

Understanding Targeted Therapy

A guide for people affected by cancer

This fact sheet has been prepared to help you understand more about targeted therapy, a treatment offered to some people with cancer. We hope this fact sheet will help you, your family and friends understand what targeted therapy is and how it may help treat cancer.

What is targeted therapy?

This is a type of drug treatment that attacks specific features of cancer cells, known as molecular targets, to stop the cancer growing and spreading.

Other names for targeted therapy include biological therapies and molecular targeted therapy.

How targeted therapy works

Targeted therapy drugs circulate throughout the body. Each drug acts on a specific molecular target within or on the surface of cancer cells (for example, a gene or protein). These molecular targets are involved in the growth and survival of cancer cells. Blocking them can kill cancer cells or slow their growth, while minimising damage to healthy cells.

Targeted therapy drugs work in a different way to chemotherapy drugs. Chemotherapy drugs also circulate throughout the body, but they particularly affect cells that divide rapidly. They kill cancer cells, but can also damage other rapidly dividing cells, such as the healthy cells in a person's mouth, stomach, skin or hair.

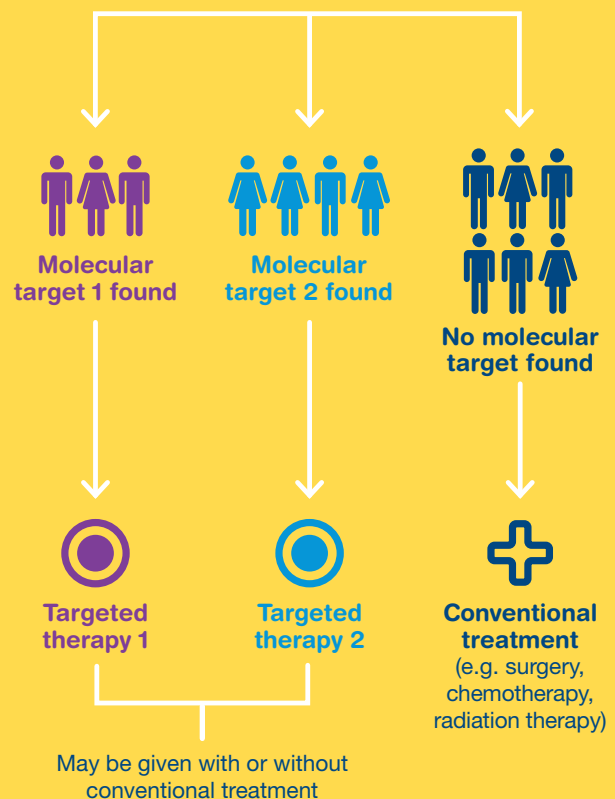
Targeted therapy drugs are used to control cancer growth. They often cause the signs and symptoms of cancer to reduce or disappear. This means many people can return to their usual activities. The drugs may need to be taken long-term, and you will need to have regular tests to monitor the cancer.

Who can have targeted therapy?

Your doctors will test the cancer to see if the cells contain a particular molecular target that is helping the cancer grow. Different people with the same cancer type may receive different treatments based on their test results.



People with the same type of cancer



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What are genes?

Genes are made up of DNA (deoxyribonucleic acid). They are found in every cell of the body and are inherited from both parents. Each human cell has about 20,000 genes. Genes tell the cell what to do, and when to grow and divide. Cells use this information to make proteins that carry out specific functions in the body.

Where do the molecular targets come from?

Cancer is caused by abnormal changes in a person's genes that can cause cancer cells to multiply and grow. These gene abnormalities are known as molecular targets. They may be acquired or inherited.

Acquired gene changes

Most cancers are not caused by inherited genetic changes but by mistakes that build up over time in the body's cells (known as acquired changes). These gene faults are in the structure of the cancerous cell, not in normal cells.

Researchers have found several gene abnormalities that play a key role in a number of cancers. For example:

- epidermal growth factor receptor (EGFR) mutations in lung cancer
- BRAF mutations in melanoma, bowel and thyroid cancers
- anaplastic lymphoma kinase (ALK) mutations in lung cancer and neuroblastoma
- KRAS mutations in bowel cancer
- NRAS mutations in melanoma, leukaemia and bowel cancer
- high levels of human epidermal growth factor receptor 2 (HER2) in breast and stomach cancers
- KIT mutations in gastrointestinal stromal tumours and melanoma.

