APPROVED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S5

DEMETEV (100 µg/ml) Concentrate for solution for Infusion

Dexmedetomidine hydrochloride

Sugar free

Read all of this leaflet carefully before you are given DEMETEV:

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet:

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

1. WHAT DEMETEV IS AND WHAT IT IS USED FOR:

DEMTREX contains an active substance called dexmedetomidine which belongs to a medicine group called sedatives. It is used to provide sedation (a state of calm, drowsiness or sleep) for adult patients in hospital intensive care

settings or awake sedation during different surgical procedures.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE DEMETEV:

DEMETEV should not be administered to you:

- if you are hypersensitive (allergic) to dexmedetomidine or any of the other ingredients of DEMETEV (listed in **section 6**)
- if you have a serious condition resulting from the presence of harmful microorganisms in the blood or other tissues and the body's response to their presence, potentially leading to the malfunctioning of various organs, shock, and death (sepsis)
- if you are an unstable trauma patient
- if you have low blood volume, for example after bleeding
- if you have uncontrolled heart failure
- if you have liver failure
- if you have some disorders of heart rhythm
- if you have recently had a stroke or other serious condition affecting blood supply to the brain
- if you have very low blood pressure which does not respond to treatment (uncontrolled low blood pressure).

Warnings and precautions:

Tell your doctor, before being given DEMETEV, if any of the following apply to you:

- if you have an abnormally slow heart rate (either due to illness or high levels of physical fitness) as it may increase the risk for cardiac arrest

- if you have low blood pressure
- if you are known to have heart disorders
- if you have had brain surgery, head or spinal cord injury
- if you have severe liver problems
- if you have ever developed a serious fever after some medicines, especially anaesthetics.

Children and adolescents:

DEMETEV should not be used in children under 18 years of age.

Other medicines and DEMETEV:

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

The following medicines may enhance the effect of DEMETEV:

- Medicines that help you sleep or cause sedation.
- Strong pain medicines (e.g. opioids such as morphine, codeine).
- Other anaesthetic medicines (e.g. sevoflurane, isoflurane).

If you are using medicines that lower your blood pressure and heart rate, co-administration with DEMETEV may enhance this effect.

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for

advice before DEMETEV is administered to you.

DEMETEV should not be administered to you if you are pregnant or breastfeeding your baby.

Driving and using machines:

DEMETEV has major impact on the ability to drive and use machines. After you have been given DEMETEV you must not drive, operate machinery, or work in dangerous situations until the effects are completely gone. Ask your doctor when you can start doing these activities again and when you can go back to this kind of work. It is not always possible to predict to what extent DEMETEV may interfere with your daily activities. You should ensure that you do not engage in driving a vehicle or use machines until you are aware of the measure to which DEMETEV affects you.

DEMETEV contains sodium:

DEMETEV contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially sodium-free.

3. HOW TO TAKE DEMETEV:

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

You will not be expected to give yourself DEMETEV. It will be given to you by a person who is qualified to do so.

DEMETEV is administered to you by a doctor or nurse in hospital intensive care.

DEMETEV is administered to you by a doctor or a nurse prior to and/or during surgical procedures requiring sedation, i.e. procedural/awake sedation.

Your doctor will decide on a suitable dose for you. The amount of DEMETEV depends on your age, size, general condition of health, the level of sedation needed and how you respond to the medicine. Your doctor will monitor your heart and blood pressure during the treatment.

DEMETEV is given to you as an infusion (drip) into your veins.

After sedation/wake-up:

- The doctor will keep you under medical supervision for some hours after the sedation to make sure that you feel well.
- You should not go home unaccompanied.
- Medicines to help you sleep cause sedation or strong painkillers may not be appropriate for some time after you have been given DEMETEV. Talk to your doctor about the use of these medicines and about the use of alcohol.

If you have been given more DEMETEV than you should:

Since a healthcare provider will administer DEMETEV, he/she will control the dosage. However, in the event of over dosage your doctor will manage the over dosage.

4. POSSIBLE SIDE EFFECTS:

DEMETEV can have side effects.

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

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

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to DEMETEV. You may need urgent medical attention or hospitalisation.

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

- chest pain or heart attack
- slow heart rate
- low or high blood pressure
- change in breathing pattern or stopping breathing
- stroke or brain bleeding.

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- low or high blood sugar
- feeling agitated
- fast heart rate
- nausea, vomiting or dry mouth

- symptoms after stopping the medicine
- high temperature.

Less frequent side effects:

- a serious electrolyte disorder characterised by an imbalance in the body's acid-base balance
- low albumin level in the blood
- hallucinations
- reduced heart function, cardiac arrest
- shortness of breath
- swelling of the stomach
- thirst, the medicine is not effective enough.

Side effects with unknown frequency:

- loss of volume of fluid from the body, such as that which occurs during bleeding
- low calcium levels in blood
- build-up of acid in the bloodstream
- a condition that develops when your blood lacks enough healthy red blood cells or haemoglobin
- heart disorders such as irregular, rapid heart rate, heart rate greater than 100 beats/min (bpm)
- breathing disorder after surgery
- an absence of enough oxygen in the tissues to sustain bodily functions
- build-up of fluid between the tissues that line the lungs and the chest

