PROPOSED CLEAN PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

Schedule 4

SIRTURO® 20 mg tablets

SIRTURO® 100 mg Tablets

Bedaquiline

SIRTURO 100 mg tablets contains sugar: each tablet contains 145 mg of lactose (as monohydrate).

Read all of this leaflet carefully before you are given SIRTURO

- Keep this leaflet. You may need to read it again.
- Do not share SIRTURO with any other person.
- Ask your health care provider or pharmacist if you need more information or advice.

What is in this leaflet

1. What SIRTURO is and what it is used for
2. What you need to know before you take SIRTURO
3. How to take SIRTURO
4. Possible side effects
5. How to store SIRTURO
6. Contents of the pack and other information

1. What SIRTURO is and what it is used for

SIRTURO is a type of antibiotic. Antibiotics are medicines that kill bacteria that cause disease.

SIRTURO is used to treat tuberculosis (TB) when it has become resistant to other antibiotics.

This is called multi-drug resistant TB.

SIRTURO must always be taken together with other medicines for treating tuberculosis.

It is used in adults and children (5 years and over, who weigh atleast 15 kg).

2. What you need to know before you take SIRTURO

Do not take SIRTURO

- If you are hypersensitive (allergic) to bedaquiline or any of the other ingredients of SIRTURO (see above WHAT SIRTURO CONTAINS).
- You have a personal or family history of a heart problem called “congenital long QT syndrome”.
- You have a serious irregular heartbeat.
- You are using medicines that can cause a heart problem called “congenital long QT syndrome” and serious irregular heartbeat.
- You have severe liver problems.

Warnings and precautions

Tell your doctor, pharmacist or nurse before taking SIRTURO, if:

Take special care with SIRTURO:

- You have had an abnormal heart tracing (ECG) or heart failure.
- You have any other diseases, including HIV infection.
- You have kidney problems.
- You have a decreased thyroid gland function. This can be seen in a blood test.

Children and adolescents

Do not give SIRTURO to children (under 5 years of age) or weighing less than 15 kg. This is because it has not been studied in this age group.

Other medicines and SIRTURO

Always tell your healthcare professional if you are taking any other medicines.

The following are examples of medicines patients with multi-drug resistant tuberculosis may take and which may potentially interact with SIRTURO:

Medicine (name of the active substance)	**Purpose of the medicine**
rifampicin, rifapentine, rifabutin	to treat some infections like tuberculosis (antimycobacterial)
ketoconazole, fluconazole	to treat fungal infections (antifungals)
efavirenz, etravirine, lopinavir/ritonavir	to treat HIV infection (antiretroviral non-nucleoside reverse transcriptase inhibitors, antiretroviral protease inhibitors)
clofazimine	to treat some infections like leprosy (antimycobacterial)
carbamazepine, phenytoin	to treat epileptic fits (anticonvulsants)
St. John's wort (*Hypericum perforatum*)	an herbal product to relieve anxiety
ciprofloxacin, erythromycin, clarithromycin	to treat bacterial infections (antibacterials)

(This includes complementary or traditional medicines).

SIRTURO with food, drink and alcohol

- Take SIRTURO with food.
- Swallow the tablets whole with water.
- Do not drink alcohol while you are using SIRTURO.

Pregnancy and Breastfeeding

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking SIRTURO.

Mothers on SIRTURO should not breastfeed their infants.

Driving and using machines

You may feel dizzy after taking SIRTURO. If this happens don't drive or operate machinery.

SIRTURO 100 mg tablets contains lactose.

SIRTURO 100 mg tablets contains lactose (a type of sugar) which may have an effect on the control of your blood sugar if you have diabetes mellitus. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking SIRTURO 100 mg tablets.

3. How to take SIRTURO

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

Always take SIRTURO exactly as your doctor has instructed you.

You should check with your doctor or pharmacist if you are not sure.

