MODULE 1.3.2 – Patient Information Leaflet

Product proprietary name:	***Accord Midazolam 5mg/5ml; 15mg/3 ml; 50mg/10 ml***
Dosage form and strength:	***5mg/5ml; 15mg/3 ml; 50mg/10 ml Midazolam Injection***
Applicant/PHCR:	***Accord Healthcare (Pty) Ltd***

SCHEDULING STATUS:

S5

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:

Accord Midazolam 5 mg/5 ml solution for injection

Accord Midazolam 15 mg/3 ml solution for injection

Accord Midazolam 50 mg/10 ml solution for injection

Read all of this leaflet carefully before you start using Accord Midazolam

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

1. WHAT ACCORD MIDAZOLAM CONTAINS:

Accord Midazolam 5 mg/5 ml: contains 5 mg midazolam as the hydrochloride, per ampoule.

Accord Midazolam 15 mg/3 ml: contains 15 mg midazolam as the hydrochloride, per ampoule.

Accord Midazolam 50 mg/10 ml: contains 50 mg midazolam as the hydrochloride, per ampoule.

Excipients:

hydrochloric acid 37 %, sodium chloride, sodium hydroxide and water for injection.

2. WHAT ACCORD MIDAZOLAM IS USED FOR:

Accord Midazolam belongs to a group of medicines known as benzodizepines. These are short-acting medicines that are used to induce sleep (a very relaxed state of calm, drowsiness or sleep) and relieves anxiety and muscle tension.

It is used:

- To make you drowsy before a diagnostic or surgical procedure that will be carried out under a local

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anaesthesia.

- As a pre-medication (medicine used to cause relaxation, and drowsiness, before putting you under anaesthesia).
- As an aid when using inhalation anaesthesia or intravenous anaesthesia.
- Long-term use in Intensive Care Units (ICU).

Accord Midazolam is only used for this purpose when the patient is in severe stress.

3. BEFORE YOU RECEIVE ACCORD MIDAZOLAM:

Do not receive Accord Midazolam if:

- You are hypersensitive to midazolam, any of the other ingredients mentioned in this leaflet or any other benzodiazepine medicine such as diazepam or nitrazepam.
- You are pregnant or breast-feeding
- You have difficulty breathing
- You have liver damage
- You suffer from shortness of breath while sleeping
- You suffer from myasthenia gravis.

Take special care with Accord Midazolam:

Please inform your doctor if you have any of the following, as a dosage reduction might be needed:

- If you are over 60 years of age
- If you are debilitated (an illness that makes you weak and short of energy)
- If you have a long-term illness (chronic illness) such as kidney, lung, liver or heart problems
- If you have obstructive pulmonary disease (a lung disease wherein the airways in your lungs are blocked resulting in difficulty breathing).
- If you receive Accord Midazolam during labour and delivery, as a single high dose of Accord Midazolam can result in your lungs collapsing, irregular heart rate in the unborn child, a poor sucking reflex in the baby and could result in the baby's body temperature dropping to a very low degree.

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Accord Midazolam should be used only in places where revival facilities are available, as intravenous administration of Accord Midazolam may weaken the heart muscle contraction and cause difficulty in breathing.

Accord Midazolam should not be used for routine intravenous induction in children under the age of 7 years. Spontaneous reactions such as hyperactivity, irritability, uncontrollable muscle movements have occurred. If any of these do occur, your doctor will monitor and adjust the dose accordingly.

Abrupt discontinuation of a prolonged intravenous dose of Accord Midazolam should be avoided, as withdrawal symptoms can occur. Your doctor will always slowly reduce your dose before ending your treatment.
Accord Midazolam should not be used for prolonged periods of time, as abuse and dependence to Accord Midazolam can occur, especially in patients with a history of alcohol and medicine abuse.
Once dependence has occurred, discontinuing use of Accord Midazolam will result in withdrawal symptoms such as headaches, muscle pain, anxiety, tension, restlessness, confusion and irritability.
In severe cases the following symptoms can occur: numbness, pins and needles of the hands and feet, sensitivity to light, noise and physical contact, seeing images or hearing sounds that don't exist, and uncontrollable shaking.

