some of the more common effects that may be experienced when peripheral nerves are damaged.

Some effects of motor peripheral neuropathy damage are:

- Inability to do up buttons easily
- Trouble in writing
- Difficulty in feeling the shape of small objects in your hand
- Unsteady gait when walking



Some effects of sensory peripheral neuropathy damage are:

- Unusual sensations or an increased sensitivity to touch – the slightest touch may cause extreme discomfort. This is frequently worse at night
- Altered sensation – such as a feeling of pain or heat when touching something cold
- Tingling, numbness or pain in your hands or feet
- Burning sensation in your hands or feet
- Trouble hearing; ringing or buzzing in your ears
- Generalised weakness
- Being unsure where your feet are on the ground, increasing the risk of falls

Some effects of autonomic nerve damage are:

- Dizziness when standing up from sitting or lying down
- Diarrhoea
- Constipation
- A feeling of being full earlier than normal when eating
- Impotence

How is myeloma associated with peripheral neuropathy?

There are many causes of peripheral neuropathy. Some are unrelated to myeloma such as: diabetes, alcoholism, vitamin deficiencies, infections (e.g. shingles) and autoimmune disorders. However, myeloma and the treatments used to manage myeloma can cause peripheral neuropathy and it is helpful to understand why it happens to best manage the symptoms and minimise further nerve damage.

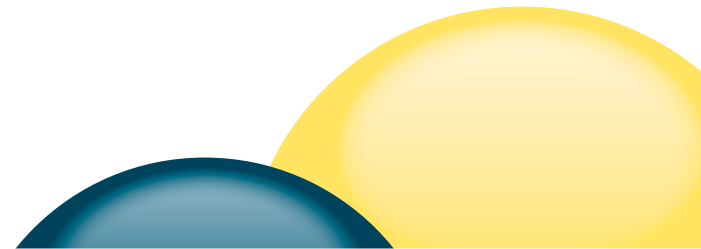
It is estimated that between 1 and 13% of people may have symptoms of peripheral neuropathy at the time of being diagnosed with myeloma, with up to 80% of patients developing some degree of peripheral neuropathy as a later complication of myeloma and its treatment.

How does the disease process of myeloma cause peripheral neuropathy?

The disease process of myeloma can cause peripheral neuropathy in a few ways. It is thought that the myeloma protein (paraprotein) produced by the malignant plasma cells, can cause direct damage to the nerve cells, resulting in symptoms of neuropathy. Sometimes, myeloma may be complicated by a condition called amyloidosis which can cause peripheral neuropathy. In some people, high levels of paraprotein can lead to thickening of the blood (hyperviscosity) and cause sluggish blood flow, which may also lead to symptoms of peripheral neuropathy. Peripheral nerves, which leave the spinal cord, may also be damaged from a fractured vertebra caused by myeloma bone disease. Other factors causing peripheral neuropathy may include weight loss, metabolic or toxic factors related to the myeloma. Peripheral neuropathy caused by the myeloma disease process should improve with treatment that controls the myeloma.

Which myeloma treatments cause peripheral neuropathy?

Many of the drugs used to treat myeloma may cause peripheral neuropathy. Older chemotherapy drugs causing peripheral neuropathy, such as vincristine and cisplatin are now rarely used to treat myeloma and have largely been replaced by more recent novel agents. Because peripheral neuropathy may also be caused by some of the newer drugs (see following page) careful management is required. The exact mechanism of damage to the nerve cells is not clearly understood and is an area of ongoing research.



How do current myeloma treatments affect the function of peripheral nerves?

There are three main drugs classified as new or novel agents currently used to treat myeloma: thalidomide (Thalomid®), bortezomib (Velcade®) and lenalidomide (Revlimid®). They are discussed below in terms of peripheral neuropathy.

1. Thalidomide (Thalomid®)

Peripheral neuropathy is one of the more common side effects of treatment with thalidomide. The severity of peripheral neuropathy is related to the dose and length of time on therapy. This is often termed a 'dose limiting toxicity' – which means a toxicity (side effect) that can limit the dose or duration of thalidomide that can be given. The risk of developing peripheral neuropathy with thalidomide increases if some nerve damage already exists at the start of thalidomide treatment.

What are the common symptoms of peripheral neuropathy caused by thalidomide?

Thalidomide-induced peripheral neuropathy can affect both your sensory and motor nerves. Mild peripheral neuropathy, causing tingling in the hands and feet, may occur within 4 months of starting thalidomide treatment. Stinging sensations and numbness in the toes more often than the fingers, are early signs. Slight trembling is also common but rarely interferes with daily activities.