The usual dose for Adults (18 years and older) is shown in table 1:

Table 1: Recommended Dosage of SIRTURO in Adult Patients

Table 1: Recommended Dosage of SIRTURO In Adult Patients	
Dosage Recommendation	
Weeks 1 and 2	**Weeks 3 to 24**
400 mg (4 of the 100 mg tablets OR 20 of the 20 mg tablets) orally **once daily**	200 mg (2 of the 100 mg tablets OR 10 of the 20 mg tablets) orally **three times per week** [a]
	After week 2, do not take a total dose of more than 600 mg SIRTURO in total during a 7-day period.

[a]= At least 48 hours between doses. For example, you may take SIRTURO on Monday, Wednesday and Friday every week from week 3 onwards.

The total duration of treatment with SIRTURO is 24 weeks. SIRTURO should be taken with food.

You may need to continue treatment beyond the 24 week course if you have extensive resistance to TB medicines in order to be cured. This may only be considered based on individual cases by your doctor.

You may need to keep taking your other medicines for TB for longer than 24 weeks. Check with your doctor or pharmacist.

Do not stop early because your TB infection could get worse or become resistant to SIRTURO and other medicines. If you have the impression that the effect of SIRTURO is too strong or too weak, tell your doctor or pharmacist.

SIRTURO must always be taken together with other medicines for treating TB. Your doctor will decide which other medicines you should take with SIRTURO.

Take SIRTURO with food.

The recommended dosage of SIRTURO in Children (5 years to less than 18 years of age) is based on body weight and shown in Table 2.

Table 2: Recommended Dosage of SIRTURO in Paediatric Patients (5 years to less than 18 years of age)

Body Weight	Dosage Recommendation	
	Weeks 1 to 2	**Weeks 3 to 24[a]**
Greater than or equal to 15 kg to less than 30 kg	200 mg **(2 of the 100 mg tablets OR 10 of the 20 mg tablets)** orally once daily	100 mg **(1 of the 100 mg tablets OR 5 of the 20 mg tablets)** orally three times per week
Greater than or equal to 30 kg	400 mg orally once daily **(4 of the 100 mg tablets OR 20 of the 20 mg tablets)** orally once daily	200 mg **(2 of the 100 mg tablets OR 10 of the 20 mg tablets)** orally three times per week

a=At least 48 hours between doses. For example, you may take SIRTURO on Monday, Wednesday and Friday every week from week 3 onwards.

The total duration of treatment with SIRTURO is 24 weeks. SIRTURO should betaken with food.

Taking this medicine:

SIRTURO 20 mg tablet

- Always take SIRTURO with food.
  - **Can swallow whole tablets:**
    - Swallow tablets whole with water **or**
    - Split tablets in half at the score line in the middle of the tablet into 2 equal parts of 10 mg each, then swallow both half parts of SIRTURO with water.

- **Cannot swallow whole tablets:**
    - Use 1 teaspoon (5ml) of water for a maximum of 5 SIRTURO tablets. Mix well in a drinking cup.
        - Swallow mixture immediately, **or**
        - To help with taking SIRTURO you may add at least 1 more teaspoon (5ml) of beverage or soft food and mix. Beverages such as water, milk products, apple juice, orange juice, cranberry juice or carbonated beverages may be used. Soft foods such as yogurt, apple sauce, mashed banana or porridge may be used.
        - Swallow mixture immediately.
        - Make sure no remaining medicine is left in the drinking cup, rinse with beverage or soft food and swallow mixture immediately.
        - If you need more than 5 tablets of SIRTURO to get your total dose, repeat the steps above until you reach your prescribed dose.

or

- Crush tablets and mix with soft food. Soft food such as yogurt, apple sauce, mashed bananas or porridge may be used. Swallow mixture immediately. Make sure no remaining medicine is left in container, add more soft food and swallow mixture immediately.

- SIRTURO 20 mg tablets may also be given through certain feeding tubes by your healthcare provider.

SIRTURO 100 mg tablet

Always take SIRTURO with food. Swallow tablets whole with water.

Do not skip doses

Skipping doses or not completing the full course of therapy may:

- make your treatment ineffective and your TB could get worse and
- increase the chance that the bacteria will become resistant to SIRTURO. This means your disease may not be treatable by SIRTURO or other medicines in the future.

