

# CLEAN PROPOSED PIL FOR ANAFRANIL 10 & 25 TABLETS AND ANAFRANIL SR 75 DIVITABS

SCHEDULING STATUS: **S5**

**ANAFRANIL® 10 tablets**

**ANAFRANIL® 25 Tablet**

**ANAFRANIL® SR 75 divitabs**

Clomipramine hydrochloride

ANAFRANIL® 10 tablets and ANAFRANIL® 25 Tablets contain sugar (lactose and sucrose).

## **Read all of this leaflet carefully before you start taking ANAFRANIL**

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

## **What is in this leaflet**

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

### **1. What ANAFRANIL is and what it is used for**

ANAFRANIL belongs to a group of medicines called tricyclic antidepressants. ANAFRANIL is believed to work by increasing the levels of two naturally occurring chemicals within the brain, noradrenaline and 5-hydroxytryptamine (also called serotonin).

ANAFRANIL is used to treat depression and mood disorders. Other psychological conditions that can be treated with ANAFRANIL are obsessions and muscular weakness (cataplexy) associated with recurrent attacks of extreme sleepiness (narcolepsy) in adults. In children aged above 5 years, ANAFRANIL is used to treat obsessive-compulsive disorders.

## **2. What you need to know before you take ANAFRANIL**

It is important to tell your doctor if you have other medical problems or if you are taking other medicines.

### **Do not take ANAFRANIL**

- If you are hypersensitive (allergic) to clomipramine, to any other tricyclic antidepressant, or any of the other ingredients of ANAFRANIL (listed in section 6).
- If you are taking certain medicines used to treat depression such as monoamine oxidase inhibitors (MAO inhibitors), selective serotonin reuptake inhibitors (SSRI), or serotonin and noradrenergic reuptake inhibitors (SNRI).
- If you have recently had a heart attack or if you suffer from a serious heart disease.
- If you have heart disorders such as abnormal heart rhythm.
- If you have any serious liver disease.
- If you have low levels of potassium in your blood (hypokalaemia).
- If you have glaucoma (increased pressure in the eye).
- If you have difficulty in passing urine.
- If you have a mental health condition called mania.

If the answer to any of these is YES, ANAFRANIL is probably not suitable for you.

If you think you may be allergic, ask your doctor for advice.

## **Warnings and precautions**

### **Take special care with ANAFRANIL:**

- If you are having thoughts of suicide.
- If you have epileptic fits.
- If you have had a head injury or have suffered brain damage.
- If you are going to have electric shock therapy (ECT).
- If you have schizophrenia or other mental disorder.
- If you have liver or kidney disease.
- If you have any blood disorder.
- If you have difficulties in passing urine (e.g. due to diseases of the prostate).
- If you have an overactive thyroid gland.
- If you have persisting constipation.
- If you easily faint or have low blood pressure.
- A history of increased eye pressure or glaucoma.
- If you have cancer in a gland called the adrenal gland, which produces hormones.
- If you are elderly, as the chances are greater that you could get side effects.

Your doctor will take these conditions into account before and during your treatment with ANAFRANIL.

If any of these apply to you, tell your doctor before you take ANAFRANIL.

## **Further safety measures**

It is important for your doctor to check your progress regularly to allow dosage adjustments and help reduce side effects. He or she may want to take some blood tests and measure your blood pressure and heart function before and during treatment.

ANAFRANIL may cause dry mouth, which can increase the risk of tooth decay. This means that during long-term treatment you should have regular dental check-ups.

If you wear contact lenses and experience eye irritation, talk to your doctor.

Before you have any kind of surgery or dental treatment, tell the doctor in charge or dentist that you are taking ANAFRANIL.

ANAFRANIL may cause your skin to be more sensitive to sunlight. Stay out of direct sunlight, and wear protective clothing and sunglasses.

**Thoughts of suicide and worsening of your depression or anxiety disorder:**

If you are depressed and/or have anxiety disorders, you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks or sometimes longer.

