1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S5

CYMGEN 30 mg capsules

Duloxetine as duloxetine hydrochloride

Contains sugar: Sucrose 55,5 mg

CYMGEN 60 mg capsules

Duloxetine as duloxetine hydrochloride

Contains sugar: Sucrose 110,6 mg

Read all of this leaflet carefully before you start taking CYMGEN

- 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.
- CYMGEN 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 CYMGEN is and what it is used for
2. What you need to know before you take CYMGEN
3. How to take CYMGEN
4. Possible side effects

5. How to store CYMGEN
6. Contents of the pack and other information

1. What CYMGEN is and what it is used for

CYMGEN belongs to a group of medicines called antidepressants.

CYMGEN is a serotonin and norepinephrine reuptake inhibitor (SNRI) and increases the levels of serotonin and noradrenaline in the nervous system.

CYMGEN is used in adults to treat:

- depression,
- diabetic peripheral neuropathic pain (often described as burning, stabbing, stinging, shooting, aching or like an electric shock. There may be loss of feeling in the affected area, or sensations such as touch, heat, cold or pressure that may cause pain).

2. What you need to know before you take CYMGEN

Do not take CYMGEN:

- if you are hypersensitive (allergic) to duloxetine or any of the other ingredients of CYMGEN (listed in section 6).
- if you have liver disease.
- if you have severe kidney disease.
- if you are taking another antidepressant medicine known as monoamine oxidase inhibitor (MAOI) or linezolid. Taking CYMGEN with a MAOI or linezolid could cause serious side effects or be life-threatening (see 'Other medicines and CYMGEN').

- if you are under 18 years of age.
- if you are pregnant or breastfeeding your baby.

Warnings and precautions

Take special care with CYMGEN:

- If you have thoughts of suicide and worsening of your depression:

  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 but sometimes longer.

  You may be more likely to think like this if you:
- have previously had thoughts about killing or harming yourself,
- are a young adult. Reports have shown an increased risk of suicidal behaviour in adults aged less than 25 years with psychiatric 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 and ask them to read this leaflet. You might ask them to tell you if they think your depressed, or if they are worried about changes in your behaviour,
- if you have had previous episodes of seizures (fits),
- if you have had previous episodes of mania (feeling elated or over-excited which causes unusual behaviour),
- if you suffer from bipolar disorder,
- if you have eye problems, such as certain kinds of glaucoma (increased pressure in the eye) and mydriasis (enlarged pupils),

- if you have kidney problems, you may need a lower dose,
- if you are taking any opioid medicines, such as buprenorphine containing medicines, tramadol and pethidine, MAOIs, other antidepressants and antipsychotics (see 'Do not take CYMGEN'). The use of these medicines together with CYMGEN can lead to serotonin syndrome, a potentially life-threating condition with symptoms that may include mental status changes (e.g. agitation, perceiving things that are not there, coma), feelings of great happiness, drowsiness, clumsiness, restlessness, feeling of being drunk, fever, sweating or rigid muscles, fits, vomiting and fast heart rate (see 'Other medicines and CYMGEN'),
- if you are taking St. John's Wort, a herbal treatment (*Hypericum perforatum*),
- if you have high blood pressure or heart disease, talk to your doctor. Your doctor will tell you if you should be taking CYMGEN. If you experience increase in blood pressure while taking CYMGEN, your doctor will tell you to reduce the dose or gradually stop taking CYMGEN,
- if you experience sexual dysfunction. CYMGEN may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued after stopping treatment,
- if you have a history of bleeding disorders (e.g. von Willebrand disease, haemophilia A, deficiency in F VIII, and haemophilia B); and comorbid bleeding disorders (e.g. multiple pregnancy, gestational hypertension or preeclampsia), or if you are pregnant (see 'Pregnancy and breastfeeding'),
- if you are at risk of low sodium levels (for example if you are taking diuretics, especially if you are elderly, dehydrated, or have liver impairment). Signs and symptoms may include dizziness, weakness, feeling sick, vomiting, confusion, drowsiness, and tiredness. Signs and symptoms associated with more severe

cases have included fainting and fits,

- if you have liver problems or are currently being treated with another medicine which may cause liver damage. You may have liver problems such as jaundice, increased liver enzymes and liver disease if you are taking CYMGEN. Most of these liver problems develop during the first months of treatment and may be linked to high alcohol intake, pre-existing liver disease, or treatment with other medicines which may cause liver damage,
- if you are feeling a sensation of restlessness or an inability to sit or stand still after taking CYMGEN. You should tell your doctor if this happens to you,
- if you are feeling sudden, severe chest pain (angina), shortness of breath, or irregular heartbeats (arrhythmias), as these may be symptoms of Takotsubo cardiomyopathy. Takotsubo cardiomyopathy (also known as stress cardiomyopathy) is a condition where your heart muscle becomes suddenly weakened, due to your body releasing stress hormones in your blood. This condition is reversible upon stopping CYMGEN and receiving appropriate treatment. It is important for you that your doctor knows about all your medical conditions.
- if you are elderly. Exercise caution when taking CYMGEN at high doses (120 mg) to treat depression.

