Viatris South Africa (Pty)Ltd	Date of amendment: 14 June 2023	Response to SAHPRA Variations email – Application SAHPRA-1E0638 Rejected
LIBRAX® (tablets)	LIBRAX® contains 5 mg 7-Chloro-2-N-methylamino-5-phenyl-3H-1,4-benzodiazepine-4-oxide (chlordiazepoxide) active substances of Librium (Trademark) and 2,5 mg 1-methyl-3-benziloyloxyquinu-clidinium bromide (clidinium bromide) per sugar-coated tablet	

1.3.2 Annotated Patient Information Leaflet- clean

SCHEDULING STATUS

S5

LIBRAX® (tablets)

Chlordiazepoxide 5 mg, Clidimium bromide 2,5 mg

Contains sugar: Lactose 131,025 mg, sucrose 130,838 mg

Read this information leaflet carefully before you start taking LIBRAX®.

- Keep this leaflet. You may need to read it again.
- LIBRAX® has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours. If you have further questions, please ask your doctor or pharmacist.

What is in this leaflet

1. What LIBRAX® is and what it is used for.

2. What you need to know before you take LIBRAX®**.**

3. How to take LIBRAX®**.**

4. Possible side effects.

5. How to store LIBRAX®**.**

6. Contents of the pack and other information.

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1.5.5.2 Annotated Patient Information Leaflet- clean

1. What LIBRAX® is and what it is used for

What LIBRAX® is:

- LIBRAX® belongs to a group of medicines called benzodiazepines.
- It affects chemical activity in your brain, to help promote sleep and to reduce anxiety and worry.
- It also works by slowing down the natural movements of your stomach and lower intestine to relieve stomach pain or discomfort.
- This helps to treat irritable bowel syndrome.

What it is used for:

- As an adjunct in the short-term treatment of non-ulcerated irritable bowel syndrome (IBS) associated with anxiety, tension or fear that something bad or unpleasant will happen in adults.
- LIBRAX® is only indicated when the above-mentioned is severe, putting the individual through extreme stress.

2. What you need to know before you take LIBRAX®

Do not take LIBRAX® if:

- you experience or have experienced a hypersensitivity to chlordiazepoxide, clidinium bromide, to other benzodiazepines, to any of the belladonna alkaloids to any of the inactive ingredients.
- you suffer from myasthenia gravis, a disorder affecting your muscles;
- you are pregnant or breastfeeding your baby;

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1.5.5.2 Annotated Patient Information Leaflet- clean

- you suffer from intestinal obstruction (a gastrointestinal condition in which digested material is prevented from passing normally through the bowel);
- you suffer from urinary obstruction (a blockage that inhibits the flow of urine through its normal path);
- you have non-cancerous (benign) tumour of the bladder;
- you have glaucoma (an eye disorder), or are at risk of developing glaucoma;
- you have any liver problems;
- you suffer from sleep apnoea syndrome (a potentially serious sleep disorder in which breathing repeatedly stops and starts);
- you suffer from a benign (not cancer) condition in which an overgrowth of prostate tissue pushes against the urethra and the bladder, blocking the flow of urine.

Warnings and precautions

Take special care with LIBRAX® if:

- you have ulcerative colitis (an inflammatory bowel disease);
- you have severe lung or breathing problems;
- you have a mental health disorder (psychosis);
- you have a hiatus hernia (a condition where the top of your stomach bulges through an opening in your diaphragm) with acid reflux;
- you are elderly or very weak and have intestinal or bowel problems;
- you have any heart instability;
- you have a history of drug abuse or dependence;

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1.5.5.2 Annotated Patient Information Leaflet- clean

- have high blood pressure;
- have an overactive thyroid (hyperthyroidism);

  have depression;
- have a type of lung disease called chronic obstructive pulmonary disease (COPD);
- have any kidney problems;
- have memory problems;
- have impaired thinking, confusion or any other type of brain damage;
- have dry mouth;
- are taking pain killers, known as opioids;
- have ever had a problem with:

- substance use, including prescribed or illegal drugs, or
- alcohol

- have ever had seizures or convulsions (violent uncontrollable shaking of the body with or without loss of consciousness);
- are sensitive to medicines known as benzodiazepines (medicines known as tranquilizers), atropine or belladonna.

Withdrawal of LIBRAX®:

- If you suddenly stop your treatment, lower your dose too fast, or switch to another medicine, you can experience withdrawal symptoms that can range from mild symptoms to severe or life threatening.
- Some of your withdrawal symptoms can last for months after you stop LIBRAX®.

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1.5.5.2 Annotated Patient Information Leaflet- clean

- Your risk of going through withdrawal is higher if you are taking LIBRAX® for a long time or at high doses. However, symptoms can still occur if you are taking LIBRAX® as directed for a short period of time or slowly reducing the dose.
- The symptoms of withdrawal often resemble the condition that you are being treated for. After stopping your treatment, it may be hard to tell if you are experiencing withdrawal or a return of your condition LIBRAX®.
- Tell your doctor or healthcare professional right away if you experience any symptoms of withdrawal after changing or stopping your treatment.