To find out if the cancer contains a change in a gene or related protein that may respond to a particular targeted therapy drug, your doctor will take a tissue sample from the cancer and send it to a laboratory for molecular testing. It may take from a few days to a few weeks before you receive the results.

Inherited faulty genes

Some genetic abnormalities are linked to a faulty gene (mutation) we inherit from our parents. Inherited faulty genes may increase a person's risk of developing cancer. However, not all people who inherit a faulty gene develop cancer.


About 5% of cancers are caused by an inherited faulty gene. Inherited genetic conditions associated with cancer continue to be discovered, for example:

- an inherited mutation in one of the BRCA genes is linked to breast, ovarian and prostate cancers
- Lynch syndrome increases the risk of developing bowel, uterine, ovarian and stomach cancers
- Li-Fraumeni syndrome increases the risk of developing breast, primary bone and adrenal cancers
- Cowden syndrome increases the risk of developing breast, thyroid and uterine cancers
- familial adenomatous polyposis (FAP) is a risk factor for bowel, stomach and thyroid cancers.

If your doctor suspects that the cancer is linked to an inherited gene fault, they will refer you to a family cancer service or genetic counsellor. A pathologist can run special tests on a blood or tissue sample to look for possible inherited gene changes. This is known as a genetic test.

Knowing whether you have a particular faulty gene may help determine suitable treatment options. Doctors may be able to recommend a targeted therapy drug that has been shown to work on cancers caused by that faulty gene.

If you are concerned about your family risk factors, talk to your doctor about having regular check-ups or ask for a referral to a family cancer clinic. To find out more, call Cancer Council 13 11 20.



Medicare rebates are available for genetic tests for some people with specific cancers. You may need to meet certain eligibility requirements to have a Medicare-funded test. For more information about genetic testing, talk to your specialist or family cancer clinic, or call 13 11 20. Visit genetics.edu.au to find a family cancer clinic near you.

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Types of targeted therapy

Each type of targeted therapy drug works on a specific molecular target. The two main groups of drugs are monoclonal antibodies and small molecule inhibitors.

Monoclonal antibodies

These medicines are manufactured (synthetic) versions of immune system proteins called antibodies, which are part of the body's natural defence against infections. The synthetic antibodies lock onto a protein on the surface of cells or surrounding tissues to interfere with the growth or survival of cancer cells in some way. Monoclonal antibodies can be classified as either a targeted therapy or immunotherapy, depending on the type of monoclonal antibody. Examples of targeted therapy monoclonal antibodies include:

Angiogenesis inhibitors	These drugs are designed to reduce the blood supply to a tumour to slow or stop it growing. They target various receptors or proteins linked with the growth of cancer cells and stop them from working. For example, bevacizumab targets vascular endothelial growth factor (VEGF), a protein that helps new blood vessels form.
HER2-targeted agents	HER2 is a protein that causes cancer cells to grow uncontrollably. Some targeted therapy drugs destroy the HER2 positive cancer cells, or reduce their ability to divide and grow. Examples include trastuzumab and pertuzumab, which are used to treat HER2 positive breast cancer.
Anti-CD20 monoclonal antibodies	These drugs target a protein called CD20 found on some B-cell leukaemias and non-Hodgkin lymphomas. Examples include rituximab and obinutuzumab.
Small molecule inhibitors	
These drugs can get inside cancer cells and block certain enzymes and proteins that tell cancer cells to grow. Examples of small molecule inhibitors include:	
Tyrosine kinase inhibitors (TKIs)	These drugs block a group of enzymes called tyrosine kinases from sending signals that tell cancer cells to grow, multiply and spread. Without this signal, the cancer cells die. Examples of TKIs include erlotinib, sunitinib, lapatinib and ibrutinib.
Mammalian target of rapamycin (mTOR) inhibitors	These drugs block mTOR, an enzyme that tells cancer cells to grow and spread. Everolimus is an mTOR inhibitor approved for use for some types of kidney cancer.
PARP inhibitors	These drugs stop the protein known as PARP from repairing damaged DNA in cancer cells. Olaparib is a PARP inhibitor approved for use in some ovarian, fallopian tube and peritoneal cancers.

Other cancer treatments

Because an individual's cancer cells are unique, different people may receive different treatments, even if their cancer type is the same. Doctors will recommend the best treatment for an individual based on the type and stage of cancer, its genetic make-up, the person's age and their general health.

Aside from targeted therapy, other treatments for cancer include surgery, chemotherapy, radiation therapy, hormone therapy, and immunotherapy.

