



**NeuroEndocrine  
Cancer** Australia

# Treatment

Being diagnosed with cancer can be a confusing and frightening time for you and your loved ones. Although your healthcare team will do their best to support you, medical appointments can be stressful and it is worth finding ways to get the most out of each appointment. The information in this section will help you to work out what questions to ask.

Each person with NETs should have an individualised treatment plan. This is because there are a number of treatment options available, depending on the type and location of the tumour, your general health and individual preferences. You may find it helpful to download your Wellness and Treatment plan from the Neuroendocrine Cancer Australia website to help you keep on track.

## Multidisciplinary teams

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The care of NETs can be complex. Your journey may involve not only a whole host of emotions, but also a whole range of investigations, treatments and healthcare professionals.

The fact that there is often not just one treatment option at diagnosis and throughout the journey means that those involved in your care need to consult with each other to work out the best treatment for you. This is called an MDT (multidisciplinary team). MDTs are used across the world in the care of cancer patients and are particularly important for a complex cancer such as NET.

With an MDT, patients can feel more confident that all aspects of their care have been discussed and that the best possible treatment plan will be formulated.

### Members of a NET MDT may include:

- Oncologist
- Radiologist
- Pain team
- Gastroenterologist
- Respiratory Physician
- Counselling staff
- Surgeon
- General practitioner/Practice nurse
- Clinic staff
- Endocrinologist
- Nurse specialist
- Cardiologist
- Nuclear medicine specialist
- Dietitian
- Clinical Trials staff
- Palliative care team
- Pathologist

## Surgery

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People with NETs often have surgery to remove the tumours. The goal of surgery depends on the type of NET cancer, its location in the body and size and whether it has spread from where it began.

Different surgeons may be involved with NETs depending on their expertise and training (e.g. endocrine, colorectal, hepatobiliary, pancreatic and cardiothoracic surgeons).

Surgery for NETs should be done in facilities which have NET specialist units where the surgeons work as part of a team including anaesthetists, oncologists, gastroenterologists, nurses, radiologists and other doctors with expertise in NET cancers.

### Curative surgery

This is surgery used when the cancer has not metastasised (spread outside the organ or area where it started). If the tumour can be removed whole and intact with a surrounding margin of clear, healthy tissue, then the surgery will potentially cure the cancer and no other treatment may be necessary.

A follow-up plan will be needed after surgery.

### Palliative surgery

When the tumour or tumours have spread or become too large to remove completely, then surgery may be considered to 'de-bulk' the tumour. This will relieve symptoms caused if the tumour is affecting other organs or producing excessive amounts of hormones.

### Cardiac and thoracic surgery

Thoracic surgery may be indicated for patients with pulmonary NETs and cardiac surgery for patients with carcinoid heart disease who may need cardiac valve replacement.

### Perioperative and anaesthetic management of NET patients

Patients with NET may be at risk of 'carcinoid crisis' in the perioperative period or during surgery. The NET specialist should discuss this with the anaesthetist before surgery.

## Medical management

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All side effects are important to discuss with your doctor and treating team, as these may need to be monitored and many can be managed with simple measures.

### Somatostatin analogues (SSA)

Daily (short acting) or monthly (long acting) injections of somatostatin analogues (Sandostatin, Lanreotide) are available to control some symptoms caused by NETs.

Short acting Octreotide may be given several times a day to control symptoms for 2 to 3 days until a correct dose of long lasting SSA can be prescribed. Sometimes the short acting SSA may be included to reduce symptoms despite the use of the long acting SSA until a treatment regime can be ordered.

Somatostatin analogues are versions of the naturally occurring somatostatin, which is a hormone produced in the brain and digestive tract. Somatostatin regulates the release of several other hormones and chemicals from our internal organs.

Injections of these analogues can stop the overproduction of hormones (e.g. serotonin) that cause symptoms such as flushing and diarrhoea. There is evidence that these injections also slow down rate of growth of tumours.

Main side effects of Somatotstatin analogues are:

- Loss of appetite
- Feeling sick
- Feeling bloated
- Stomach pain
- Tiredness (fatigue)
- Increased diarrhoea (this is rare)
- Soreness at the injection site
- Fat Malabsorption (stools that appear pale, oily, float or are hard to flush).

View our Factsheet on Vitamin and Mineral deficiencies for more info:

<https://neuroendocrine.org.au/factsheets>

You might have raised or lowered blood sugar levels. If you are a diabetic you need to check your blood sugar more often. You might also need fewer diabetic tablets and less insulin.

Having octreotide over many months can cause gallstones. So you might have an ultrasound scan of your gallbladder before you start treatment, and then every 6 to 12 months. Between 10 and 50 out of 100 people (10 to 50%) develop gallstones while they are having octreotide. Most people have no symptoms from the gallstones.