More severe and painful peripheral neuropathy is less common and usually happens after taking thalidomide for longer periods of time (9–12 months or longer). Seventy percent of patients taking thalidomide for 12 months or more will develop symptoms. Severe symptoms are less likely to be reversible so it is important that those receiving thalidomide are monitored for early signs of neuropathy during therapy.

What happens when symptoms occur?

As there is no known cure for peripheral neuropathy, its management concentrates on reducing the risk of occurrence and managing the symptoms as they occur. To minimise the risk of peripheral neuropathy, the length and dose of thalidomide therapy should be carefully considered against the potential benefit of the drug. Reducing the dosage, delaying treatment or gradually increasing the dose, are approaches your doctor may use to help control symptoms.

In addition, thalidomide treatment may need to be stopped and alternative treatments offered before peripheral neuropathy becomes severe. This is particularly important as the symptoms of peripheral neuropathy may continue even after thalidomide has been stopped.

2. Bortezomib (Velcade®)

Bortezomib-induced peripheral neuropathy is one of this drug's most common side effects. The exact mechanism of damage is unknown. Although the peripheral neuropathy mostly affects sensory nerves, it sometimes affects autonomic nerves. Usually bortezomib-induced peripheral neuropathy is reversible but in some people the symptoms continue after treatment has ended.

What are the symptoms of peripheral neuropathy caused by bortezomib?

Patients most often describe sensory neuropathy symptoms of pain, numbness, tingling and burning, more commonly in the feet than the hands. About 10% of patients experience an autonomic neuropathy causing a drop in their blood pressure when standing up from the sitting or lying position. This is called postural hypotension. Other symptoms

of autonomic neuropathy are diarrhoea or constipation, a feeling of being full earlier than normal when eating, and impotence. If symptoms of bortezomib-induced peripheral neuropathy are going to occur, they usually start during the first few cycles of bortezomib treatment and stabilise around cycle five. It does not appear to increase in later cycles and peripheral neuropathy rarely starts later.

What happens when symptoms occur?

In most patients the symptoms improve or disappear when the dose of bortezomib is reduced or ceased. Therefore, reducing the frequency of doses or reducing the dose itself can help keep symptoms at a low grade during treatment with bortezomib.

Strategies to help manage the autonomic symptoms of lowered blood pressure or dizziness include regular blood pressure monitoring and making sure your fluid intake is up to 2–3 litres daily. You may need to sit upright for a minute before standing up from the sitting or lying position. Report any symptoms of dizziness to your doctor. For digestive upsets monitor your appetite and bowel habits and report any changes from what is normal for you to your doctor.

Improvement or disappearance of symptoms may take up to 6 months after completion of therapy. In a few patients, the damage is permanent. Patients who have symptoms of peripheral neuropathy before starting bortezomib appear to have a greater risk of developing bortezomib-induced peripheral neuropathy. Careful assessment of the risks and benefits of this drug is required when considering treatment with bortezomib in patients with pre-existing symptoms of



peripheral neuropathy. It is important that any symptoms are assessed before starting bortezomib treatment and the peripheral neuropathy assessment should be repeated regularly during treatment to monitor any changes.

3. Lenalidomide (Revlimid®)

The risk of developing peripheral neuropathy with lenalidomide is low (2–3%). Lenalidomide is a newer drug in the same family as thalidomide. It is a potentially effective myeloma treatment for patients with peripheral neuropathy symptoms and is unlikely to make those symptoms worse.

Can I prevent or lessen the impact of peripheral neuropathy?

Before starting any treatment that may cause peripheral neuropathy, it is important to be assessed for existing signs of sensory and motor nerve damage. Any changes in nerve function can then be assessed against this baseline. Early peripheral neuropathy symptoms can be treated by dose reduction or delay, so tell your doctor about any symptoms you may experience.

Because early recognition of peripheral neuropathy is important, it is a good idea to monitor your symptoms weekly using an assessment questionnaire such as the one on the following page. Keep a record in a diary or on dated copies of the questionnaire and take this with you when you visit the clinic.

Circle one number per line to indicate how true each statement has been for you during the last 7 days

Date: ___ / ___ / ___

	None	A little bit	Somewhat	Quite a bit	Very much
I have numbness or tingling in my hands	0	1	2	3	4
I have numbness or tingling in my feet	0	1	2	3	4
I feel discomfort in my hands	0	1	2	3	4
I feel discomfort in my feet	0	1	2	3	4
I have joint or muscle cramps	0	1	2	3	4
I feel weak all over	0	1	2	3	4
I have trouble hearing	0	1	2	3	4
I get a ringing or buzzing in my ears	0	1	2	3	4
I have trouble with fine control hand movements, e.g. doing up buttons	0	1	2	3	4
I have trouble feeling the shape of small objects in my hands	0	1	2	3	4
I have trouble walking	0	1	2	3	4

Reference: International Myeloma Foundation Nurse Leadership Board, June 2008.