If you take more SIRTURO than you should

If you take more SIRTURO than you should, talk to your doctor straight away. Take the medicine pack with you.

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

If you forget to take SIRTURO

During the first two weeks

- Do not take a double dose to make up for a forgotten dose.
- Take the next dose as usual.

From week 3 onwards

- Take the missed dose as soon as possible and continue taking SIRTURO on the 3 times a week schedule.
- Make sure that there is at least 24 hours between taking the missed dose and the next scheduled dose.
- Do not take more than the prescribed weekly dose in a 7-day period.

If you have missed a dose and you are not sure what to do, talk to your doctor or pharmacist.

If you stop taking SIRTURO:

Do not stop taking SIRTURO without first talking to your doctor. If you stop taking SIRTURO earlier than you should, your TB infection could get worse or become resistant to SIRTURO and other medicines.

If you have further questions on the use of SIRTURO, ask your doctor, pharmacist or nurse.

4. Possible side effects

SIRTURO can have side effects.

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

Serious heart rhythm changes (QT prolongation):

Tell your healthcare provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you faint.

Liver problems (hepatotoxicity):

Call your healthcare provider right away if you have unexplained symptoms such as nausea or vomiting, stomach pain, fever, weakness, itching, unusual tiredness, loss of appetite, light coloured bowel movements, dark coloured urine, yellowing of your skin or the white of your eyes (jaundice).

Frequent side effects:

- headache
- joint pain
- feeling dizzy

- feeling sick (nausea) or being sick (vomiting).
- diarrh**o**ea
- increased liver enzymes shown in blood tests
- aching muscles, tender or weak muscles, not caused by exercise
- abnormal ECG called “QT prolongation”

Additional side effects in children

- Increased liver enzymes (shown in blood tests).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via “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 SIRTURO.

Alternatively, you may report side effects experienced with SIRTURO directly to Janssen Pharmaceutica (see section ‘Holder of the Certificate of Registration’ for contact details or visit www.janssen.com).

5 How to store SIRTURO

- Store at or below 25 °C.
- Store SIRTURO in the original container in order to protect from light.
- Do not use SIRTURO after the expiry date which is stated on the carton after “EXP”. The expiry date refers to the last day of the month.
- Store all medicines out of reach of children
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6 Contents of the pack and other information

What SIRTURO contains:

- The active substance is bedaquiline.

SIRTURO 20 mg tablets.

- Each SIRTURO tablet contains bedaquiline fumarate equivalent to 20 mg of the active substance bedaquiline.
- The other ingredients are: microcrystalline cellulose, crospovidone, colloidal anhydrous silica, hypromellose, polysorbate 20, sodium stearly fumarate.

SIRTURO 100 mg tablets

- Each SIRTURO tablet contains bedaquiline fumarate equivalent to 100 mg of the active substance bedaquiline.

- The other ingredients are colloidal anhydrous silica, croscarmellose sodium, hypromellose 2910, lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose and polysorbate 20.

What SIRTURO looks like and contents of the pack

SIRTURO 20 mg tablets.

Uncoated, white to almost white oblong tablet with score line on both sides, debossed with “2” and “0” on one side and plain on other side.

The tablets may be split along the break-mark into 2 halves to facilitate dosing.

60 tablets packaged in a white high-density polyethylene (HDPE) bottle with a child resistant polypropylene (PP) closer with induction seal liner.

SIRTURO 100 mg tablets

Uncoated, white to almost white round biconvex tablet, 11 mm in diameter, with debossing “T” over ‘207” on one side and “100” on the other side.

188 tablets packaged in a white high density polyethylene (HDPE) bottle

with a child resistant polypropylene (PP) closer with induction seal liner.

OR

An aluminium/aluminium blister with heat seal coating. Each packaging contains one or more blister(s) of six (6) tablets.

Holder of certificate of registration

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This leaflet was revised in

04 July 2023

Registration number

SIRTURO 20 mg tablets.

56/20.2.3/0799

SIRTURO 100 mg tablets

47/20.2.3/1182

Access to the corresponding Professional Information

Included in the carton, accompanying this patient information leaflet.