You may be more likely to think like this:

- If you have previously had thoughts about killing or harming yourself.
- If you are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in young adults (less than 25 years old) with mental health conditions who were treated with an antidepressant.

If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.

You may find it helpful to tell a relative or close friend that you are depressed or have an anxiety disorder, and ask them to read this leaflet. You might ask them to tell you if they think your depression or anxiety is getting worse, or if they are worried about changes in your behaviour.

### **Information for families, and caregivers**

You should monitor whether your depressed child/patient shows signs of behavioural changes such as unusually anxiety, restlessness, sleeping problems, irritability, aggressiveness, over-excitedness or other unusual changes in behaviour, worsening of depression or thinking about suicide. You should report any such symptoms to the patient's doctor, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms before. You should evaluate the emergence of such symptoms on a day-to-day basis, especially early during antidepressant treatment and when the dose is increased or decreased, since changes may be abrupt.

Symptoms such as these may be associated with an increased risk for suicidal thinking and behaviour and indicate a need for very close monitoring and possibly changes in the medication.

### **Children and adolescents**

ANAFRANIL is only indicated for the use of obsessive–compulsive syndromes in children 5 years of age and older.

### **Other medicines and ANAFRANIL**

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

Since many medicines interact with ANAFRANIL, it may be necessary to adjust the dosage or stop one of the medicines. It is especially important for your doctor and pharmacist to know if you drink alcohol every day, if you change your smoking habits or if you are taking any of the following:

- Other antidepressants, particularly MAOIs (see section “Do not take” above).
- Diuretics, also known as “water pills”.

- Medicines to treat heart disorders, particularly those used to treat an abnormal heart rhythm e.g. disopyramide, procainamide, epinephrine (adrenaline), isoprenaline, amiodarone, quinidine, diltiazem and verapamil.
- Terbinafine, used orally to treat skin, hair or nail infections due to fungus.
- Medicines used to treat ulcer/heartburn such as cimetidine.
- Medicines containing oestrogens, e.g. contraceptive pill.
- Sedatives, tranquillisers and other medicines for other mental health conditions such as schizophrenia or bipolar disorder e.g. thioridazine, lithium, clozapine, pimozide, benzodiazepines e.g. alprazolam.
- Disulfiram, used to help you stop drinking alcohol.
- Medicines, used to treat attention deficit/hyperactivity disorder (ADHD) such as methylphenidate.
- Anticonvulsants used to stop seizures (e.g. barbiturates such as phenobarbital, phenytoin, carbamazepine or valproate).
- Rifampicin, used to treat some infections including tuberculosis (TB).
- Nicotine e.g. if you smoke or are using nicotine replacement therapy.
- Colestipol, cholestyramine, used to treat high cholesterol levels.
- St. John's wort (*Hypericum perforatum*), a herbal product used to treat depression and other conditions.
- Medicines used to treat allergies, called antihistamines.
- Medicines used to treat Parkinson's disease e.g. biperiden, entacapone or selegiline.
- Atropine or similar medicines (including eye drops).
- Medicines used to control high blood pressure e.g. guanethidine, betanidine, reserpine, clonidine or alpha methyl dopa.
- Beta-blockers e.g. sotalol.
- Anaesthetics, used for the temporary loss of bodily sensation.
- Norepinephrine (noradrenaline), used to treat low blood pressure.

- Decongestants used for colds and flu such as ephedrine, phenylephrine or phenylpropanolamine.
- Medicines used to thin blood (anticoagulants).
- Quinine, for cramp or malaria treatment.
- Pentamidine, a medicine used to treat pneumonia.
- Aspirin and similar pain killing non-steroidal anti-inflammatory drugs (NSAIDs).
- Altretamine, used to treat cancer.
- Strong painkillers such as tramadol, nefopam or opioid analgesics.
- Levacetylmethadol, used to treat addiction to opioid drugs, such as heroin.
- Baclofen, used in the treatment of multiple sclerosis and spinal damage.
- Thyroid preparations.