- excess fluid in the lungs
- wheezing, abnormal slow breathing
- passing abnormal amount of urine
- fever, chills, swelling of the legs and arms
- bleeding after surgery
- decreased urine output
- abdominal swelling, swelling, pain, shivering or shaking, very high fever
- heart disorders such as blood pressure fluctuation, increased high blood pressure, abnormal heart rhythm, chest pain, drop in blood pressure upon standing, extra, abnormal heartbeats that begin in one of the heart's two lower chambers, partial or complete interruption of impulse transmission from the atria to the ventricles
- abnormal sensation, typically tingling or pricking (‘pins and needles’), muscle weakness of paralysis, speech disorder
- headache, intense, typically intermittent pain along the course of a nerve, especially in the head or face, inflammation of a nerve
- dysfunction of one or more peripheral nerves, typically causing numbness or weakness
- stomach pain, diarrhoea, belching, ulcer on mucous membranes
- liver disorders such as increased liver enzymes and inflammation of the liver (jaundice)
- condition that occurs when the lungs cannot remove all of the carbon dioxide the body produces, diabetes mellitus
- reduced or increased potassium levels
- very low levels of protein in the blood, impaired renal function

- blood disorders such as blood clotting, a condition affecting the blood's ability to clot and stop bleeding, collection of blood outside of a blood vessel
- low or abnormal number of platelets in the blood, a high level of white blood cells in the blood
- anxiety, confusion, delirium, depression, illusion, nervousness
- renal disorders (blood in urine, renal failure, urine retention)
- increased need to pass urine
- infections, fungal infections
- lung disease, coughing, increased sputum, too much carbon dioxide in your bloodstream, high-pitched, wheezing sound caused by disrupted airflow, infection of the lungs, coughing up blood, collapsed lung
- inflammation of the tissues that line the lungs and chest cavity, throat infection, type of chronic obstructive pulmonary disease (emphysema), bronchospasm, condition in which the lungs cannot take in sufficient oxygen or expel sufficient carbon dioxide to meet the needs of the cells of the body
- rash or increased sweating
- any abnormal condition of the blood vessels (arteries and veins)
- double vision, abnormal vision, presence of perceived flashes of light in the field of vision.

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 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 DEMETEV.

5. HOW TO STORE DEMETEV:

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Store at or below 25 °C.

Store in the original package in order to protect from light.

After dilution:

Chemical and physical in-use stability has been demonstrated for 24 hours at 25 °C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to the use are the responsibility of the user and would not normally be longer than 24 hours at 2 ° to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

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

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 DEMETEV contains:

The active substance is dexmedetomidine hydrochloride.

Each 1 ml of concentrate for solution for infusion contains dexmedetomidine hydrochloride equivalent to 100 micrograms of dexmedetomidine.

Each 2 ml vial contains dexmedetomidine hydrochloride equivalent to 200 micrograms of dexmedetomidine.

Each 4 ml vial contains dexmedetomidine hydrochloride equivalent to 400 micrograms of dexmedetomidine.

Each 10 ml vial contains dexmedetomidine hydrochloride equivalent to 1000 micrograms of dexmedetomidine

The other ingredients are sodium chloride and water for injection.

What DEMETEV looks like and contents of the pack:

DEMETEV is a clear colourless solution.

DEMETEV 200 micrograms/2 ml: Type I transparent, sulphur treated, glass vial (3 ml or 2R) closed with grey chlorobutyl rubber stopper and green-blue polypropylene cover.

DEMETEV 400 micrograms/4 ml: Type I transparent, sulphur treated, glass vial (6R) closed with grey chlorobutyl rubber stopper and white polypropylene cover.

DEMETEV 1000 micrograms/10 ml: Type I transparent, sulphur treated, glass vial (10R) closed with grey chlorobutyl rubber stopper and white polypropylene cover.

Pack sizes: 1, 5, 25 x 2 ml; 4 x 4 ml and 4 x 10 ml.

Not all pack sizes may be marketed.

Holder of Certificate of Registration:

Teva Pharmaceuticals (Pty) Ltd

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The following information is intended for healthcare professionals only:

DEMETEV 100 micrograms/ml concentrate for solution for infusion

Method of administration

DEMETEV should be administered by healthcare professionals skilled in the management of patients requiring intensive care or in the anaesthetic management of patients in the operating room. It must be administered only as a diluted intravenous infusion using a controlled infusion device.

Preparation of solution

DEMETEV can be diluted in glucose 50 mg/ml (5 %), Ringers, mannitol or sodium chloride 9 mg/ml (0,9 %) solution for injection to achieve the required concentration of either 4 micrograms/ml or 8 micrograms/ml prior to administration. Please see below in tabulated form the volumes needed to prepare the infusion.

In the case the required concentration is 4 micrograms/ml:

Volume of DEMETEV 100 micrograms/ml concentrate for solution for infusion	**Volume of diluent**	**Total volume of infusion**
2 ml	48 ml	50 ml
4 ml	96 ml	100 ml
10 ml	240 ml	250 ml
20 ml	480 ml	500 ml

In the case the required concentration is 8 micrograms/ml:

Volume of DEMETEV 100 micrograms/ml concentrate for solution for infusion	**Volume of diluent**	**Total volume of infusion**
4 ml	46 ml	50 ml
8 ml	92 ml	100 ml
20 ml	230 ml	350 ml
40 ml	460 ml	500 ml

The solution should be shaken gently to mix well. DEMETEV should be inspected visually for particulate matter and discoloration prior to administration. DEMETEV has been shown to be compatible when administered with the following intravenous fluids and medicines: Lactated Ringers, 5 % glucose solution, sodium chloride 9 mg/ml (0,9 %) solution for injection, mannitol 200 mg/ml (20 %), thiopental sodium, etomidate, vecuronium bromide, pancuronium bromide, succinylcholine, atracurium besylate, mivacurium chloride, rocuronium bromide, glycopyrrolate bromide, phenylephrine HCl, atropine sulfate, dopamine, noradrenaline, dobutamine, midazolam, morphine sulfate, fentanyl citrate, and a plasma-substitute. ***Shelf life*** Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to the use are the responsibility of the user and would not normally be longer than 24 hours at 2 ° to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.	