Severe symptoms of withdrawal include:

- Feeling like you cannot move or respond (catatonia);
- severe confusion, shivering, an irregular heartrate and excessive sweating (delirium tremens);
- feeling depressed;
- feeling disconnected from reality (dissociation);
- seeing or hearing things that are not there (hallucinations);
- overactive behaviour and thoughts (mania);
- believing in things that are not true (psychosis);
- convulsions (seizures), including some that do not stop;
- thoughts or actions of suicide

For other symptoms of withdrawal, see section 4 ‘Possible side effects’ and what to do about them (below).

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1.5.5.2 Annotated Patient Information Leaflet- clean

To reduce your chances of going through withdrawal:

- Always contact your doctor before stopping or reducing your dose of LIBRAX® or changing medicines;
- always follow your doctor's instructions on how to reduce your dose carefully and safely;
- tell your doctor right away if you experience any unusual symptoms after changing or stopping your treatment.

LIBRAX® with opioids:

Taking LIBRAX® with opioid medicines can cause severe drowsiness and breathing problems *(see section 'Other medicines and LIBRAX®*).

Tell your doctor if you:

- are taking opioid medicines;
- are prescribed an opioid medicine after you start taking LIBRAX®.

Monitoring and Tests:

- During your treatment with LIBRAX®, your healthcare professional may do tests to monitor your blood cell count and your liver function.

Children/ and adolescents

Do not give LIBRAX® to children.

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1.5.5.2 Annotated Patient Information Leaflet- clean

Other medicines and LIBRAX®

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

Tell your doctor if you are taking any of the following medicines:

- Alcohol;
- sedative antihistamines (medicines which teat allergies and colds and make you sleepy);
- medicines used to treat epilepsy (anticonvulsants);
- medicines used to manage psychosis (antipsychotics);
- medicines used to treat depression (antidepressants);
- medicines that affect your mind, emotions, or behaviour (psychotropics);
- cimetidine, a medicine used to treat heartburn and stomach ulcers;
- erythromycin, a medicine used to treat bacterial infections;
- ketoconazole or itraconazole, which are medicines used to treat fungal infections;
- nefazodone, a medicine used to treat depression;
- certain medicines used to treat HIV/AIDS.

Taking LIBRAX® and opioids may cause:

- Severe drowsiness;
- trouble breathing;
- coma;

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1.5.5.2 Annotated Patient Information Leaflet- clean

- death.

LIBRAX with food and drink and alcohol

- Do not take LIBRAX® with alcohol.
- Take LIBRAX® before meals.

Pregnancy and breastfeeding and fertility

You should not take LIBRAX® if you are pregnant or breastfeeding your baby.

LIBRAX® may harm your unborn baby (e.g. birth defects) if you take them while you are pregnant.

During labour LIBRAX® crosses the placenta and may cause the “floppy-infant” syndrome characterised by difficulty in breathing, a potentially dangerous drop in body temperature and poor sucking.

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

Women of childbearing potential should use effective contraceptive measures while being treated with LIBRAX® and for 7 months following completion of treatment.

If you suspect to be pregnant or intend to become pregnant contact your doctor or healthcare professional to discuss discontinuation of LIBRAX®.

Men are recommended to use effective contraceptive measures and to not father a child while receiving LIBRAX® and for 4 months following completion of treatment.

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1.5.5.2 Annotated Patient Information Leaflet- clean

Driving and using machinery

LIBRAX® may cause drowsiness, sleepiness, loss of memory, impaired concentration, and impaired muscular function and may affect mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision e.g. driving, riding, flying, sailing, operating machines/equipment (*see 'Possible side- effects*'**).**

LIBRAX® contains lactose and sucrose

LIBRAX® contains lactose and sucrose, which may have an effect on the control of your blood sugar if you have diabetes mellitus.

Lactose warning:

Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption intolerance should not take LIBRAX®.

Sucrose warning:

Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take LIBRAX®.

3. How to take LIBRAX®

- Do not share medicines prescribed for you with any other person.
- Always take LIBRAX® exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

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1.5.5.2 Annotated Patient Information Leaflet- clean

- Treatment should be started with the lowest recommended dose.
- The maximum dose should not be exceeded.
- Treatment should be as short as possible.
- The overall duration of treatment generally should not be more than 8 – 12 weeks, including a tapering off process.
- Your doctor will slowly decrease your dose and will tell you when to stop taking this medicine (see *'If you stop taking LIBRAX®'*).
- If you have the impression that the effect of LIBRAX® is too strong or too weak, tell your doctor or pharmacist.

