NOVARTIS

TEGRETOL® (carbamazepine)

200 mg tablet

200 mg and 400 mg controlled release, film-coated tablet

100mg/5 ml suspension

Patient Information Leaflet

Document status: Final

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SCHEDULING STATUS: S3

TEGRETOL® 200 Tablets

TEGRETOL® CR 200 Divitabs

TEGRETOL® CR 400 Divitabs

TEGRETOL® S Suspension

Carbamazepine

(Tablets: Sugar-free)

(Suspension: Contains sweetener (saccharin sodium and sorbitol))

Read all of this leaflet carefully before you start taking TEGRETOL

- 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.
- TEGRETOL 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 TEGRETOL is and what it is used for

What TEGRETOL is

The active substance of TEGRETOL is carbamazepine.

TEGRETOL belongs to a group of medicines called antiepileptics (medicine for seizures). TEGRETOL is used to treat certain types of seizures (epilepsy). It is also used to treat some neurological diseases (such as a painful condition of the face called ‘trigeminal neuralgia’) as well as certain psychiatric conditions (mania episodes of bipolar mood disorders and a certain type of depression).

2. What you need to know before you take TEGRETOL

The risk of serious skin reactions in patients of Han Chinese or Thai origin associated with carbamazepine or chemically related compounds may be predicted by testing a blood sample of these patients. Your doctor should be able to advise if a blood test is necessary before taking TEGRETOL.

Do not take TEGRETOL:

If you think you may be hypersensitive (allergic) to carbamazepine or similar medicines such as oxcarbazepine (Trileptal), or to any of a related group of medicines known as tricyclic antidepressants (such as amitriptyline or imipramine). If you are allergic to carbamazepine there is a one in four (25 %) chance that you could also have an allergic reaction to oxcarbazepine.

- If you are **allergic** (hypersensitive) to carbamazepine or to any of the other ingredients of TEGRETOL listed in this leaflet.

  Signs of a hypersensitivity reaction include swelling of the face or mouth (angioedema), breathing problems, runny nose, skin rash, blistering or peeling.

- If you have **severe heart disease.**
- If you have had **serious blood illnesses** in the past.
- If you have a **disturbance in the production of porphyrin**, a pigment important for liver function and blood formation (also called ‘porphyria’).
- If you have taken medicines belonging to a group of antidepressants called **monoamine-oxidase inhibitors (MAOIs),** within the last 14 days**.**
- Do not breastfeed your baby if you are taking TEGRETOL.
- If you previously developed a serious skin rash (Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN).

If this applies to you, **tell your doctor before taking TEGRETOL**. If you think you may be allergic, ask your doctor for advice.

Warnings and Precautions:

Take special care with TEGRETOL:

- **If you have blood illnesses** (including those caused by other medicines).
- If you have ever shown **unusual sensitivity** (rash or any other signs of allergy) to **carbamazepine, oxcarbazepine or to any other medicines**. It is important to note that if you are allergic to carbamazepine, the chances are approximately 1 in 4 (25 %) that you could also have an allergic reaction to oxcarbazepine.
- If you have or have had **heart, liver or kidney disease** in the past.
- If you have **increased pressure in the eye** (glaucoma) or if you have difficulty or pain when passing urine.

- If you were told by your medical practitioner that you suffer from a **mental disorder called psychosis** that may be accompanied by confusion or agitation.
- If you are a female of childbearing age, you should use an effective method of contraception throughout your treatment and for 2 weeks after your last dose. If you are **taking a hormonal contraceptive** (birth control medicine), TEGRETOL may render this contraceptive ineffective. Therefore, you should use a different or additional non-hormonal method of contraception while you are taking TEGRETOL.

Tell your doctor at once if you get irregular vaginal bleeding or spotting. If you have any questions about this, ask your doctor or health professional.

Tell your doctor if you are pregnant or plan to become pregnant. Your doctor will discuss with you the potential risk of taking TEGRETOL during pregnancy since it may cause harm or abnormalities in the unborn child (see section “Pregnancy”).

If any of the following applies to you, **tell your doctor immediately**.

