

<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd		Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i>	Each film-coated tablet contains 50 mg delamanid.

PROPOSED CLEAN PATIENT INFORMATION LEAFLET – Feb 2020

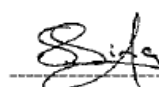
SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

DELTYBA™ (film-coated tablets)

Read this leaflet carefully before you start using DELTYBA.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- **DELTYBA** 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.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

1. WHAT DELTYBA CONTAINS:

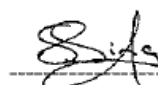
Each **DELTYBA** film-coated tablet contains 50 mg delamanid.

Contains sugar (Lactose monohydrate) 100 mg

Contains antioxidant (All-*rac*- α -tocopherol)

The other ingredients are: carmellose calcium, cellulose microcrystalline, hypromellose phthalate, magnesium stearate, povidone (K-25), silica colloidal hydrated, sodium starch glycolate (type A)

Film-coat {Hypromellose, iron oxide yellow (E172), macrogol 8000, titanium dioxide, talc}.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

2. WHAT DELTYBA IS USED FOR:

DELTYBA belongs to a group of antimicrobials, used in the treatment of tuberculosis in the lung caused by mycobacteria that are not killed by the most commonly used antimicrobials to treat tuberculosis.

3. BEFORE YOU TAKE DELTYBA:

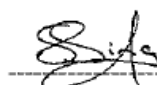
Do not take DELTYBA:

- If you have an allergy to delamanid or any of the ingredients in the **DELTYBA** tablets.
- If you have severe liver disease.
- If you have heart rhythm disturbances (slow or fast rate or palpitations)
- If you take other medicines that prolong the QT time on your electrocardiogram to unsafe values.
- If you have heart failure.
- If you have congenital QT prolongation.
- If you have very low levels of albumin, in the blood.
- If you are taking medicines that strongly induce a certain liver enzyme called "CYP 450 3A4" (e.g Carbamazepine)

Take special care with DELTYBA:

Tell your doctor if you have any of the following conditions:

Before you start taking **DELTYBA**, and during the treatment, your doctor may check your heart's electrical activity using an ECG (electrocardiogram) machine (electrical recording of



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

the heart).

Your doctor may also perform a blood test to check the concentration of some minerals and proteins which are important for the function of your heart.

Tell your doctor if you have one of the following conditions:

- you have been told that you have reduced levels of albumin, potassium, magnesium or calcium in the blood
- you have been told that you have heart problems, for example a slow heart rhythm (bradycardia) or have a history of heart attack (myocardial infarction)
- if you have a condition called congenital long QT syndrome or have a serious heart disease or problems with heart rhythm.
- you have liver disease or kidney disease.
- you have HIV.

Taking DELTYBA with food and drink:

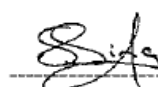
DELTYBA can be taken during or just after a meal. Swallow the tablets with water.

Pregnancy and breast-feeding:

Safety in pregnancy and breastfeeding women has not been established.

Pregnancy:

You must not take **DELTYBA** during pregnancy.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

If you are a woman who could become pregnant during treatment with **DELTYBA**, you must use an effective method of contraception for the duration of treatment to avoid becoming pregnant.

Breast-feeding:

It is not known whether **DELTYBA** passes into breast milk. You should not breastfeed your baby if you are on treatment with **DELTYBA**.

If you are pregnant or breast-feeding your baby while taking DELTYBA, please consult your doctor, pharmacist or other health care professional for advice.

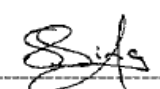
Driving and using machinery:

DELTYBA may have an influence on your ability to drive and use machines. Make sure you know how you react to **DELTYBA** before you drive, use machines, or do anything else that could be dangerous.

Important information about some of the ingredients of DELTYBA tablets:

DELTYBA tablets contain lactose. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking **DELTYBA**.

Taking other medicines with DELTYBA:

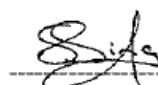


<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

Tell your doctor, pharmacist or healthcare professional about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements.

