SCHEDULING STATUS

S4

Venclexta 10 mg film-coated tablets

Venclexta 50 mg film-coated tablets

Venclexta 100 mg film-coated tablets

Venetoclax

Sugar free

Read all of this leaflet carefully before you start taking Venclexta

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, nurse or other healthcare provider.
- Venclexta has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What Venclexta is and what it is used for

What Venclexta is

Venclexta is medicine used to treat cancer and contains the active substance venetoclax. It belongs to a group of medicines called “BCL-2 inhibitors”.

What Venclexta is used for

Venclexta is used to treat patients with:

- chronic lymphocytic leukaemia (CLL). Venclexta may be given to you in combination with other medicines or alone.
- acute myeloid leukaemia (AML). Venclexta will be given in combination with other medicines

CLL is a type of cancer affecting white blood cells called lymphocytes and the lymph nodes. In CLL, the lymphocytes multiply too quickly and live for too long, so that there are too many of them in the blood.

AML is a type of cancer affecting white blood cells called myeloid cells. In AML, myeloid blood cells multiply and grow very quickly in bone marrow and blood, so that there are too many of them and not enough red blood cells in the blood.

How Venclexta works

Venclexta works by blocking a protein in the body called “BCL-2”. This protein helps cancer cells survive. Blocking this protein helps to kill and lower the number of cancer cells. It also slows down the worsening of the disease.

2. What you need to know before you take Venclexta

Do not take Venclexta if:

- you are allergic to the active substance venetoclax or any of the other ingredients of this medicine (listed in section 6).

- you are pregnant or breastfeeding your baby.

- you are to receive immunisation with a live attenuated viral of bacterial vaccine.

- you have CLL and are taking any of the medicines listed below when you start your treatment and while your dose is gradually being increased (usually over 5 weeks). This is because serious and life-threatening effects can occur when Venclexta is taken with these medicines:

    - itraconazole, ketoconazole, posaconazole, or voriconazole for fungal infections
    - clarithromycin for bacterial infections
    - ritonavir for HIV infection.

  When your Venclexta dose has been increased to the full standard dose, check with your doctor if you can start taking these medicines again.

- you are taking any of the medicines listed below. This is because they can lower the activity of Venclexta when taken together:
    - nafcillin and rifampicin for bacterial infections
    - efavirenz and etravirine for HIV infection
    - carbamazepine and phenytoin – medicines used to prevent seizures or to treat epilepsy
    - bosentan – a medicine used to treat a lung condition called pulmonary arterial hypertension
    - modafinil – a medicine used to treat sleep disorder (narcolopsy)

- you are taking a herbal medicine called St. John's wort, used for depression. If you are not sure about this, talk to your doctor, pharmacist or nurse before taking Venclexta.

It is important that you tell your doctor, pharmacist, or nurse about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Your doctor may need to stop certain medicines when you first start taking Venclexta and during the first five weeks when your dose is gradually increased to the full standard dose.

Warnings and precautions

Talk to your doctor or healthcare provider before taking Venclexta if:

- you have any kidney problems as your risk for a side effect called tumour lysis syndrome may increase
- you have liver problems as this may increase your risk for side effects. Your doctor may need to reduce your dose of Venclexta
- you think you may have an infection or have had a long-lasting or repeated infection

- you are due to have a vaccine.

If any of the above apply to you, or you are not sure, talk to your doctor, pharmacist, or nurse before taking Venclexta.

Tumour Lysis Syndrome

You may develop unusual levels of some body salts (such as potassium and uric acid) in the blood caused by the fast breakdown of cancer cells during treatment. This may lead to changes in kidney function, abnormal heartbeat, or seizures. This is called tumour lysis syndrome (TLS). The risk for TLS is in the first 5 weeks of treatment with Venclexta.

Your doctor, pharmacist or nurse will do blood tests to check for TLS when you first start treatment and during treatment with Venclexta. It is important to keep your appointments for blood tests.

<u>If you have CLL</u>

Your doctor may also give you medicines to help prevent the build up of uric acid in your body before you start treatment with Venclexta.

Drinking plenty of water, at least 1.5 to 2 litres per day, helps to remove cancer cell breakdown products from your body through urine, and may decrease your risk of getting TLS (see section 3).

Tell your doctor, pharmacist or nurse immediately if you get any of the symptoms of TLS listed in section 4.

