

Treatments for chronic lymphocytic leukaemia

What does the guidance say?

Acalabrutinib, obinutuzumab, venetoclax and zanubrutinib are recommended for listing on the Medication Assistance Fund (MAF) for government funding when used as part of specific treatment regimens for patients with chronic lymphocytic leukaemia or small lymphocytic lymphoma who meet certain criteria.

Ibrutinib has not been recommended for subsidy for this condition.

What is chronic lymphocytic leukaemia?

Chronic lymphocytic leukaemia (CLL) is a cancer that affects the blood and bone marrow and causes white blood cells (B-cell lymphocytes) to grow uncontrollably and produce "leukaemia cells". As the number of leukaemia cells increases in the blood and bone marrow, there is less room for healthy blood cells, making patients more susceptible to infections. CLL is most common in older adults, affecting up to 40 people each year in Singapore.

Small lymphocytic lymphoma (SLL) is very similar to CLL except the leukaemia cells are mostly found in the lymph nodes, rather than in the blood and bone marrow. SLL and CLL are usually treated in the same way.

Many people do not have any symptoms at first because the leukaemia cells usually build up slowly. However, overtime as the cells spread to other parts of the body, symptoms may include swollen lymph nodes, fatigue, fever, night sweats, weight loss and frequent infections.

Patients often do not need treatment at first if they do not have any symptoms. Once symptoms develop, the type of treatment needed will depend on how fast the cancer cells are growing, which treatments have been tried before, the age of the patient and their general health. Doctors also test patients for genetic mutations (such as del17p or TP53) to determine which treatment is likely to work best.

After treatment, sometimes the cancer can come back (relapsed CLL). Some treatments can also stop working well after patients have been taking them for a while, and the cancer can begin to worsen. This is known as refractory or resistant CLL.

What are acalabrutinib and zanubrutinib?

Acalabrutinib and zanubrutinib belong to a group of targeted medicines called Bruton's tyrosine kinase (BTK) inhibitors which bind to BTK proteins on cancer cells and stop them from growing. Both treatments are taken orally each day.

Your doctor will tell you how much you need to take and how long you need to take either of these treatments for.



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Who can have acalabrutinib or zanubrutinib?

Acalabrutinib or zanubrutinib are used to treat patients with CLL or SLL if:

- they have not had treatment for CLL or SLL before and cannot have fludarabine-based chemotherapy; or
- they have had at least one previous treatment, but their cancer has come back or continued to worsen.

Acalabrutinib has only been recommended for funding when it is used on its own.

Your doctor will tell you if acalabrutinib or zanubrutinib is a suitable treatment for you.

What are obinutuzumab and venetoclax?

Obinutuzumab belongs to a group of targeted medicines called monoclonal antibodies that help the immune system find and destroy leukaemia cells that have a CD20 protein on their surface. It is given as a drip into a vein (intravenously), usually in combination with other cancer medicines when used to treat CLL.

Venetoclax belongs to a group of targeted medicines called B-cell lymphoma 2 (BCL2) inhibitors that help the immune system find and destroy leukaemia cells that have a BCL2 protein on their surface. It is taken orally, on its own or in combination with other cancer medicines when used to treat CLL.

Who can have obinutuzumab or venetoclax?

Venetoclax is used in combination with obinutuzumab or on its own after six cycles of obinutuzumab have been completed to treat patients with CLL if:

- they have not had treatment for CLL before and cannot have fludarabine-based chemotherapy; and
- venetoclax is taken for up to 12 months and obinutuzumab is given for up to 6 cycles.

Venetoclax is used in combination with rituximab biosimilar or on its own after six cycles of rituximab have been completed to treat patients with CLL if:

- they have had at least one previous treatment, but their cancer has come back or continued to worsen; and
- venetoclax is taken for up to 24 months and rituximab biosimilar is given for up to 6 cycles.

Obinutuzumab has not been recommended for funding when it is used in combination with chlorambucil or with acalabrutinib. Venetoclax has not been recommended for funding when it is used in combination with unsubsidised brands of rituximab. Your doctor will tell you if venetoclax or obinutuzumab is a suitable treatment for you.



Plain English Summary

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Why were these treatments recommended for funding?

ACE evaluates how well a treatment works in relation to how much it costs compared to other treatments. Acalabrutinib, obinutuzumab, venetoclax and zanubrutinib were recommended for funding because their benefit in improving survival for certain patients with CLL, when used as part of specific treatment regimens, justifies their costs.

Ibrutinib was not recommended for subsidy because its benefit does not justify its cost. If you need ibrutinib for CLL, you can speak to a medical social worker to find out if there is other financial assistance available to help with the cost of treatment.

What does listing on MAF mean for me?

The MAF helps people pay for expensive treatments that are clinically effective and cost effective. If your doctor prescribes acalabrutinib, obinutuzumab, venetoclax or zanubrutinib for CLL, and you meet the MAF criteria, your treatment cost will be subsidised by 40% to 75%.

All four drugs have also been included on the Cancer Drug List (CDL) and are claimable under MediShield Life. The subsidy class and MediShield Life claim limits are available at <u>go.gov.sg/moh-cancer-drug-list</u>.

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