Pregnancy and breastfeeding:

Safety in pregnancy and lactation has not been established.
Accord Midazolam has been shown to cross the placenta and enter the blood circulation of the unborn child, and therefore should not be used in pregnant women.
Accord Midazolam passes into breast milk and should not be administered to breastfeeding mothers.
Tell your doctor if you become pregnant while using this medicine.

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

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Driving and using machinery:

Since Accord Midazolam can cause drowsiness and sedation, you should not drive a vehicle or operate any

4. HOW ACCORD MIDAZOLAM IS ADMINISTERED:

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

Your doctor will tell you how long your treatment with Accord Midazolam will last. If you have the impression that the effect of Accord Midazolam is too strong or too weak, tell your doctor or pharmacist.

Accord Midazolam is a potent sleeping medicine which requires slow administration and individualised dosing, and will always be administered by a healthcare professional. Your doctor will determine how much of Accord Midazolam you will require based on your age, weight, other medicines you are taking, and the reason why you are being treated. If you are elderly (adults over 60 years) and suffer from a heart or lung function problem, weakness or long-term illnesses, your doctor will adjust your dosage in relation to your health condition.

Your treatment will always start with the lowest possible dose. However, if you require more Accord Midazolam, your doctor will increase your dosage accordingly.

Basal sedation (inducing drowsiness)

Intravenous (injection into the vein) administration:

Intravenous injections must be given slowly (approximately 1 mg in 30 seconds for sedation). The medicine takes effect in about two minutes after the injection is given.

For basal sedation in procedures performed under local anaesthesia:

In adults below the age of 60, the initial dose is 2,5 mg (0,04 mg/kg) 5-10 minutes before the beginning of the procedure. Further doses of 1 mg may be given as necessary. A total dose greater than 5 mg is not usually necessary to reach the desired endpoint.

In adults over 60 years, very weak, or chronically ill patients, the initial dose will be reduced to 1 to 1,5 mg and given 5-10 minutes before the beginning of the procedure. Further doses of 0,5 to 1,0 mg may be given as necessary. Total doses greater than 3,5 mg are not usually necessary.

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Pre-medication before an operation:

Intramuscular administration (injecting into a muscle):

Pre-medication with Accord Midazolam given shortly before an operation causes you to sleep or feel drowsy.

Adults below the age of 60:

0,07-0,1 mg/kg body weight given intramuscularly according to the general condition of the patient. The usual dose is about 5 mg.

Children:

(between ages 1 and 15) proportionately higher doses are required than in adults in relation to bodyweight. The dose range from 0,08 to 0,20 mg/kg body weight has been shown to be effective and safe. These doses should be administered into a large muscle mass about 30 to 60 minutes before induction of anaesthesia.

In adults over 60 years, who are very weak and have a long-term illness:

0,025-0,05 mg/kg bodyweight given intramuscularly. The usual dose is 2 to 3 mg.

Induction and maintenance of anaesthesia:

Intravenous injection:

Induction: intravenous injections must be given slowly (approximately 2,5 mg in 10 seconds for induction of anaesthesia). A deep level of sleep is generally achieved after 2-3 minutes. In non pre-medicated adults below the age of 60, the dose may be higher (0,3 to 0,35 mg/kg body weight), but a total dose greater than 20 mg is usually not necessary. Lower doses will be required in adults over 60 years of age, who are very weak or have long-term illnesses

Maintenance:

Intravenous continuous infusion:

The maintenance dose usually ranges from 0,03 to 0,1 mg/kg/hr when used in combination with other medicines known as narcotics or ketamines. In high-risk surgical patients, adults over 60 years, very weak and ill patients, lower doses will be required.

Sedation in intensive care units (ICU):

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Intravenous sedation in ICU:

For sedation in ICU, your doctor will determine the dosage required for you, according to your age, weight, other medicines you are taking, and the reason why you are being treated.