Children and adolescents

CYMGEN should not be used for children and adolescents under 18 years (see 'Do not take CYMGEN'). Also, you should know that patients under 18 years and young adults (< 25 years of age) have an increased risk of side effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines.

If your doctor has prescribed CYMGEN for a patient under 18 years and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 years are taking CYMGEN. Also, the long-term safety effects concerning growth, maturation, and mental and behavioural development of duloxetine, as in CYMGEN, in this age group have not yet been established.

Other medicines and CYMGEN

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:

- Monoamine oxidase inhibitors (MAOIs): You should not take CYMGEN if you are taking or have recently taken (within the last 14 days) another antidepressant medicine called a monoamine oxidase inhibitor (MAOI). Examples of MAOIs include moclobemide (an antidepressant) and linezolid (an antibiotic). Taking a MAOI together with CYMGEN can cause serotonin syndrome, a potentially life-threating condition. You must wait at least 14 days after you have stopped taking an MAOI before you can take CYMGEN. Also, you need to wait at least 5 days after you stop taking CYMGEN before you take a MAOI.
- Medicines that increase the level of serotonin: triptans, tryptophan, SSRIs (such as paroxetine and fluoxetine), SNRIs (such as venlafaxine), tricyclic antidepressants (such as clomipramine, amitriptyline), St. John's Wort, MAOIs (such as moclobemide and linezolid) and opioid medicines such as buprenorphine containing medicines, tramadol and pethidine. These medicines increase the risk of side effects such as serotonin syndrome (see

‘Warnings and precautions’); if you get any unusual symptoms taking any of these medicine together with CYMGEN, you should see your doctor.

- Medicines that cause sleepiness: These include medicines prescribed by your doctor including benzodiazepines, strong painkillers, antipsychotics, phenobarbitone and antihistamines.
- Oral anticoagulants or antiplatelet medicines: Medicines which thin the blood or prevent the blood from clotting (e.g. warfarin). These medicines might increase the risk of bleeding.
- Fluvoxamine used for treatment of obsessive-compulsive disorder.
- Quinolone antibiotics used to treat bacterial infections.
- Risperidone used to treat schizophrenia and bipolar disorder.
- Flecainide, propafenone, and metoprolol used to prevent and treat abnormally fast heart rates.
- Oral contraceptives used for birth control.
- Highly protein-bound medicines such as phenobarbitone, diazepam, and cefazolin. CYMGEN is highly protein-bound, therefore if you are taking CYMGEN with other highly protein-bound medicines, the medicines may negatively affect one another.

CYMGEN with food, drink and alcohol

CYMGEN may be taken with or without food. Care should be taken if you drink alcohol while you are being treated with CYMGEN.

Pregnancy and breastfeeding

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

- CYMGEN may increase the risk of a serious condition in babies, called

persistent pulmonary hypertension of the newborn (PPHN), making the baby breathe faster and appear bluish. These symptoms usually begin during the first 24 hours after the baby is born. If this happens to your baby, you should contact your midwife and/or doctor immediately.

- If you take CYMGEN near the end of your pregnancy, your baby might have some symptoms when it is born. These usually begin at birth or within a few days of your baby being born. These symptoms may include floppy muscles, trembling, jitteriness, not feeding properly, trouble with breathing and fits. If your baby has any of these symptoms when it is born, or you are concerned about your baby's health, contact your doctor or midwife who will be able to advise you.
- If you take CYMGEN near the end of your pregnancy there is an increased risk of excessive vaginal bleeding shortly after birth, especially if you have a history of bleeding disorders. Your doctor or midwife should be aware that you are taking CYMGEN so they can advise you.

Driving and using machines

CYMGEN may make you feel sleepy or dizzy. You should not drive, use machinery or perform any tasks that require concentration until you are certain that CYMGEN does not adversely affect your ability to do so safely (see section 4).

It is not always possible to predict to what extent CYMGEN may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which CYMGEN affects you (see section 4).

CYMGEN contains sucrose

If you have been told by your doctor that you have an intolerance to some sugars,

contact your doctor before taking this medicine.

3. How to take CYMGEN

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

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

CYMGEN is for oral use.