- If an **allergic reaction** happens, such as swelling of lips, eyelids, face, throat, mouth, or sudden breathing problems, fever with lymph nodes swelling, rash or skin blistering, **tell your doctor immediately or go to the emergency department at your nearest hospital** (see section 4 - *Possible side effects*).
    - Serious skin rashes (Stevens- Johnson syndrome, toxic epidermal necrolysis) have been reported with the use of carbamazepine. Frequently, the rash can involve ulcers of the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These serious skin rashes are often preceded by influenza-like symptoms fever, headache, body ache (flu-like symptoms). The rash may progress to widespread

blistering and peeling of the skin. The highest risk for occurrence of serious skin reactions is within the first months of treatment.

- If you develop a rash or these skin symptoms, stop taking carbamazepine and contact your doctor immediately or go to the emergency department at your nearest hospital (see Possible side effects).
- These reactions may be more frequent in patients from some Asian countries (e.g. Taiwan, Malaysia and the Philippines) and in patients with Chinese ancestry. Studies found a strong correlation between serious skin reactions associated with TEGRETOL and the presence in these patients of the Human Leukocyte Antigen HLA-B*1502 allele.
- If you are a patient with a genetically at-risk population (populations for example, patients of the Japanese and Caucasian populations, patients who belong to the indigenous populations of the Americas, Hispanic populations, people of southern India, and people of Arabic descent), consider testing for the presence of HLA-A*3101. Before starting you on TEGRETOL your doctor should consider testing for the presence of HLA-B*1502 allele if you have ancestry in genetically at-risk populations.
- If you experience **an increase in the number of seizures**, tell your doctor immediately.
- If you notice **symptoms suggestive of hepatitis**, such as jaundice (yellowing of skin and eyes), tell your doctor immediately.
- A small number of people being treated with anti-epileptics such as carbamazepine have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.
- If you have **kidney problems** associated with low sodium blood level or if you have kidney problems and you are taking also certain medicines that lower sodium blood level (diuretics such as hydrochlorothiazide, furosemide).

- If you experience dizziness, drowsiness, decrease in blood pressure, confusion, due to TEGRETOL treatment, which may lead to falls.

Do not stop your treatment with TEGRETOL without first checking with your doctor. To prevent sudden worsening of your seizures, do not discontinue your medicine abruptly.

Other medicines and TEGRETOL

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

The use of TEGRETOL with these medicines may cause undesirable interactions.

Remember also, those not prescribed by a doctor. It is particularly important for TEGRETOL, since many other medicines interact with it. This includes in particular:

- Medicines that can raise carbamazepine levels: ibuprofen, danazol, macrolide antibiotics (e.g. erythromycin, clarithromycin), ciprofloxacin, desipramine, fluoxetine, fluvoxamine, nefazodone, paroxetine, stiripentol, vigabatrin, azoles (e.g. itraconazole, ketoconazole, fluconazole, voriconazole), olanzapine, isoniazid, acetazolamide, diltiazem, verapamil, cimetidine, omeprazole. Oxybutynin, dantrolene, ticlopidine, nicotinamide.
- Medicine that may raise the active metabolite 10,11–epoxide levels: loxapine, quetiapine, primidone, progabide, valproic acid, valnoctamide, valpromide and brivaracetam.
- Medicine that may decrease carbamazepine and/or carbamazepine-10,11-epoxide plasma levels: felbamate, methsuximide, oxcarbazepine, phenobarbitone,

phensuximide, phenytoin, primidone, clonazepam, cisplatin, doxorubicin, rifampicin, theophylline, aminophylline, isotretinoin, St John's Wort.

- The dosage of the following medicines may have to be adjusted to clinical requirements: buprenorphine, methadone, paracetamol, oral anticoagulants (e.g. warfarin, rivaroxaban and dabigatran), bupropion, citalopram, mianserin, nefazodone, trazodone, tricyclic antidepressants (e.g. imipramine, amitriptyline, nortriptyline, clomipramine), aprepitant, clobazam, clonazepam, ethosuximide, felbamate, lamotrigine, primidone, tiagabine, topiramate, valproic acid, zonisamide, phenytoin, itraconazole, praziquantel, albendazole, imatinib, cyclophosphamide, lapatinib, temsirolimus, clozapine, haloperidol and bromperidol, quetiapine, risperidone, ziprasidone, olanzapine, aripiprazole, paliperidone, alprazolam, theophylline, hormonal contraceptives, calcium channel blockers (felodipine, digoxin), corticosteroids, tadalafil, ciclosporin, everolimus, tacrolimus, sirolimus.