### **ANAFRANIL with food, drink and alcohol**

Take care when eating grapefruit, or drinking grapefruit juice or cranberry juice as this may increase your chance of experiencing side effects. Be careful when drinking alcohol - it may affect you more than usual.

### **Pregnancy, breastfeeding and fertility**

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 health care provider for advice before taking this medicine.

### **Pregnant women**

Tell your doctor if you are pregnant or breastfeeding. ANAFRANIL should not be used during pregnancy or by women able to have children, who are not using contraception.

Your doctor will discuss with you the potential risk of taking ANAFRANIL during pregnancy.

### **Breastfeeding mothers**

The active ingredient of ANAFRANIL passes into the breast milk. Mothers are advised not to breast feed their babies while taking ANAFRANIL.

### **Fertility**

The active ingredient of ANAFRANIL does not appear to have any significant effects on fertility and general reproductive performance.

### **Driving and using machines**

ANAFRANIL may affect your ability to drive or use machines. You should not drive during the first few days of starting treatment with ANAFRANIL, until you know how it affects you, as it may affect your ability to make decisions whilst driving, which could cause an accident.

ANAFRANIL may make some people drowsy or less alert, or it may cause blurred vision. Other side effects, such as attention difficulty, feeling confused, feeling disorientated and feeling more depressed have been reported. If you experience these side effects, you should not drive, use machinery, or perform other tasks that need full attention. Drinking alcohol may increase drowsiness.

### **ANAFRANIL contains lactose and sucrose**

ANAFRANIL 10 mg and 25 mg tablets contain lactose and sucrose.

Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take ANAFRANIL 10 mg and 25 mg tablets.

If you have been told by your doctor that you have an intolerance to some sugars (e.g. lactose, sucrose), contact your doctor before taking ANAFRANIL 10 mg and 25 mg tablets.

### **3. How to take ANAFRANIL**

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

Always take ANAFRANIL exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

If you have low blood potassium levels (hypokalaemia), your doctor will treat this before you can start treatment with ANAFRANIL.

Your doctor will decide on the most suitable dosage for your particular case.

Take ANAFRANIL as directed by your doctor. Do not take more of it, and do not take it more often or for longer than your doctor ordered. In some cases, the doctor may decide to treat you with injections of ANAFRANIL.

The 75 mg SR divitabs can be halved, but should not be chewed. You can take ANAFRANIL with or without food.

For depression and obsessive-compulsive disorders, the daily dosage is normally between 75 mg and 150 mg. Max daily dose is 250 mg.

For muscular weakness (cataplexy) accompanied by extreme sleepiness (narcolepsy), the daily dose is between 25 mg to 75 mg.

### **ANAFRANIL and older people**

Elderly patients generally need lower doses than young and middle-aged patients. Side effects are more likely to occur in older patients. Your doctor will provide any special information about careful dosage and close observation needed.

### **ANAFRANIL and children**

ANAFRANIL should not be given to children or adolescents unless specifically prescribed by a doctor. Your doctor will provide any special information about careful dosage and close observation needed.

The starting dose for children/adolescents for the treatment of obsessive disorders is 25 mg daily. The maximum dose is 3 mg/kg or 200 mg, whichever is smaller.

### **If you take more ANAFRANIL than you should**

In the event of an overdose, consult your doctor or pharmacist. If neither is available, rush the patient to the nearest hospital or poison centre.

The following symptoms of overdose usually appear within a few hours: severe drowsiness, poor concentration, fast, slow, or irregular heartbeat, the inability of the heart to pump as much blood as it should, low blood pressure, restlessness and agitation, loss of muscle coordination and muscle stiffness, shortness of breath, fits, vomiting or fever. Breathing difficulty, cyanosis (low levels of oxygen in your blood), mydriasis (widening of the pupils of the eyes), sweating, and very low or no urine being created by your body, may also occur.

### **If you forget to take ANAFRANIL**

If you forget to take a dose of ANAFRANIL, take the missed dose as soon as possible and then go back to your normal dosage schedule. If it is almost time for your next dose, skip the missed dose and continue with your normal dosage schedule. Do not take a double dose to make up for forgotten individual doses. If you have any questions about this, ask your doctor.