If you are at risk of TLS you may be treated in hospital so that you can be given fluids into the vein if needed, have blood tests done more often and to check for side effects. This is to see if you can continue to take this medicine safely.

If you have AML

You may be treated in hospital and your doctor or nurse will make sure that you have enough water/fluids, give you medicines to prevent the build-up of uric acid in your body and do blood tests before you start to take Venclyxto, while they increase your dose and when you start to take the full dose.

Children and adolescents

Venclexta should not be used in children and adolescents 18 years of age or below. Venclexta has not been studied in these age groups.

Other medicines and Venclexta

Tell your doctor or pharmacist if you take any of the following medicines as they can increase or decrease the amount of venetoclax in your blood (This includes all complementary or traditional medicines):

- medicines for fungal infections – fluconazole, itraconazole, ketoconazole, posaconazole, or voriconazole
- antibiotics to treat bacterial infections – ciprofloxacin, clarithromycin, erythromycin, nafcillin, or rifampicin
- medicines to prevent seizures or to treat epilepsy – carbamazepine, phenytoin
- medicines for HIV infection – efavirenz, etravirine, ritonavir
- medicines to treat raised blood pressure or angina – diltiazem, verapamil

- medicines to lower cholesterol levels in the blood – cholestyramine, colestipol, colesevelam
- a medicine used to treat a lung condition called pulmonary arterial hypertension – bosentan
- a medicine to treat sleep disorder (narcolepsy) known as modafinil
- a herbal medicine known as St. John's wort

Your doctor may change your dose of Venclexta.

Tell your doctor if you take any of the following medicines as Venclexta may affect how they work:

- medicines that prevent blood clots, warfarin, dabigatran
- a medicine used to treat heart problems known as digoxin
- a medicine for cancer known as everolimus
- a medicine used to prevent organ rejection known as sirolimus
- medicines to lower cholesterol levels in the blood known as statins

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, herbal medicines and supplements. This is because Venclexta may affect the way some other medicines work. Also some other medicines can affect the way Venclexta works.

Venclexta with food and drink

Do not eat grapefruit products, Seville oranges (bitter oranges), or starfruit (carambola) while you are taking Venclexta – this includes eating them, drinking the juice or taking a

supplement that might contain them. This is because they can increase the amount of venetoclax in your blood.

Pregnancy

- Venclexta should not be used during pregnancy as the possibility of serious harm to your unborn baby cannot be excluded.

- Do not get pregnant while you are taking Venclexta. If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist, or nurse for advice before taking Venclexta.

- There is no information about the safety of venetoclax in pregnant women.

Contraception

- Women of childbearing age must use a highly effective method of contraception during treatment and for at least 30 days after receiving Venclexta to avoid becoming pregnant. If you are using hormonal contraceptive pills or devices, you must also use a barrier method of contraception (such as condoms) as the effect of hormonal contraceptive pills or devices may be affected by Venclexta.
- Tell your doctor immediately if you become pregnant while you are taking Venclexta.

Breastfeeding

Do not breastfeed while you are taking Venclexta. It is not known whether the active substance in Venclexta passes into human breast milk and the potential of serious harm to your baby cannot be excluded.

Fertility

Based on findings in animals, Venclexta may cause male infertility (low or no sperm count) which may not be reversible after stopping treatment. This may affect your ability to father a child. Ask your doctor for advice on sperm storage before starting treatment with Venclexta.

Driving and using machines

Treatment with Venclexta may affect your ability to drive and use machines. You should not drive and use machines until you know how treatment with Venclexta affects you.
You may feel tired or fatigued after taking Venclexta, which may affect your ability to drive or use tools or machines.

3. How to take Venclexta

Do not share medicines prescribed for you with any other person.

Always take Venclexta exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take

<u>If you have CLL</u>

You will begin treatment with Venclexta at a low dose for 1 week. Your doctor will gradually increase the dose over the next 4 weeks to the full standard dose. You will receive the first 4 weeks of medicine in a “Starting Pack”. Follow the instructions below for the first 4 weeks. After that use the 100 mg tablets from bottles to take 400 mg (four 100 mg tablets) once a day.

- the starting dose is 20 mg (two 10 mg tablets) once a day for 7 days.
- the dose will be increased to 50 mg (one 50 mg tablet) once a day for 7 days.
- the dose will be increased to 100 mg (one 100 mg tablet) once a day for 7 days.
- the dose will be increased to 200 mg (two 100 mg tablets) once a day for 7 days.
- the dose will be increased to 400 mg (four 100 mg tablets) once a day for 7 days.
    - When you are receiving Venclexta therapy alone, you will stay on the 400 mg daily dose, which is the standard dose, for as long as necessary.
    - When you are receiving Venclexta therapy in combination with rituximab, you will receive the 400 mg daily dose for 24 months.