Are there other factors that may make peripheral neuropathy worse?

- **Smoking** – interferes with peripheral circulation and nerves so consider stopping. Ask your GP or practice nurse for advice and/or local support. Alternatively ring the Quitline on 137 848.
- **Diabetes** – if you have diabetes, make sure your blood sugar levels are carefully monitored. Chronically elevated blood sugar levels can damage the peripheral circulation and nerves.

How might my doctor manage peripheral neuropathy?

The management of peripheral neuropathy in myeloma focuses on close assessment of any pre-existing neuropathy; timely dose adjustments of nerve-damaging drugs; ongoing assessment to monitor for worsening neuropathy and strategies to minimise unpleasant symptoms. Changing myeloma treatment schedules or stopping treatment can be difficult to accept, especially if the treatment is working well against the myeloma. Therefore, it is essential to discuss fully with your doctor or nurse what other treatment options are available to you.

If neuropathy is severe, especially the pain associated with some neuropathy, your doctor may refer you to a neurologist, to assess the extent of your nerve damage and give advice on prescription medications and strategies that can ease the pain.

Neuropathy caused by fractures of the spine that have trapped or damaged nerves is treated with painkillers (analgesics), radiotherapy and in some cases spinal surgery to stabilise and increase the height of the vertebrae.

What can I do to relieve the symptoms of peripheral neuropathy?

There are a variety of remedies that patients have reported as being useful in easing their symptoms. Most patients learn what helps through trial and error. For some patients, one option will work whereas other patients find a combination of methods may be the answer. Patients need to tell their doctor/nurse what methods help or don't so that a plan of management can be recorded.

In general, maintaining a healthy lifestyle will help: eating a well-balanced diet, getting regular gentle exercise and limiting alcohol intake. Giving up smoking is very important. Smoking constricts the blood vessels that supply nutrients to your peripheral nerves, which can make symptoms worse.

Unfortunately, there is little scientific evidence to support one or more effective management strategies. Here we discuss methods your doctor may order, anecdotal methods that have benefited some patients, and sensible lifestyle choices.



Managing pain

The pain associated with peripheral neuropathy can vary in intensity and is often described as 'sharp', 'burning', or 'jabbing'. Pain-relieving medications and treatments that may be ordered by your doctor include low-dose antidepressant drugs (such as amitriptyline) and antiepileptic drugs (such as gabapentin or carbamazepine).

Other pain-relieving treatments include:

- Opioid drugs (such as codeine or morphine)
- Local anaesthetic injections or patches (such as lignocaine), which can be effective in blocking the pain from the damaged nerves
- Transcutaneous electrical nerve stimulation (TENS) machines, which sometimes help reduce pain by delivering tiny electrical impulses to specific nerve pathways through small electrodes placed on the skin

Supplements for cramps

- Drinking tonic water may help with cramps. Your doctor may also check your blood electrolyte (salts) levels and order magnesium or potassium supplements if indicated.

Strategies to help manage autonomic symptoms

- If low blood pressure or dizziness is a problem, regularly monitor blood pressure and make sure your fluid intake is up to 2–3 litres daily. You may need to sit upright for a minute before standing up from the sitting or lying position. Report any symptoms of dizziness to your doctor.
- For digestive upsets, monitor your appetite and bowel habits and report any changes from what is normal for you to your doctor.
- Report any signs of erectile dysfunction to your doctor.

Supplements that may help your nerves repair damage

- Vitamin B complex that includes B₁, B₆, B₁₂ and folic acid
- Vitamin E
- Amino acids: Acetyl L-carnitine; Alpha-lipoic acid
- Fish and vegetable oils: Omega-3 fatty acids (EPA and DHA); flax seed oil

Please note: While the use of high doses of vitamin C is not mentioned here, caution is recommended if taking bortezomib (Velcade®). Vitamin C may interfere with the action of bortezomib, reducing its anti-myeloma effect.

The above supplements are all available over the counter at chemist shops, supermarkets or health food shops. There is no firm research evidence as yet to support the use of these supplements, so they must always be used with caution and supervision. **We strongly advise that you discuss any supplement you wish to take with your doctor before you start, to make sure they are safe and do not interact with other medicines.**

Strategies for better circulation

Massage

Gentle massage with cocoa butter cream (rich in vitamin E) may help relieve pain and discomfort. Massaging twice a day can increase circulation and promote relaxation.



Start massaging at the toes or fingers working your way gently up the limb. This promotes circulation and enhances lymphatic drainage from the affected area. Some patients find wooden foot massagers helpful for self-massage to increase circulation in their feet. If swelling of your feet is a problem, elevating the feet when resting or sitting down is a good idea. This uses gravity to assist fluid drainage in the legs. Pressure stockings will also help reduce swelling. Reducing the pressure of fluid in the legs may help peripheral neuropathy symptoms.