### **Sandostatin LAR® (depot preparation of octreotide)**

Long Acting Octreotide (an analogue of the naturally occurring somatostatin) is the active ingredient in Sandostatin LAR®. Sandostatin LAR® blocks the somatostatin receptors and can slow the tumour growth and treat the symptoms of NETs. Sandostatin LAR must be mixed immediately prior to injection. It is usually given by a health professional however some patients and / or carers give the injection. There is a home program available whereby a GP or nurse can administer it in the patients home or when travelling around Australia.

### **Somatuline® Autogel (depot preparation of Lanreotide)**

Lanreotide (an analogue of the naturally occurring somatostatin) is the active ingredient in Somatuline® LA. Lanreotide may be used instead of somatostatin because it is more potent, lasts longer in the body and is given as a monthly injection. Somatuline® Autogel blocks the somatostatin receptors and can slow the NET tumour growth and treat the symptoms of NETs. Lanreotide comes premixed and is usually given by a health professional, however, some patients can self-inject or receive injection by carer.

### **Targeted molecular therapies**

Sunitinib (Sutent) is a medication that comes in capsule form. It is mainly used in patients with pancreatic neuroendocrine tumours. It works mainly by blocking a process called angiogenesis (the process of making new blood vessels). Tumours need a good blood supply to grow and Sutent helps stop that process. The drug comes under an umbrella group of drugs known as tyrosine kinase inhibitors.

Everolimus (Affinitor®) is another medication for patients with pancreatic, lung and gastrointestinal neuroendocrine tumours – however funding has not been approved for all these NETs at time of publication. It also comes in a capsule form and is a type of drug that interferes with the mTOR enzyme in cells that regulates growth and metabolism. Blocking the action of this enzyme has been shown to slow the growth of neuroendocrine tumour cells in patients with progressive disease.

## Chemotherapy

Chemotherapy may be an option, especially for NET patients with pancreatic, bronchial or high-grade (G2/G3) NETs. Not all NETs respond equally to chemotherapy, so your doctor may or may not recommend it as part of your treatment.

Many chemotherapy treatments involve intravenous drugs that are given in hospital as a day procedure; however, there are also oral chemotherapy agents—your NET doctor or MDT will discuss the best option with you. Chemotherapy, either oral or intravenous, will cause side effects and special care is required to prevent and or minimise these side effects. You will be given specific information relevant to the treatment you will be receiving from your treatment team.

The histology of the tumour (i.e. how it looks under the microscope after biopsy or operation) may help determine the type of treatment you receive.

Chemotherapy may sometimes be recommended after surgery (adjuvant therapy) for high grade NETS. You may be asked if you would like to join a clinical trial researching chemotherapy for different types of NET cancer.



## Peptide receptor radionuclide therapy (PRRT) or Lutate

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PRRT is an outpatient therapy that is effective for some patients with NETs.

Lutetium-177 Octreotate Therapy (Lutate) is primarily used to treat people with NETs when other types of treatment, such as surgery or chemotherapy, are not suitable or are ineffective. This may be due to the size, location and number of tumours present. Lutetium-177 Octreotate is a very specific therapy that can only be used when tumours express a large number of somatostatin receptors. Most NETs show an increase in somatostatin receptors. Other tumours such as head and neck cancers, non-small cell lung cancer, small cell lung cancer and Merkel cell cancer may also express somatostatin receptors. If this therapy is being considered, a diagnostic scan is performed (Gallium 68 PET scan) to distinguish if the tumours are positive for somatostatin receptors

If having this treatment, you may have a dose of chemotherapy to prepare or sensitise the tumour cells for the PRRT. You will also have an infusion of amino acids to help protect your kidneys.

Depending on the treatment regimen, PRRT is given as an induction course of four treatments separated by 6 to 8 weeks. You may have more PRRT later: your doctor will advise you about this.

You may have nausea, fatigue, some hair loss (not baldness), risk of carcinoid syndrome flare and minor changes in the production of your blood as side effects of this treatment. You should contact your treatment team if you do experience any of these side effects as these side effects can be managed.

## Liver directed therapies

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### Hepatic artery embolization (HAE)/ transcatheter arterial chemoembolisation (TACE)

If the NET tumour has spread to the liver, you may be offered hepatic artery embolisation (HAE), which will aim to block the blood supply to the tumours in the liver.

You will have local anaesthetic (and sedation). The radiologist will access an artery in the groin and then direct a catheter, with the help of x-ray imaging, into the main supply of the liver (hepatic artery) and into the artery that supplies blood to the NET tumours in the liver. Tiny particles called microspheres are then injected

through the catheter into the artery. These particles block the blood supply to the tumour, which can cause the tumour to shrink or even die.