The usual dose is:

Adults:

- The usual dose is one (1) tablet three (3) or four (4) times a day administered before meals and at bedtime.
- A maximum daily dose of 8 tablets should not be exceeded.

Elderly and debilitated patients:

- Initially one (1) tablet twice a day.

If you take more LIBRAX® than you should

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

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1.5.5.2 Annotated Patient Information Leaflet- clean

If you forget to take dose of LIBRAX®

Do not take a double dose to make up for forgotten individual doses.

If you stop taking LIBRAX®

Do not stop treatment early because you will experience withdrawal symptoms with LIBRAX®:

Long-term treatment with LIBRAX®, especially in high doses, may lead to dependence, with withdrawal symptoms after stopping treatment. Your doctor will slowly decrease your dose and will tell you when to stop taking this medicine.

Your doctor will tell you how long your treatment with LIBRAX® will last.

Withdrawal effects may occur if the medicine is stopped suddenly. This is less likely if your dose is gradually reduced towards the end of your treatment.

Withdrawal symptoms may include:

- Difficulty sleeping;
- depression;
- nervousness;
- irritability;
- restlessness;
- extreme anxiety;
- sweating;
- diarrhoea;

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1.5.5.2 Annotated Patient Information Leaflet- clean

- confusion;
- headaches and muscle pain.

In severe cases the following symptoms may occur:

- Changes in mood and behaviour or the way you are feeling;
- tingling sensations and numbness of a limb of the body, such as the arm or leg;
- over-sensitivity to light, noise and touch;
- feeling of unreality or being separated from the body;
- hallucinations;
- fits (seizures and convulsions);
- if you are woken up soon after taking the medicine your memory may be temporarily affected.

4. Possible side effects

LIBRAX® can have side effects.

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

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

- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing;

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1.5.5.2 Annotated Patient Information Leaflet- clean

- rash (skin eruptions, hives) or itching;
- fainting;
- difficulty breathing;
- thoughts of self-harm (suicidal ideation);
- yellowing of the skin and eyes (jaundice), dark urine, light coloured stool;
- coma;
- uncontrolled rolling of the eyes.

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

- Ataxia - symptoms include unsteadiness and clumsiness, slurred speech;
- difficulty controlling movements;
- balance disorder;
- confusional states;
- decreased/depressed level of consciousness;
- dependence;
- emotional disturbances e.g irritability, rages and violent behaviour

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

Tell your doctor if you notice any of the following:

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1.5.5.2 Annotated Patient Information Leaflet- clean

The following side effects have been reported frequently:

- Drowsiness and light-headedness the next day;
- sleepiness and dizziness;
- tiredness (fatigue) or sometimes blackouts.

The following side effects have been reported less frequently:

- Changes in sex drive;
- difficulty passing urine;
- incontinence (loss of bladder control);
- impotence;
- reduced alertness;
- headache;
- problems with your eye sight including double vision;
- stomach upsets;
- menstrual disorder;
- blood disorders;
- lowering of blood pressure (hypotension) - symptoms include light-headedness, feeling dizzy or faint.

The following side effects have been reported but the frequency is unknown:

- Forgetfulness, memory loss;
- aggressive outbursts, inappropriate behaviour;

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1.5.5.2 Annotated Patient Information Leaflet- clean

- restlessness, agitation, delusion, irritability, nightmares, depression;
- increased liver enzymes;
- changes in the way you walk and muscle weakness;
- paradoxical reactions (e.g. saliva altered, anxiety, sleep disorders, insomnia);
- tremors, stiffness and slow movement;
- hallucinations, if you are woken up soon after taking this medicine your memory may be partially affected;
- increased appetite;
- constipation.

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

Reporting of side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions 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 LIBRAX.

5. How to store LIBRAX®

Store all medicines out of reach of children.

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1.5.5.2 Annotated Patient Information Leaflet- clean

Store at or below 25 °C.

Store in the original package / container.

Keep the container tightly closed.

Do not store in a bathroom.

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

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 LIBRAX® contains:

The active substance is chlordiazepoxide and clidinium bromide.

The other ingredients are acacia gum spray-dried, indigo carmine 85 %, yellow iron oxide, lactose anhydrous, magnesium stearate, maize (white corn) starch, oil of paraffin of low viscosity, paraffinum sodium FP 50/52, rice starch, sucrose (crystallized sugar) and talc.

What LIBRAX® looks like and contents of the pack:

What LIBRAX® looks like:

Round, biconvex and green to yellow-green sugar-coated tablets.

Contents of the pack:

Sugar-coated tablets in amber glass bottles containing 30, 100 or 500 tablets.

Holder of Certificate of Registration and Manufacturer

Viatris South Africa (Pty) Ltd

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4 Brewery Street

Isando

Gauteng

This leaflet was last revised in

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Registration number

B/11.2/994

Access to the corresponding Professional Information

Can be obtained on the SAHPRA website.