Especially tell your doctor, pharmacist or healthcare professional if you take:

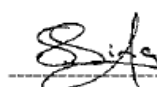
- if you are taking medicines to treat an abnormal heart rhythm (e.g. amiodarone, disopyramide, dofetilide, ibutilide, procainamide, quinidine, hydroquinidine, sotalol).
- if you are taking medicines to treat psychoses (e.g. phenothiazines, sertindole, sultopride, chlorpromazine, haloperidol, mesoridazine, pimozone, or thioridazine) or depression.
- if you are taking certain antimicrobial medicines (e.g. erythromycin, clarithromycin, moxifloxacin, sparfloxacin, bedaquiline or pentamidine,
- if you are taking triazole antifungal medicines (e.g. fluconazole, itraconazole, voriconazole).
- if you are taking certain medicines to treat allergic reactions (e.g. terfenadine, astemizole, mizolastine).
- If you are taking certain medicines to treat malaria (e.g. halofantrine, quinine, chloroquine, artesunate/amodiaquine, dihydroartemisinin/piperaquine)
- if you are taking any of the following: cisapride (used to treat stomach disorders), droperidol (used against vomiting and migraine), domperidone (used against nausea and vomiting), diphemanil (used to treat stomach disorders or excessive sweating), probucol (lowers the level of cholesterol in the bloodstream), levomethadyl or methadone (used for the treatment of opiate addiction), vinca alkaloids (anti-cancer medicines), or arsenic trioxide (used to treat certain types of leukaemia).



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd		Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i>	Each film-coated tablet contains 50 mg delamanid.

- if you are taking HIV-medicines containing lopinavir/ritonavir or saquinavir.
- You may be more at risk for dangerous changes of the heart rhythm

Keep a complete list of all the medicines that you are taking. Make a new list when medicines are added or stopped. Give copies of this list to your doctor, pharmacist or healthcare professional **EVERY TIME** you visit them or fill a prescription.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTIBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

4. HOW TO TAKE DELTYBA:

Always take **DELTIBA** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Adults:

The usual dose for adults of **DELTIBA** is two 50 mg tablets taken twice a day (morning and evening) as advised by your doctor. The tablets should be taken during or just after a meal.

Swallow the tablets with water.

If you have the impression that the effect of **DELTIBA** is too strong or too weak, talk to your doctor or pharmacist.

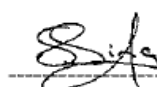
If you take more DELTYBA tablets than you should:

In the event of an overdose, consult your doctor or pharmacist. If neither is available, seek assistance at the nearest hospital or poison control centre.

Remember to take the pack with you so that it is clear what medicine you have taken.

If you forget to take your DELTYBA:

It is important that you do not miss any doses. If you miss a dose of **DELTIBA**, take it as soon as possible and then take your next scheduled dose at its regular time. If it is almost time for your next dose, do not take the missed dose. Wait and take the next dose at the regular time. Do not double the next dose.

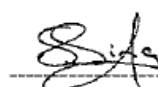


<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTIBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

Effects when treatment with DELTYBA is stopped:

You should not stop treatment unless your doctor instructs you to. When your **DELTIBA** supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of bacteria in your blood may increase if the medicine is stopped for even a short time. The bacteria may develop resistance to **DELTIBA** and become harder to treat.

Do not share medicines prescribed for you with others.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTIBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

5. POSSIBLE SIDE-EFFECTS:

DELTIBA can have side-effects.

Not all side effects reported for **DELTIBA** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **DELTIBA**, please consult your doctor, pharmacist or other healthcare professional for advice.

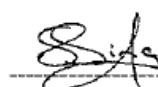
If any of the following happens, stop taking **DELTIBA** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Sudden swelling of the skin hands, face, lips, mouth, tongue and throat or mucous membranes [(e.g. throat or tongue)] with difficulty breathing and/or itching and rash.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to DELTYBA.

- Serious liver problems. The following are signs of the liver problems:
 - Yellow discolouration of the skin and the white part of your eyeballs
 - Darkening of your urine
 - Your bowel movements turn lighter in colour
 - You feel sick to your stomach (nausea)
 - You have stomach pain

You may need urgent medical attention or hospitalisation.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

Tell your doctor immediately or go to casualty department at your nearest hospital if you notice any of the following:

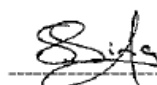
- changes in the way you heart beats, for example, if you notice it beating faster (palpitations)
- Signs of QT prolongation:
 - unexplained fainting
 - seizures
 - fluttering feelings in the chest

These are all serious side effects. You may need urgent attention.