The dose should be reduced or omitted in patients who have a low blood volume, whose blood vessels are narrowed, or whose body temperature is very low.

The maintenance dose ranges from 0,03 to 0,2 mg/kg/hr. In these patients the maintenance dose will be reduced, at times to as low as 25 % of the usual dose. The level of sedation should be assessed regularly by the patient's condition.

If you receive more Accord Midazolam than you should:

Using more Accord Midazolam than required can result in confusion, lethargy, sleepiness, muscle weakness and long periods of sleep. In these cases, observation by a healthcare professional of the vital functions (such as heart rate, blood pressure and oxygen levels) will be necessary.

Extreme overdosage may lead to coma (unconscious state), lost reflexes, loss of breathing and weakness of the heart and lung function. If these occur, ventilation and cardiovascular support will be necessary.

Since a healthcare professional will administer this medicine, he/she will control the dosage. However in the event of overdosage your doctor will manage the overdosage.

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5. POSSIBLE SIDE EFFECTS:

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

Accord Midazolam can have side effects.

The following side effects can occur:

Psychiatric problems

- impairment of psychomotor skills
- hallucinations (hearing or seeing things that aren't really there)
- an excessive feeling of happiness or excitation

Nervous system problems

- dizziness, light headedness, feeling faint, numbness, tingling, pain or weakness in hands and feet, uncontrolled or jerky movements, unusual excitement, irritability, restlessness
- over sedation, headaches, anterograde/prolonged memory loss, seizures in premature infants and babies

Heart problems

- decrease in blood pressure
- change in pulse
- local effects on the veins, heart collapse

Eye problems

- change in vision

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Lung and breathing problems

- difficulty in breathing/ shortness of breath
- hiccups, wheezing, coughing

Stomach problems

- nausea, vomiting

Skin problems

- skin rash, hives, itching

Immune system

- hypersensitivity including serious allergic reactions

Muscle problems

- muscle tremor.
- ataxia (an uncontrollable muscle movement, resulting in shaking or tremors)

General problems and problems at the site of administration

- pain at injection site, redness, lumps and hardness**.**

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

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6. STORING AND DISPOSING OF ACCORD MIDAZOLAM:

Store at or below 25 ˚C. Protect the ampoules from light. Do not refrigerate.

Keep the ampoules in the outer carton until required for use.

Store all medicines out of reach of children.

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

Return all unused medicine to your pharmacist.

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

7. PRESENTATION OF ACCORD MIDAZOLAM:

Accord Midazolam 5 mg/5 ml solution for injection: Type I, clear, colourless glass ampoule, with a blue ring and white OPC dot (10 ampoules are packed in a unit carton).

Accord Midazolam 15 mg/3 ml solution for injection: Type I, clear, colourless glass ampoule, with a blue ring and white OPC dot (10 ampoules are packed in a unit carton).

Accord Midazolam 50 mg/10 ml solution for injection: Type I, clear, colourless glass ampoule, with a red ring and white OPC dot OR a blue ring and white OPC dot (1 ampoule per carton).

8. IDENTIFICATION OF ACCORD MIDAZOLAM:

Accord Midazolam 5 mg/5 ml solution for injection: Clear colourless to pale yellow solution, free from foreign particles

Accord Midazolam 15 mg/3 ml solution for injection: Clear colourless to pale yellow solution, free from foreign particles

Accord Midazolam 50 mg/10 ml solution for injection: Clear colourless to pale yellow solution, free from foreign particles

9. REGISTRATION NUMBER/REFERENCE NUMBER:

Accord Midazolam 5 mg/5 ml solution for injection: 42/26/0329

Accord Midazolam 15 mg/3 ml solution for injection: 42/26/0327

Accord Midazolam 50 mg/10 ml solution for injection: 42/26/0328

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10. NAME AND ADDRESS OF REGISTRATION HOLDER:

Accord Healthcare (Pty) Ltd

Tuscany Office Park

6 Coombe Place

Rivonia, Gauteng

South Africa

11. DATE OF PUBLICATION:

14 September 2012

5 February 2015

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