For depression and diabetic peripheral neuropathic pain:

The usual dose of CYMGEN is 60 mg once a day. Your doctor will prescribe the dose that is right for you.

If you suffer from depression, CYMGEN may take 2 to 4 weeks to start working. Talk to your doctor if you do not start to feel better after this time.

If you have diabetic peripheral neuropathic pain, it can take some weeks before you feel better. Talk to your doctor if you do not feel better after 2 months.

Your doctor will tell you how long your treatment with CYMGEN will last. Do not stop treatment early. If you have the impression that the effect of CYMGEN is too strong or too weak, tell your doctor or pharmacist.

If you stop treatment early, you may have withdrawal symptoms, especially if you stop suddenly. Common withdrawal symptoms include dizziness, sensory disturbances (including pins and needles or electric shock-like sensations, especially in the head), sleep disturbances (including lack of sleep and intense dreams, nightmares), tiredness, drowsiness, agitation or anxiety, feeling sick and/or vomiting, tremor, headache, muscle aches and pain, irritability, diarrhoea, excessive sweating, and spinning sensation.

If you take more CYMGEN 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.

Symptoms of overdose include sleepiness, coma, serotonin syndrome (a rare reaction which may cause feelings of great happiness, drowsiness, clumsiness, restlessness, feeling of being drunk, fever, sweating or rigid muscles), fits, vomiting and fast heart rate.

If you forget to take CYMGEN

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

If you stop taking CYMGEN

Do not stop taking CYMGEN without the advice of your doctor even if you feel better.

If your doctor thinks that you no longer need CYMGEN, your doctor will ask you to reduce your dose over at least 2 weeks before stopping treatment altogether.

Some patients who stop taking CYMGEN suddenly have had symptoms such as: dizziness, tingling feelings like pins and needles or electric shock-like feelings (particularly in the head), sleep disturbances (vivid dreams, nightmares, inability to sleep), fatigue, sleepiness, feeling restless or agitated, feeling anxious, feeling sick (nausea) or being sick (vomiting), shaking (tremor), headaches, muscle pain, feeling irritable, diarrhoea, excessive sweating or vertigo.

These symptoms are usually not serious and occur within the first few days of stopping treatment. But they may be severe in some patients. These symptoms have also been reported in patients who have missed a dose. If you have symptoms that are troublesome you should ask your doctor for advice.

4. Possible side effects

CYMGEN can have side effects.

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

If any of the following happens, stop taking CYMGEN 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,
- rash or itching,
- fainting,
- blistering of the skin, mouth, eyes and genitals as these may be due to a serious allergic reaction known as Stevens-Johnson Syndrome (SJS).

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

- Thoughts of harming or killing yourself (suicidal behaviour), perceiving things that are not there (hallucinations),
- fit, seizure (convulsions),
- a rare reaction which may cause feelings of great happiness, drowsiness, clumsiness, restlessness, feeling of being drunk, fever, sweating or rigid muscles (serotonin syndrome),

- fast/slow or irregular heartbeat,
- increase in blood pressure that can lead to a stroke (hypertensive crisis),
- chest pain, dry cough, shortness of breath, especially with activity,
- bleeding in the stomach, passing of fresh blood in the stools, inflammation of the large intestine that causes persistent watery diarrhoea,
- liver disease with symptoms of stomach pain and swelling, and yellowing of the skin or whites of the eyes (jaundice),
- lesions and/or ulcers in the skin,
- excessive vaginal bleeding shortly after birth (postpartum haemorrhage).

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:

- Lack of appetite including anorexia which is an eating disorder causing people to obsess about weight and what they eat,
- trouble sleeping (insomnia),
- less sex drive, abnormal orgasm,
- problems getting an erection, and with ejaculation,
- anxiety, feeling agitated, also includes feeling jittery, nervousness, restlessness, tension,
- sleep disorder, unusual dreams, nightmares,
- headache, dizziness, feeling sluggish (lethargy, asthenia, fatigue), drowsiness, increased yawning, tremor,
- impaired sense of taste, numbness, tingling, pins and needles,
- blurred eyesight,
- ringing in the ears (tinnitus),

- increased blood pressure (hypertension), flushing (also includes hot flush),
- constipation, dry mouth, feeling sick (nausea), diarrhoea, being sick (vomiting), heartburn or indigestion, stomach pain, breaking wind,
- increased sweating,
- muscle pain, muscle spasm,
- falls,
- feeling tired,
- frequent urination,
- difficulty or inability to pass urine,
- weight loss.