Tell your doctor if you notice any of the following:

Frequent:

- Decreased appetite
- Sensations of irregular and/or forceful beating of the heart
- Vomiting
- Nausea
- Diarrhoea
- Stomach pain
- Headache
- A tingling, burning or pricking sensation or numbness of the skin (paresthesia)
- Shaking (tremor)
- Dizziness

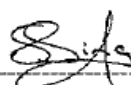


<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

- Hearing a persistent sound in your ear when no sound exists (tinnitus)
- Joint or muscle pain
- Weakness or lack of energy
- Difficulties with falling or staying asleep (Insomnia)
- Increase in immature red blood cells (Reticulocytosis)
- Low blood potassium level (Hypokalaemia)
- Increased blood uric acid level (Hyperuricaemia)
- Coughing up blood
- Changes found in investigations (electrocardiogram, ECG) of the heart

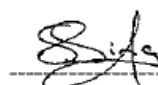
Less frequent:

- Anaemia
- Increase of certain white blood cells (eosinophilia)
- Increased blood triglycerides
- Psychotic disorder
- Agitation
- Anxiety
- Depression
- Restlessness
- Nerve damage causing numbness or pain (burning) or tingling feeling in hands or feet
- Drowsiness



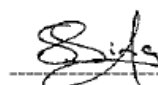
<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

- Reduced sensation
- Dry eye
- Decreased tolerability of the eyes for bright light
- Ear pain
- Increase of blood pressure (hypertension)
- Decrease of blood pressure (hypotension)
- Bruising
- Hot flushes
- Shortness of breath
- Cough
- Pain in the mouth or throat
- Throat irritation
- Dry throat
- Runny nose
- Gastritis
- Constipation
- Indigestion
- Dermatitis
- Hives
- Itching
- Papules (small skin elevations)



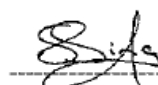
<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

- Rash
- Acne
- Increased sweating
- A bone disease called osteochondrosis
- Muscular weakness
- Pain in bones
- Flank pain
- Pain in arms or legs
- Blood in urine
- Fever
- Chest pain
- Feeling unwell
- Chest discomfort
- Foot, leg or ankle swelling
- Increased values for blood investigations for the hormone cortisol
- Shingles
- Oral thrush
- Yeast infection of the skin (tinea versicolor)
- Low white blood cell count (leukopenia)
- Low blood platelets count (thrombocytopenia)
- Dehydration



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

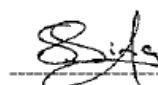
- Low blood calcium level
- High blood cholesterol level
- Aggression
- Paranoia
- Panic attacks
- Adjustment disorder with depressed mood
- Neurosis
- Feeling of emotional and mental discomfort
- Mental aberration
- Problems with sleeping
- Increase of libido
- Lethargy
- Balance disorder
- Regional pain
- Allergic conjunctivitis
- Heart rhythm problems
- Swallowing problems
- Abnormal feeling in the mouth
- Tenderness in the abdomen
- Hair loss
- Itchy or red skin including around the hair roots.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

- Urine retention
- Painful urination
- Increased need to urinate at night
- Feeling hot
- Abnormal values for blood investigations related to coagulation (prolonged APPT)
- Abnormal blood values related to the function of the liver, biliary system or pancreas
- Decreased values for blood investigations for the hormone cortisol
- Increased blood pressure

If you notice any side effects not mentioned in this leaflet, please inform the medical practitioner or pharmacist.



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

6. STORAGE AND DISPOSAL OF DELTYBA:

Store at or below 30 °C. Store in the original container. Protect from light. Do not remove from carton until required for use.

KEEP OUT OF REACH AND SIGHT OF CHILDREN

Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist.

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

Do not remove the tablets from the blister strips until required for use.

7. PRESENTATION OF DELTYBA:

DELTYBA film-coated tablets is supplied as follows:

The tablets are packaged in silver aluminum/aluminum foil blisters. Each blister strip contains 8 separately blistered tablets. 6 blister strips are placed into a carton. Pack size 48's.

8. IDENTIFICATION OF DELTYBA:

DELTYBA 50 mg film-coated tablets are round, and yellow, debossed with "DLM" and "50" on one side.

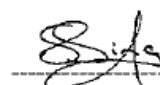
9. REGISTRATION NUMBER/REFERENCE NUMBER:

52/20.2.3/0460

10. NAME AND BUSINESS ADDRESS OF REGISTRATION HOLDER:

Mylan (Pty) Ltd

Building 6, Greenstone Hill Office Park



<i>Applicant/PHRC:</i>	Mylan (Pty) Ltd	Date of approval: 25 March 2019 SRN update: May 2019 PV update: January 2020 Minor changes as per Jana: February 2020
<i>Product proprietary name:</i>	DELTYBA	<i>Dosage form and strength:</i> Each film-coated tablet contains 50 mg delamanid.

<p>Emerald Boulevard</p> <p>MODDERFONTEIN, 1645</p> <p>Republic of South Africa</p>
<p>11. DATE OF PUBLICATION:</p> <p>25 March 2019</p>