You may need a change in your dose or, sometimes, to stop one of the medicines.

Irregularity of the menstrual period may occur in women taking hormonal contraceptives (birth control medicines) and TEGRETOL. Hormonal contraceptives may become less effective, and you should consider using other effective contraceptive methods (non-hormonal).

TEGRETOL with food and drink:

Do not drink alcohol when you are on TEGRETOL.

Do not drink grapefruit juice or eat grapefruit since this can increase the effect of TEGRETOL. Other juices, like orange juice or apple juice, do not have this effect.

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 healthcare provider for advice before taking TEGRETOL, as TEGRETOL may harm your baby.

It is important to control epileptic seizures during pregnancy. However, there is a possible risk to your baby if you take antiepileptic medication (medicine for seizures) including TEGRETOL during pregnancy.

Risk of neurodevelopmental disorders cannot be excluded among children born to women with epilepsy treated with carbamazepine alone or in combination with other antiepileptic medicines during pregnancy.

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

Do not stop your treatment with TEGRETOL during pregnancy without first checking with your doctor.

Breastfeeding

Tell your doctor if you are breastfeeding. The active ingredient in TEGRETOL passes into the breast milk. Mothers on TEGRETOL should not breastfeed their infants.

Women of child-bearing potential

You should use an effective method of contraception throughout your treatment with TEGRETOL and for 2 weeks after the last dose. Irregularity of the menstrual period may occur in women taking hormonal contraceptives (birth control medicines) and TEGRETOL.

The hormonal contraceptive may become less effective, and you should consider using a different or additional non-hormonal contraceptive method.

Driving and using machines

TEGRETOL may make you feel sleepy or dizzy or may cause blurred vision, double vision, or you may have a lack of muscular coordination especially when starting treatment or increasing the dose. Therefore, be careful when driving a vehicle or operating a machine or doing other activities requiring careful attention.

TEGRETOL S Suspension contains sorbitol and parahydroxybenzoates

One ml of TEGRETOL oral suspension contains 175 mg of sorbitol. When taken according to the dosage recommendations, the maximum daily dose contains 17.5 g of sorbitol.

Sorbitol may cause stomach upset and diarrhoea. Patients with rare hereditary problems of fructose intolerance should not take TEGRETOL.

TEGRETOL oral suspension contains parahydroxybenzoates which may cause allergic reactions (possibly delayed).

3. How to take TEGRETOL

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

Always take TEGRETOL exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are not sure.
This will help you to get the best results and reduce the chance of serious side-effects. Do not take extra unprescribed doses of TEGRETOL, do not take it more often, and do not take it for a longer time than your doctor tells you.

Your doctor will tell you how long your treatment with TEGRETOL will last. If you are taking TEGRETOL, do not suddenly stop taking it without first checking with your doctor.
If you have the impression that the effect of TEGRETOL is too strong or too weak, tell your doctor or pharmacist.

Treatment of **epilepsy** with all forms of tablets and oral suspension is usually started at 100 to 200 mg once or twice a day in adults. The dosage is then gradually increased to 800 to 1 200 mg a day (in some patients 1600 mg a day may be needed), divided in 2 or 3 intakes.

Treatment in children is usually started at 100 to 200 mg day (based on 10 to 20 mg/kg body weight daily) and kept at 400 to 600 mg a day. Adolescents may receive between 600 and 1 000 mg a day.

For **trigeminal neuralgia** the starting dosage of 200 to 400 mg a day is slowly raised until there is no pain (usually 200 mg 3 to 4 times a day). For elderly patients a lower starting dose, 100 mg twice a day, is recommended.

For **acute mania and maintenance treatment of bipolar affective disorders** the usual dosage is 400 to 600 mg a day (dosage range: about 400 to 1 600 mg a day).
Your doctor will tell you exactly how many doses of TEGRETOL to take.

TEGRETOL is always (except possibly on the first day) given in divided daily doses, i.e. 2 to 4 times a day, depending on your medical condition.

The dose prescribed by your doctor may be different from those listed above. In this case follow your doctor's instructions.

Take TEGRETOL during or after a meal. Swallow the tablets with some liquid; if necessary, the tablets may be broken in half along the line.