Your dose may need to be adjusted for side effects. Your doctor will advise what your dose should be.

<u>If you have AML</u>

You will begin treatment with Venclexta on a lower dose. Your doctor will gradually increase the dose each day for the first 3 days. After 3 days you will take the full standard dose. Your doctor will give you Venclexta in combination with another medicine for the first 3 days. The dose (tablets) is taken once a day.

Doses are listed in the table below

Day	Venclexta daily dose
1	100 mg (One 100 mg tablet)
2	200 mg (Two 100 mg tablets)
3 and after	400 mg (Four 100 mg tablets)

You will keep taking Venclexta at the full dose until either your AML gets worse or you cannot take Venclexta as it is causing serious side effects.

How to take Venclexta

- Take the tablets with a meal at around the same time each day
- Swallow the tablets whole with a glass of water
- Do not chew, crush, or break the tablets
- During the first 5 weeks of treatment, you should take the tablets in the morning to help you follow-up with blood tests, if needed.

If you vomit after taking Venclexta, do not take an extra dose that day. Take the next dose at the usual time the next day. If you have problems taking Venclexta, talk to your doctor.

Drink plenty of water

<u>If you have CLL</u>

It is very important that you drink plenty of water when taking Venclexta during the first 5 weeks of treatment. This will help to remove cancer cell breakdown products from your blood through your urine.

You should start drinking at least 1.5 to 2 litres of water daily two days before starting Venclexta. You may also include non-alcoholic and non-caffeinated drinks in this amount, but exclude grapefruit, Seville orange, or starfruit (carambola) juices. You should continue to drink at least 1.5 to 2 litres of water on the day you start Venclexta. Drink the same amount of water (at least 1.5 to 2 litres daily) two days before and on the day that your dose is increased.

If your doctor thinks that you are at risk of TLS, you may be treated in the hospital so that you can be given extra fluids into the vein if needed, have your blood tests more often and be checked for side effects. This is to see if you can continue to take this medicine safely.

If you have AML

It is very important you drink plenty of water when taking Venclexta especially when you start treatment and increase your dose. Drinking water will help to remove cancer cell breakdown products from your blood through your urine. Your doctor or nurse will give you fluids into the vein if needed if you are in hospital to make sure this happens.

If you take more Venclexta than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take Venclexta

- If it is less than 8 hours since the time you usually take your dose, take it as soon as possible.
- If it is more than 8 hours since the time you usually take your dose, do not take the dose that day. Return to your normal dose schedule the next day.
- Do not take a double dose to make up for a forgotten dose.
- If you are not sure talk to your doctor, pharmacist or nurse.

Do not stop taking Venclexta

Do not stop taking Venclexta unless your doctor tells you to. If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Not all side effects reported for Venclexta are included in this leaflet. Should your general health worsenor if you experience any untoward effects while taking Venclexta, please consult your health care provider for advice.

Venclexta can cause side effects. The following serious side effects may happen with Venclexta:

Tumour lysis syndrome (Frequent)

Stop taking Venclexta and seek medical attention immediately if you notice any of the symptoms of TLS:

- fever or chills
- feeling or being sick (nausea or vomiting)
- feeling confused
- feeling short of breath
- irregular heart beat
- dark or cloudy urine
- feeling unusually tired
- muscle pain or uncomfortable joints
- fits or seizures
- abdominal pain and distension

Low white blood cell count (neutropenia) (Frequent)

Your doctor will check your blood count during treatment with Venclexta. Low white blood cell count can increase your risk for infection. Signs may include fever, chills, feeling weak or confused, cough, pain or burning feeling when passing urine. Some infections can be serious

and may lead to death. Tell your doctor immediately if you have signs of an infection while taking Venclexta.