This procedure may be combined with the injection of chemotherapy or the use of microspheres that contain chemotherapy. This is called transcatheter arterial chemoembolisation (TACE). For this procedure, you will probably be admitted to hospital overnight. The side effects can include fatigue, nausea, vomiting and pain especially around the liver.

### Selective internal radiation therapy (SIRT)

This is the use of radiotherapy to treat liver metastases that cannot be removed with surgery.

It is similar to hepatic artery embolisation. An experienced interventional radiologist will insert a catheter into the hepatic artery supplying blood to the NET tumours and tiny beads containing a radioactive substance will be injected. These interfere with the tumour cell DNA and slow tumour growth.

### Radiofrequency ablation (RFA)

This is a treatment for metastatic or primary NET and is done by a radiologist. Using ultrasound or CT guidance, a needle (under local anaesthetic and sedation) is inserted through the abdominal wall and into the liver tumour. Once the needle is localised within the tumour, a generator is used to deliver a rapidly alternating current (radiofrequency energy) producing high temperatures (heat) that destroy the cancer cells (necrosis).

## Symptom Management

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### Telotristat etipirate (Xermelo)

Telotristat is a novel oral drug. It inhibits an enzyme that is responsible for the production of serotonin. Excessive blood levels of serotonin cause carcinoid syndrome (diarrhoea, flushing, abdominal pain); therefore, decreasing its production can reduce these symptoms. The recent TELESTAR trial enrolled patients with carcinoid syndrome and 4+ bowel movements per day. The patients who received telotristat reported significantly fewer bowel movements. It is worth noting, however, that telotristat improved bowel motions by approximately 1/day over placebo i.e. patients on telotristat may still have multiple bowel



movements per day. Urinary 5-HIAA (reflecting serotonin production) was also reduced with telotristat. This is a promising option for treatment of patients who have diarrhoea from carcinoid syndrome despite SSAs.

This drug does not act on the tumours to control their growth.

## Watchful Waiting

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No treatment, or watchful waiting, may be the best option for some NET patients especially if the NET is not causing symptoms or problems, the disease is stable, or the tumour is low grade (G1).

For some people, poor general health or complications secondary to treatments may also make further NET treatment inadvisable.

## Clinical trials

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Clinical trials are medical research trials involving patients. They are done to try to find new and better treatments. Clinical trials are the only sure way to find out if a new approach to cancer care is better than the standard treatment currently available. They are heavily regulated to ensure that results are meaningful and reliable. For further information refer to

<https://www.tga.gov.au/community-qa/clinical-trials-information-consumers> or  
<https://www.australianclinicaltrials.gov.au/consumers>

[www.neuroendocrine.org.au](http://www.neuroendocrine.org.au)

[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

## Palliative Care

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Involving Palliative Care team members as part of the multidisciplinary team is extremely beneficial from diagnosis onward as this can improve the patient's and family's quality of life psychologically and physically. Palliative care is care that helps people live their life as fully and as comfortably as possible and provide services which can meet the individual needs by –

- Relief of pain and other symptoms e.g. vomiting, shortness of breath
- Resources such as equipment needed to aid care at home

- Assistance for families to come together to talk about sensitive issues
- Links to other services such as home help and financial support
- Support for people to meet cultural obligations - Aboriginal and Torres Strait Islander (ATSI), Cultural and Linguistic Diverse (CALD) populations and preferences
- Support for emotional, social and spiritual concerns
- Counselling and grief support
- Referrals to respite care services

Please refer to [www.palliativecare.org.au](http://www.palliativecare.org.au) for further information

## Prognosis

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Many patients have an excellent prognosis from NET. If low-grade disease is completely cut out (resected), there is a good chance that it will not come back. However, these patients may need follow-up over a long period to monitor for recurrence.

Even for patients with advanced (unresectable) disease, there can be a wide range of outcomes. The average outcome is quite dependent on the histological (tissue-based) grade of the NET. Patients with low-grade (Grade 1) disease may survive for many (even 10+) years. Patients with high grade (grade 3) disease that is aggressive have an average survival time measured in the range of many months to a few years, despite best treatment.

It is important to realise two things about prognosis:

1. There is a big variation in prognosis - there is a lot of variation in outcomes and no “magic number” for a particular patient. Some patients find discussion of ranges in prognosis (best case/worse case/expected scenarios) very helpful.
2. New treatments and insights can improve care and hence prognosis for all NET patients. Therefore, prognoses based on the available information are a rough estimate.



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