Less frequent side effects:

- Throat inflammation that causes a hoarse voice,
- high blood sugar,
- dehydration, low levels of sodium in the blood mostly in elderly people; the symptoms may include feeling dizzy, weak, confused, sleepy or very tired, or feeling or being sick, more serious symptoms are fainting, fits or falls, syndrome of inappropriate secretion of antidiuretic hormone (SIADH), a condition that causes the body to retain water instead of excreting it normally in urine,
- excessive grinding of the teeth or clenching of the jaw (bruxism), confusional state (disorientation), feeling indifferent or lacking emotion (apathy),
- over activity, racing thoughts, extremely elevated and excitable mood (mania), aggression and anger,
- difficulty concentrating, sudden involuntary jerks or twitches of the muscles, uncontrolled urge to move the legs (restless legs syndrome), poor quality

sleep,

- large pupils, wide eyes, problems with eyesight, or increased pressure in the eye (glaucoma),
- ear pain, spinning feeling (vertigo),
- Takotsubo cardiomyopathy (a condition affecting heart muscle)
- feeling cold,
- low blood pressure,
- throat tightness, nose bleeds,
- painful swelling and sores inside the mouth, inflammation of the stomach and/or intestine, a stomach infection marked by diarrhoea, cramps, nausea, vomiting and fever leading to bad breath, burping,
- night sweats, sensitivity to sunlight, cold sweat, a skin rash caused by contact with a certain substance, hives, increased tendency to bruise,
- muscle tightness, muscle twitching, restriction of the range of motion of the jaws,
- difficulty to start urinating, needing to pass urine during the night, needing to pass more urine than normal, having a decreased urine flow, abnormal urine odour,
- menopausal symptoms, abnormal production of breast milk in men or women,
- pain in the testicles,
- abnormal vaginal bleeding, abnormal periods, including heavy, painful, irregular or prolonged periods, unusually light or missed periods,
- sexual dysfunction,
- feeling abnormal, feeling hot, malaise, thirst, gait disturbance,
- elevated liver enzymes seen on blood tests with symptoms of stomach pain, dark urine, feeling tired, itching, loss of appetite, nausea and vomiting,

- too much fatty substance in your blood (increased blood cholesterol) shown on blood tests,
- high potassium levels in your blood with symptoms of tiredness and muscle weakness,
- decreased thyroid gland activity which can cause tiredness or weight gain.

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 Reactions Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/+27 (0)11 239-6200

By reporting side effects, you can help provide more information on the safety of CYMGEN.

5. How to store CYMGEN

Store all medicines out of reach of children.

Store at or below 30 °C in blister packs.

Do not store in a bathroom.

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 and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What CYMGEN contains

CYMGEN 30

The active substance is duloxetine hydrochloride equivalent to 30 mg of duloxetine.

The other ingredients are carmoisine (E122), FD&C blue no. 2 aluminium lake (E132), gelatin, hypromellose, hypromellose acetate succinate, iron oxide yellow (E172), patent blue V (E131), propylene glycol, shellac (E904), sodium lauryl sulfate, sucrose, sugar spheres, talc, triethyl citrate, titanium dioxide (E171).

Contains sugar: Sucrose 55,5 mg

CYMGEN 60

The active substance is duloxetine hydrochloride equivalent to 60 mg of duloxetine.

The other ingredients are carmoisine (E122), gelatin, hypromellose, hypromellose acetate succinate, iron oxide yellow (E172), patent blue V (E131), povidone, propylene glycol, shellac (E904), sodium lauryl sulfate, sucrose, sugar spheres, talc, triethyl citrate, titanium dioxide (E171).

Contains sugar: Sucrose 110,6 mg

What CYMGEN looks like and contents of the pack

CYMGEN 30,

Hard gelatin capsule size ‘3’ opaque blue cap and opaque white body, imprinted with ‘F38’ on cap and body in green ink that contains white to light greyish white pellets.

CYMGEN 60,

Hard gelatin capsule size ‘1’ opaque blue cap and opaque green body, imprinted with ‘F39’ on cap and body in white ink that contains white to light greyish white pellets.

CYMGEN capsules are supplied in blister packs composed of cold-form aluminium laminate on one side and aluminium foil on the other side and packed in cartons of 28 capsules.

Holder of Certificate of Registration

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

Hotline: 0800 122 912/+27 (0)11 239-6200

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Registration numbers

CYMGEN 30: 41/1.2/1029

CYMGEN 60: 41/1.2/1030

Access to the corresponding Professional Information

SAHPRA Repository of Professional Information and

Patient Information Leaflets:

https://www.sahpra.org.za/pi-pil-repository/

Aspen Pharmacare:

E-mail: Medinfo@aspenpharma.com

Tel: 0800 118 088

Namibia: NS3
CYMGEN 30: 16/1.2/0201
CYMGEN 60: 16/1.2/0202

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