These treatments may be used on their own or in combination. For example, you may have surgery to remove a tumour, followed by a targeted therapy drug to kill any remaining cancer cells.

For more information about other cancer treatments, read Cancer Council's publications on *Understanding Radiation Therapy*, *Understanding Chemotherapy*, *Understanding Surgery* and *Understanding Immunotherapy*. Call 13 11 20 or download copies from your local Cancer Council website (see page 6).

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🗨️ When I was first diagnosed I was put on imatinib, but I had severe side effects so my haematologist put me on dasatinib. I've been on this for over eight years with excellent results. As the leukaemia is still detected in the regular blood tests, there's no plan to discontinue treatment in the foreseeable future. 🗨️ *Patricia*

Who may benefit?

Targeted therapy drugs have been approved for use in Australia for bowel, breast, cervical, kidney, lung, ovarian, stomach and thyroid cancers, as well as melanoma and some forms of leukaemia, lymphoma and myeloma.

The development of targeted therapy drugs has led to improved survival rates for several types of cancer and some people have had very encouraging outcomes. These drugs are becoming an increasingly important part of cancer treatment.

Targeted therapy drugs may be used:

- after surgery to destroy any remaining cancer cells
- to treat advanced cancer that hasn't responded to other treatment, or cancer that has come back
- as maintenance treatment for advanced cancer to try to prevent the cancer coming back.

Less commonly, targeted therapy drugs are used as the first treatment for primary cancer or in combination with radiation therapy.

Many targeted therapy drugs are not safe to use during pregnancy or while breastfeeding. Ask your doctor for advice about contraception. If you become pregnant, let your medical team know immediately.

Challenges of targeted therapy

While many people respond well, targeted therapy is suitable for only a small number of cancers.

Will it work? – The cancer must contain the particular molecular target or the drug won't work. However, even if the cancer is shown to contain the target, there is no guarantee the drug will kill the cancer cells. The response to targeted therapy varies widely depending on the cancer type and molecular target. In some cancers, four out of five people assessed as suitable for a particular targeted therapy drug will respond.

Some cancer cells can become resistant to the targeted therapy even if it works at first. If this happens, another type of targeted therapy or another treatment may be offered.

How much will it cost? – The Pharmaceutical Benefits Scheme (PBS) subsidises the cost of many prescription medicines, including some targeted therapy drugs. The PBS has approved a number of targeted therapy drugs for use in Australia, under specific circumstances and for certain cancers. Medicines or treatments that are not on the PBS are usually very expensive, however, you may be able to access them as part of a clinical trial.

How targeted therapy is given

Targeted therapy drugs are usually prescribed by a medical oncologist or haematologist. They are commonly given in repeating cycles, with rest periods in between. Some drugs may be taken daily for many months or even years. They may be given on their own or in combination with chemotherapy drugs.

These drugs are generally given in different ways:

- as tablets that you can swallow
- through a drip into a vein in your arm (IV infusion)
- as an injection under the skin.

How long you take the drugs will depend on the aim of the treatment, how the cancer responds, and the side effects you experience. Your treatment team can give you more details.

⚠️ Some people can react to the infusion process (e.g. difficulty breathing, nausea and skin rashes). Reactions can occur during or several hours after the infusion. You will be monitored and may be given medicine to help prevent this. Reactions are more common with the first infusion, so it may be given more slowly than later treatments.

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“When my non-Hodgkin lymphoma came back I was treated with radiation therapy and then put on rituximab for maintenance therapy. This was of great benefit – I had no worrying side effects and have felt very well in the five years since my last treatment.” *Jennifer*

Possible side effects

Although targeted therapy minimises harm to healthy cells, it can still have side effects. These vary greatly for each person depending on the drug you have and how your body responds. Some people don't experience any side effects, while others have several.

Targeted therapy drugs commonly cause skin problems, for example:

- sensitivity to sunlight, skin redness, swelling and dry, flaky skin
- a rash that looks like acne or pimples on the face, scalp or upper body (acneiform rash)
- a skin reaction on the palms and soles causing tenderness and blisters (hand-foot syndrome).

Other common side effects include fever, tiredness, joint aches, nausea, headaches, diarrhoea, heavy bleeding and bruising, and high blood pressure.

Less commonly, some targeted therapy drugs can affect the way the heart, thyroid or liver works, or increase the risk of getting an infection.

Let your treatment team know about side effects

As targeted therapy drugs have the potential to cause serious life-threatening side effects, such as heart and lung complications, it's important for your treatment team to monitor your response. Ask the doctor or nurse which side effects to watch out for or report, and who to contact after hours.