If you take more TEGRETOL than you should

If you experience difficulty in breathing, a fast and irregular heartbeat, loss of consciousness, fainting, shakiness, sickness and/or vomiting, your dose may be too high. Stop taking your medicine and inform your doctor without delay.

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

If you forget to take TEGRETOL

If you forget to take a dose, take it as soon as possible. However, if it is almost time for your next dose, do not take the missed one; just go back to your regular dosing timetable. Do not double the dose to make up for the forgotten dose.

4. Possible side effects

TEGRETOL can have side-effects.

Not all side effects reported for TEGRETOL are included in this leaflet. Should your general

health worsen while taking TEGRETOL, please consult your health care provider for advice.

If any of the following happens, stop taking TEGRETOL and tell your doctor immediately or go to the casualty department at your nearest hospital:
They may be early signs of serious damage to your blood, liver, kidneys or other organs and may urgently need medical treatment.

- If you have swelling of the face, eyes, or tongue, difficulty swallowing, wheezing, hives and generalised itching, rash, fever, abdominal cramps, chest discomfort or tightness, difficulty breathing, unconsciousness (signs of angioedema and severe allergic reactions).
- If you have fever, sore throat, rash, ulcers in the mouth, swollen glands or more easily getting infections (signs of lack of white blood cells).
- If you have tiredness, headache, being short of breath when exercising, dizziness, looking pale, frequent infections leading to fever, chills, sore throat or mouth ulcers; bleeding or bruising more easily than normal, nose bleeds (lack of all blood cells).
- If you have red blotchy rash mainly on the face which may be accompanied by fatigue, fever, nausea, loss of appetite (signs of systemic lupus erythematosus).
- If you have any yellowing of the white of your eyes or your skin (signs of hepatitis).
- If you have darkening of urine (signs of porphyria or hepatitis).
- If you have severe decreased urine output due to kidney disorders, blood in the urine.
- If you have severe upper abdominal pain, vomiting, loss of appetite (signs of pancreatitis).
- If you have skin rash, redness of the skin, blistering of the lips, eyes or mouth, skin peeling, accompanied by fever, chills, headache, cough, body aches (signs of

serious skin reactions).

- If you have lethargy, confusion, muscular twitching or significant worsening of convulsions (symptoms that may be linked to low sodium levels in the blood).
- If you have fever, nausea, vomiting, headache, stiff neck and extreme sensitivity to bright light (signs of meningitis).
- If you have muscular stiffness, high fever, altered consciousness, high blood pressure, excessive salvation (signs of neuroleptic malignant syndrome).
- If you have irregular heartbeat, chest pain.
- If you have disturbed consciousness, fainting.
- If you have diarrhoea, abdominal pain and fever (signs of an inflammation of the colon). The frequency of this side effect is not known.
- If you experience a fall due to dizziness, drowsiness, decrease in blood pressure, confusion.

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

Frequent: loss of muscle coordination, allergic skin reactions

Less frequent: swelling of the ankles, feet or lower legs (oedema), changes in behaviour, confusion, weakness, increase in seizures (fits, due to insufficient amount of sodium in your body), blurred vision, double vision, itching with redness and swelling of the eye (conjunctivitis), feeling pressure/pain in the eye (signs of increased pressure in the eye), trembling, uncontrolled body movements, muscle spasms, uncontrolled eye movements, itching, swollen glands, agitation or hostility (especially in the elderly), fainting, difficulty in

speaking or slurred speech, depression with restlessness, nervousness or other mood or mental changes, hallucinations (seeing/hearing things that are not there), ringing or other unexplained sounds in the ears, decreased hearing, troubled breathing, chest pain, fast or unusually slow heartbeat, numbness, tingling in hands and feet, frequent urination, sudden decrease in amount of urine, taste disturbances, unusual secretion of breast milk, breast enlargement in men, swelling and redness along a vein which is extremely tender when touched, often experienced as painful (thrombophlebitis), increased sensitivity of the skin to sun, softening or thinning or weakening of bones causing an increased risk of broken bones (lack of vitamin D, osteoporosis).