Tell your doctor if you notice any of the following side effects:

For patients with CLL

Frequent

- pneumonia (lung infection)
- upper respiratory tract infection – signs include runny nose, sore throat or cough
- diarrhoea
- feeling or being sick (nausea or vomiting)
- constipation
- feeling tired/fatigued
- dizziness
- headache
- difficulty sleeping
- muscle pain
- joint pain
- skin rash

Blood tests may also show:

- lower number of red blood cells
- lower number of white blood cells called lymphocytes
- lower number of platelets
- higher level of potassium
- higher level of a body salt (electrolyte) called phosphate

- lower level of calcium
- lower level of blood sugar
- lower or higher level of body salt (electrolyte) called sodium
- increased level of a liver enzyme

Frequent

- severe infection in the blood (sepsis)
- urinary tract infection
- low number of white blood cells with fever (febrile neutropenia)
- stomach pain
- sores in mouth
- fever
- swelling

Blood tests may also show:

- higher level of creatinine
- higher level of urea
- lower level of calcium
- lower level of body salt (electrolyte) called phosphate
- higher level of bilirubin
- lower level of albumin

For patients with AML

Frequent

- feeling or being sick (nausea or vomiting)
- diarrhoea

- mouth sores
- feeling tired or weak
- infection of lung or blood
- decreased appetite
- joint pain
- dizziness or fainting
- headache
- shortness of breath
- bleeding
- low blood pressure
- urinary tract infection
- weight loss
- pain in belly (abdominal pain)

Blood tests may also show

- lower number of platelets (thrombocytopenia)
- lower number of white blood cells with fever (febrile neutropenia)
- lower number of red blood cells (anaemia)
- higher level of total bilirubin
- low level of potassium in the blood

Frequent

- gall stones or gall bladder infection

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist, or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications" https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of Venclexta.

5. How to store Venclexta

Store all medicines out of reach of children.

Do not use Venclexta after the expiry date which is stated on the carton and blister after EXP.

Venclexta does not require any special storage conditions.

Return all unused Venclexta to your pharmacist.

Do not dispose of unused Venclexta in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What Venclexta contains

The active substance is venetoclax.

- Venclexta 10 mg film-coated tablets: Each film-coated tablet contains 10 mg venetoclax.
- Venclexta 50 mg film-coated tablets: Each film-coated tablet contains 50 mg venetoclax.

- Venclexta 100 mg film-coated tablets: Each film-coated tablet contains 100 mg venetoclax.

The other ingredients are:

- In the tablet core: copovidone (K 28), polysorbate 80 (E433), colloidal anhydrous silica (E551), anydrous calcium hydrogen phosphate (E341 (ii)), sodium stearyl fumarate.

In the film-coating:

- Venclexta 10 mg film-coated tablets: iron oxide yellow (E172), polyvinyl alcohol (E1203), titanium dioxide (E171), macrogol 3350 (E1521), talc (E553b).
- Venclexta 50 mg film-coated tablets: iron oxide yellow (E172), iron oxide red (E172), iron oxide black (E172), polyvinyl alcohol (E1203), titanium dioxide (E171), macrogol 3350 (E1521), talc (E553b)
- Venclexta 100 mg film-coated tablets: iron oxide yellow (E172), polyvinyl alcohol (E1203), titanium dioxide (E171), macrogol 3350 (E1521), talc (E553b).

What Venclexta looks like and contents of the pack

Venclexta 10 mg film-coated tablet is pale yellow, round 6 mm diameter, with V on one side and 10 on the other.

Venclexta 50 mg film-coated tablet is beige, oblong 14 mm long, with V on one side and 50 on the other.

Venclexta 100 mg film-coated tablet is pale yellow, oblong 17.2 mm long with V on one side and 100 on the other.

Venclexta is available as follows:

Packaging Presentation	Number of Tablets
CLL Starting Pack	Each pack contains four weekly wallet blister packs: • Week 1 (14 x 10 mg tablets) • Week 2 (7 x 50 mg tablets) • Week 3 (7 x 100 mg tablets) • Week 4 (14 x 100 mg tablets)
Wallet containing 10 mg tablets	14 x 10 mg tablets
Wallet containing 50 mg tablets	7 x 50 mg tablets
Unit dose blister containing 10 mg tablets	2 x 10 mg tablets
Unit dose blister containing 50 mg tablet	1 x 50 mg tablet
Unit dose blister containing 100 mg tablet	1 x 100 mg tablet
Bottle containing 100 mg tablets	120 x 100 mg tablets

Not all pack sizes may be marketed.

Holder of the Certificate of Registration

AbbVie (Pty) Ltd

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Venclexta 50 mg: 51/26/0581

Venclexta 100 mg: 51/26/0582

Access to the corresponding Professional Information

For the professional information please email medicalinfo.za@abbvie.com

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