Side effects can be better managed when they are reported early. Your doctor may be able to prescribe medicine to prevent or reduce them. If they are not treated, side effects may become serious, and treatment may need to be stopped for a period of time. Once the side effects have gone away, you may be able to restart the targeted therapy on an adjusted dose, or try a different drug.

Managing side effects

Your health care team will monitor you while you are taking targeted therapy drugs. Side effects can sometimes begin within days of starting treatment, but more commonly they occur weeks or even months later. Your treatment team can help you manage any side effects.

Side effects may last from a few weeks to a few months. Most are temporary and will improve once you stop taking the drug; however some may be permanent. In some cases, your treatment team will reduce the dose of the targeted therapy drug to see if that helps ease the side effects.

Many side effects of targeted therapy drugs may need to be managed differently. For example, skin reactions may be more severe or last longer than with other types of treatment, and you may be prescribed an antihistamine or steroid cream to help with the itching and dryness.

Targeted therapy drugs can interact with many common medicines and cause harmful side effects. It is important to let your doctor know about any other medicines or supplements you are taking so they can check for any known interactions. It is also a good idea to talk with your cancer specialist before having any vaccinations.

How will I know whether the targeted therapy drug is working?

You will have regular check-ups with your doctor, blood tests and different types of scans to see whether the cancer has responded to treatment.

If the treatment is working, the cancer will stop growing. A good response from targeted therapy will make the cancer shrink. In some cases, the cancer remains stable, which means it doesn't grow in size on scans, but also does not shrink or disappear. People with stable disease can continue to have a good quality of life.

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How do I access targeted therapy?

Ask your oncologist or haematologist if there is a suitable targeted therapy drug for you. Targeted therapy drugs are becoming more available on the Pharmaceutical Benefits Scheme (PBS) for specific cancers including melanoma, bowel cancer, stomach cancer, ovarian cancer, non-Hodgkin lymphoma, thyroid cancer, breast cancer and lung cancer. You will need a test to see if you are suitable for one of these drugs.

Many more targeted therapy drugs are being studied in clinical trials. Talk with your doctor about the latest developments and whether you are a suitable candidate. For more information on clinical trials, call 13 11 20 and ask for a copy of the *Understanding Clinical Trials and Research* booklet.

Question checklist

- Is targeted therapy available as part of my treatment plan? If not, why not?
- Which targeted therapy drug are you recommending?
- What do you expect the targeted therapy drug to do to the cancer?
- Will it be my only treatment or will I also have other treatments?
- How often will I have targeted therapy?
- How long will I receive treatment?
- Where will I have treatment?
- What side effects should I watch out for or report?
- Will it affect my immune system or vaccinations?
- Who do I contact if I get side effects?
- How can side effects be managed?
- What clinical trials are available?
- How will I know if the treatment is working?

Useful websites

The internet has many useful resources, although not all websites are reliable. The websites listed below are good sources of information.

- Cancer Australia
canceraustralia.gov.au
- Cancer Council Online Community
cancerCouncil.com.au/OC
- Centre for Genetics Education
genetics.edu.au
- eviQ Cancer Treatments Online
eviq.org.au
- The *Thing About Cancer* podcast
cancerCouncil.com.au/podcasts
- Australian Cancer Trials
australiancancertrials.gov.au
- American Cancer Society
cancer.org

Where to get help and information

Call Cancer Council **13 11 20** for more information about targeted therapy. Health professionals can listen to your concerns, provide information, put you in touch with local services, and send you free copies of our booklets. You can also visit your local Cancer Council website:

ACT..... actcancer.org
 NSW cancerCouncil.com.au
 NT..... nt.cancer.org.au
 QLD cancerqld.org.au
 SA..... cancersa.org.au
 TAS cancertas.org.au
 VIC..... cancervic.org.au
 WA..... cancerwa.asn.au
 Australia..... cancer.org.au

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Note to reader

Always consult your doctor about matters that affect your health. This fact sheet is intended as a general introduction and is not a substitute for professional medical, legal or financial advice. Information about cancer is constantly being updated and revised by the medical and research communities. While all care is taken to ensure accuracy at the time of publication, Cancer Council Australia and its members exclude all liability for any injury, loss or damage incurred by use of or reliance on the information provided in this fact sheet.



For information and support on cancer-related issues, call Cancer Council **13 11 20**. This is a confidential service.