Some side effects are of unknown frequency: reactivation of herpes virus infection (can be serious when the immune system is depressed), complete loss of the nails, bone fracture, decrease in the bone density.
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: vomiting, nausea, dizziness, sleepiness, unsteadiness, weight gain.
Less frequent side effects: headache, dry mouth, constipation, diarrhoea, abdominal pain, aching joints or muscles, increased sweating, loss of appetite, loss of hair, sexual disturbances, male infertility, red and sore tongue, mouth sores, alterations in skin pigmentation, acne.
Some side effects are of not known frequency: drowsiness, memory loss, purple or reddish-purple bumps that may be itchy.
If any of these affects you severely, tell your doctor.
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 or pharmacist. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

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

5. How to store TEGRETOL

TEGRETOL® 200

Store at or below 30 °C and protect from moisture.

TEGRETOL CR® 200 and TEGRETOL® CR 400

Store at or below 30 °C and protect from moisture.

TEGRETOL® S

Store below 30 °C and protect from light.

Store all medicines out of the reach of children.

Return any 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 TEGRETOL contains

TEGRETOL 200 Tablets: The active substance is 200 mg carbamazepine.

The other ingredients are colloidal anhydrous silica, microcrystalline cellulose, magnesium stearate, sodium carboxymethylcellulose.

TEGRETOL CR 200 and TEGRETOL CR 400 Controlled release, film-coated divisible tablets: The active substance is 200 mg and 400 mg carbamazepine.

The other ingredients are colloidal anhydrous silica, ethylcellulose aqueous dispersion, microcrystalline cellulose, polyacrylate dispersion, magnesium stearate, croscarmellose sodium, talc.

Coating: hypromellose, macrogolglycerol hydroxystearate, iron oxide red, iron oxide yellow, talc, titanium dioxide.

TEGRETOL S Suspension: The active substance is 100 mg/5 ml carbamazepine.

The other ingredients are microcrystalline cellulose + sodium carboxymethylcellulose, caramel aroma 52929 A, methylparaben, hydroxyethylcellulose, propylene glycol, polyethylene glycol 400 stearate, propylparaben, saccharin sodium, sorbic acid, sorbitol solution, purified water.

What TEGRETOL looks like and contents of the pack

TEGRETOL® 200

White, round tablet, flat on both sides, with slightly bevelled edges. Imprinted CG on one side, and G/K with a score on the other. Diameter approximately 9,0 mm. Thickness approximately 3,7 mm.

TEGRETOL® CR 200

Beige orange, ovaloid shaped, convex, film coated tablets, scored on both sides. Imprinted C/G on one side and H/C on the other. Approximately 12,2 x 5,6 mm and approximately

5,0 mm thick.

TEGRETOL® CR 400

Brownish orange, ovaloid shaped, convex, film coated tablets, scored on both sides. Imprinted CG/CG on one side and ENE/ENE on the other. Approximately 16,7 x 6,7 mm and approximately 6,0 mm thick.

TEGRETOL® S

A milky white, viscous suspension with the odour and taste of caramel.

TEGRETOL® 200 is supplied as tablets in packs of 50.

TEGRETOL® CR 200 and TEGRETOL® CR 400 are supplied in packs of 30.

TEGRETOL® S is supplied in bottles of 250 ml.

Holder of the Certificate of Registration

Novartis South Africa (Pty) Ltd

Magwa Crescent West,

Waterfall City, Jukskei View

Johannesburg, 2090

South Africa

+2710 347 6600

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TEGRETOL® 200	B1530 (Act 101/1965)
TEGRETOL® CR 200	V/2.5/321
TEGRETOL® CR 400	V/2.5/322
TEGRETOL® S	D/2.5/204

Access to the corresponding Professional Information

Can be obtained on the SAHPRA website

Tegretol S	Botswana	BOT 0400641	S2	Delpharm Huningue S.A.S 26, rue de la Chapelle, 68330 Huningue, France
	Namibia	90/2.5/00728	NS2	
Tegretol CR 200	Botswana	BOT 0400643	S2	Novartis Pharma S.p.A Via Provinciale Schito 131, 80058 Torre Annunziata, Italy
	Namibia	90/2.5/00726	NS2	
Tegretol CR 400	Botswana	BOT 0400644	S2	
	Namibia	90/2.5/00727	NS2	
Tegretol 200	Botswana	BOT 0400642	S2	
	Namibia	08/2.5/0131	NS2	