### **If you stop taking ANAFRANIL**

Depression and obsessive-compulsive disorders require long-term treatment with ANAFRANIL. Do not change or stop the treatment without first asking your doctor. Your doctor may want you to reduce the dosage gradually before stopping completely. This is to prevent any worsening of

your condition and reduce the risk of withdrawal symptoms such as headache, nausea, vomiting, stomach pain, diarrhoea, sleeping difficulty, nervousness and feeling anxious.

#### **4. Possible side effects**

ANAFRANIL can have side effects.

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

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

- A lower than normal level of sodium in the blood, which may make you feel weak and confused with sudden contraction of the muscles, muscle spasms. This may be due to inappropriate ADH secretion, a hormone that causes the body to retain water and dilute the blood, reducing the amount of sodium.
- Seeing or hearing things that are not really there.
- Allergic reactions with/without coughing and difficulty in breathing, skin reactions (itching or reddening), fast heartbeat (racing, pounding), swelling of the hands, face, tongue, neck or throat, increased fluid in tissues and very low blood pressure.
- Stomach pain.
- Loss of appetite.
- Muscle weakness or stiffness.
- Difficulty in speaking.
- Confusion, delirium.
- Inability to coordinate movement.
- Irregular heartbeat (racing, pounding), and fainting (especially if you have low potassium levels in your blood).

- Fits.
- A nervous system disorder characterized by muscle stiffness, high fever and impaired consciousness. These may be the symptoms of a serious condition known as neuroleptic malignant syndrome.
- Disease of the liver (known as hepatitis), this may result in jaundice. You may feel sick, be sick, generally feel unwell, lose your appetite, have a fever, yellowing of the skin or whites of the eyes, light coloured stools and dark-coloured urine.
- Frequent infection with fever and sore throat (due to decreased number of white blood cells).
- Increase pressure in the eye.
- Difficulty in passing urine.
- Thoughts of suicide or self-harm (see section 2 for more information).
- Serotonin syndrome (caused by an increase in naturally occurring messenger, serotonin, in the brain; symptoms include agitation, confusion, diarrhoea, high temperature, increased blood pressure, excessive sweating and rapid heartbeat).
- Breakdown of muscle, causing muscle pain, weakness or tenderness accompanied by dark urine (rhabdomyolysis).

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

**Frequent side effects:**

- Drowsiness.
- Tiredness.
- Dizziness.
- Restlessness.
- Increase in appetite.
- Dry mouth.

- Constipation.
- Problem with your eye sight including blurred vision.
- Trembling.
- Headache.
- Nausea.
- Sweating.
- Weight gain.
- Changes in the amount of sugar in the blood.
- Sexual difficulties.
- Anxiety.
- Changes to the amount of urine you produce or frequency of urination.
- Disorientation.
- Agitation.
- Palpitations.
- Minor changes to your electrocardiogram (ECG – a test, which shows how your heart conducts electricity) may show up if your heart is tested.
- Disturbance in attention.
- Sleep disturbances.
- Over-excitedness.
- Aggressiveness.
- Poor memory.
- Yawning.
- Nightmares.
- Numbness or tingling of the extremities.
- Hot flushes.
- Dilated pupils.
- Fall in blood pressure associated with dizziness after abrupt standing or sitting up.
- Vomiting, abdominal disorders, diarrhoea.

- Skin sensitivity to sunlight.
- Rash, hives or itching.
- Worsening depression.
- Swelling of the breasts and discharge of milk.
- Women may not be able to orgasm.
- Unpleasant taste.
- Ringing in the ears.
- Feeling detached from a situation (like watching it from afar).
- Changes in liver function tests.