Other creams may ease local symptoms. Menthol-based creams such as many sports injury creams can provide relief in areas that are overly sensitive. Capsicum cream (capsaicin cream) can be used in areas that are painful.

Exercise

Gentle and regular exercise may help reduce the symptoms of neuropathy. Keeping active helps maintain good blood flow to the hands and feet. Walk and exercise within your limits (if you exercise beyond your limit, the muscle fatigue and lactic acid build-up may worsen peripheral neuropathy symptoms). If you are not exercising regularly and would like to start, talk to your nurse or doctor about seeing a physiotherapist or exercise physiologist who can design an exercise plan for you. This plan should consider your level of fitness, pain if present and any other limitations. If your doctor refers you to a physiotherapist as part of your Enhanced Primary Care (EPC) plan, you are eligible for a Medicare rebate. Some private health insurers also provide a rebate.

Keeping comfortable overnight

Friction of bedsheets overnight can cause irritation to sensitive areas and prevent a good night's sleep. Some people wear support stockings to stop the sheets from rubbing on their legs. Silk sheets may also help reduce this friction; alternatively, use a pillow or frame at the end of the bed to lift the sheets from the legs.

Relaxation techniques

Techniques such as meditation, visualisation, relaxation or a combination of these can be helpful in reducing muscle tension, which may be contributing to your pain. These therapies also help temporarily distract you from your discomfort by providing an alternative focal point.

Acupuncture and reflexology may also help to relieve some of your symptoms.



What safety issues should I consider?

Symptoms of peripheral neuropathy may increase your risk of accidents or injuries because of the lack of sensation, weakness, or clumsiness that may come with damage to the nerves of the skin and muscles.

The table on the next page outlines safety measures you should consider.

Please think about the following safety measures:

Safety concern	Preventative measures
Falls	Make sure the lights are on when entering a room
	Remove small rugs and loose floor mats. Clear walkways of clutter such as toys and footstools
	Wipe spills immediately
	Use skid-free shower and bathroom mats
	Use liquid soap instead of bar soap (to avoid dropping and picking up in bath/shower)
	Avoid slippers and running shoes with thick soles that may increase your chance of tripping
	Wear supportive, well-fitting shoes
	Clear garages and work areas of oil spills. Store rakes, nails and garden tools out of the walkways
Skin injuries	Use a cane or walking stick if you find you are limping or having difficulty walking (or use a walker if arms are weak)
	Use protective gloves when washing dishes
	Wear warm socks and gloves during cold weather
	Trim nails carefully, avoid leaving nails long or with sharp edges (see hand and foot care below)
	Moisturise skin daily to prevent cracking
	Dry well in between toes to prevent tinea (fungal infection)
	Lower water temperature in your home water heater to avoid burns
	Be sure you can feel brake pedals and steering wheel. Be alert for changes in your reaction time
Driving	Be sure you have sufficient strength and coordination when driving
Fine motor tasks	Use a lighted key ring to unlock doors



Adaptive aids

If weakness of your hands or feet interferes with your daily activities, special equipment may be needed to aid with activity. An occupational therapist can advise on equipment to help overcome the effects of muscle weakness. If your doctor refers you to an Occupational Therapist as part of your Enhanced Primary Care (EPC) plan, you are eligible for a Medicare rebate. Some private health insurers also provide a rebate.

Foot and hand care

It is important to maintain healthy skin when sensory nerves are involved. You may have reduced sensation and not be able to feel the discomfort that would normally alert you that a problem is present.

- Inspect hands and/or feet for sores or blisters.
- Moisturise feet and hands daily.
- Dry in between toes after bathing to avoid fungal infections.
- Keep toenails carefully trimmed and filed smooth. Do not leave them long or with sharp edges. If hand weakness makes this difficult, see a podiatrist.

If your doctor refers you to a podiatrist as part of your Enhanced Primary Care (EPC) plan, you are eligible for a Medicare rebate. Some private health insurers also provide a rebate.

Conclusion

Peripheral neuropathy is increasingly recognised as a problem that potentially limits treatment options and severely impacts quality of life. Current research is looking into the mechanisms that cause peripheral neuropathy and how best to control its different presentations and symptoms. People with myeloma are living longer with their disease and so the control of side effects caused by treatments has become even more important. It is now understood that keeping the symptoms of peripheral neuropathy at a low level is the most important strategy in preventing severe symptoms that impact on quality of life and treatment options.

Resources



www.quitnow.info.au



www.diabetesaustralia.com.au

For further information or to discuss any of the information contained in this booklet, call the Myeloma Support Line on 1800 MYELOMA or 1800 693 566.

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