**Less frequent side effects:**

- Higher than normal level of white blood cells (eosinophilia) as seen in a blood test.
- Swelling of the lungs which can cause flu-like effects such as coughing, chest tightness, chills, wheezing and difficulty breathing.
- Blue or purplish spots on the skin (ecchymosis or purpura).
- Abnormal reading of the electrical activity of the brain (as seen in an electroencephalogram).
- Changes in how you think and feel.
- Vaginal bleeding.
- Oedema (swollen ankles and/or hands and/or swelling of any other part of the body).
- Hair loss.
- Patients aged 50 years or older and taking a medicine of this group are more likely to experience bone fractures.

**The frequency of the following side effects are unknown:**

- Repetitive, uncontrollable movements.
- Inability to ejaculate or a delay in ejaculation.
- Increase in prolactin (a hormone) level in the blood.

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 ANAFRANIL.

### **5. How to store ANAFRANIL**

ANAFRANIL<sup>®</sup> 10 tablets and ANAFRANIL<sup>®</sup> 25 Tablets: Store at or below 30 °C and protect from moisture and light.

ANAFRANIL<sup>®</sup> SR 75 divitabs: Store at or below 30 °C and protect from moisture.

KEEP OUT OF REACH AND SIGHT OF CHILDREN.

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

Return all used ANAFRANIL to your pharmacist.

Do not dispose of unused ANAFRANIL in drains or sewerage system.

### **6. Contents of the pack and other information**

#### **What ANAFRANIL contains**

The **active substance** of ANAFRANIL is clomipramine.

ANAFRANIL<sup>®</sup> 10 tablets and ANAFRANIL<sup>®</sup> 25 Tablets contain 10 mg and 25 mg clomipramine hydrochloride respectively.

ANAFRANIL<sup>®</sup> SR 75 divitabs contain 75 mg clomipramine hydrochloride in a slow release formulation.

The other ingredients are:

ANAFRANIL<sup>®</sup> 10 tablets and ANAFRANIL<sup>®</sup> 25 Tablets: copovidone (vinylpyrrolidone-vinylacetate copolymer), hypromellose (hydroxypropyl methylcellulose), iron oxide yellow (E172), lactose monohydrate, macrogol 8000 (polyethylene glycol 8000), magnesium stearate, maize starch, microcrystalline cellulose, povidone (polyvinylpyrrolidone), silicon dioxide, sucrose, talc, titanium dioxide (E171).

ANAFRANIL<sup>®</sup> 25 Tablets also contain glycerol (85 %) and stearic acid.

ANAFRANIL<sup>®</sup> SR 75 divitabs: calcium phosphate dibasic, calcium stearate, hypromellose (hydroxypropyl methylcellulose), iron oxide red, macrogolglycerol hydroxystearate (polyoxyl 40 hydrogenated castor oil), polyacrylate dispersion 30%, silicon dioxide, talc, titanium dioxide.

#### **What ANAFRANIL looks like and contents of the pack**

ANAFRANIL<sup>®</sup> 10 tablets: light yellow, triangular, biconvex, sugar-coated tablets. Apex to base of triangle approximately 5,8 mm. Thickness approximately 3,3 mm.

ANAFRANIL<sup>®</sup> 25 Tablets: light yellow, sugar-coated, round, biconvex tablets. Diameter approximately 5,6 mm. Thickness approximately 3,5 mm.

ANAFRANIL<sup>®</sup> SR 75 divitabs: rose coloured, film-coated, capsule-shaped, biconvex, divisible tablets. Imprinted C/G with a score on one side, and G/D with a score on the other side. Length approximately 13,2 mm. Width approximately 5,2 mm. Thickness approximately 4,6 mm.

ANAFRANIL<sup>®</sup> 10 tablets and ANAFRANIL<sup>®</sup> 25 Tablets are supplied as 10 mg and 25 mg tablets in blister packs of 50, and ANAFRANIL<sup>®</sup> SR 75 divitabs in blister packs of 30.

**Holder of Certificate of Registration**

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ANAFRANIL<sup>®</sup> 25 Tablets: B1532 (Act 101/1965)

ANAFRANIL<sup>®</sup> SR 75 divitabs: W/1.2/140

**Access to the corresponding Professional Information**

Not applicable.