

Patient package insert according to Pharmacists' Regulations (Preparations) - 1986

This medicine can be sold with a physician's prescription only

Rephenidate® LA

10, 20, 30, 40, 60 mg

Modified-release capsules

Each capsule contains Methylphenidate hydrochloride 10, 20, 30, 40 or 60 mg respectively. Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine".

Read this entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is the same as yours.

1. What is the medicine intended for?

For treatment of Attention Deficit Hyperactivity Disorder (ADHD).

Therapeutic group: Central nervous system stimulant. **Rephenidate LA** capsules contain the active ingredient methylphenidate hydrochloride. Methylphenidate hydrochloride is a central nervous system stimulant.

Rephenidate LA capsules are used to treat Attention Deficit Hyperactivity Disorder (ADHD or hyperkinetic disorder) which is a behavioral disorder in children, adolescents, and adults. About 3% of children suffer from this disorder, which makes them unable to sit still or concentrate on tasks for any length of time. Children with this disorder may have difficulty in learning and doing homework.

It may frequently be difficult to manage them both in school and at home.

Adults with ADHD often find it hard to concentrate. They often feel restless, impatient, inattentive and become bored easily. They may experience difficulty organizing their private life and work.

Methylphenidate is assumed to work by regulating specific chemicals in the brain that affect behavior. It helps focus attention, shuts out distraction and allows impulsive people to think before they act. If treatment is successful, it improves the person's natural ability to be attentive.

This medicine is part of a treatment program which usually also includes psychological, educational and social therapy.

If you have any question about how **Rephenidate LA** works or why this medicine has been prescribed for you or your child, refer to your doctor.

2. Before using the medicine

Do not use the medicine:

- If you are hypersensitive (allergic) to the active ingredient (Methylphenidate) or to any of the other ingredients this medicine contains (see section 6). Some of the symptoms of an allergic reaction may include shortness of breath, wheezing or breathing difficulties; swelling of the face, lips, tongue or other parts of the body; rash, itching or hives on the skin.

Do not take Rephenidate LA if you are suffering from the following medical conditions:

- periods of anxiety, tension or agitation
- Tourette's syndrome (a condition of uncontrolled body movements and speech or tics) or if you have a family history of this disorder
- increased pressure in the eye (glaucoma)
- an overactive thyroid or other thyroid problems
- heart problems such as heart attack, irregular heartbeat, chest pain (angina pectoris), heart failure, heart disease or congenital heart problem
- very high blood pressure (hypertension) or narrowing of the arterial blood vessels (arterial occlusive disease, that may cause pain in the arms and legs)
- a rare tumor of the adrenal gland, known as pheochromocytoma

If you are unsure if you are suffering from any of the medical conditions listed above, ask the doctor.

Do not take Rephenidate LA if you are taking a medicine from the monoamine oxidase (MAO) inhibitors group or if you took MAO inhibitors within the 14 days before starting Rephenidate LA treatment (see section "Drug interactions"). Taking **Rephenidate LA** together with medicines from the MAO inhibitors group may cause a severe reaction, which includes a sudden rise in body temperature, extremely high blood pressure and severe convulsions.

If you are not sure if you took any of these medicines, ask the doctor.

Special warnings regarding the use of the medicine
Tell the doctor if you are allergic to any other medicine, food, dyes or preservatives.

The doctor will want to know if you are prone to allergies.

Before treatment with Rephenidate LA, tell the doctor if you are suffering from any of the listed medical conditions or behaviors:

- heart defects (e.g., structural cardiac abnormality)
 - tics (muscle twitching which is usually in the face or shoulders) or if your brothers or sisters have tics
 - family history of sudden death or irregular heartbeat
 - hardening of the arteries
 - any other current or previous heart problem
 - abnormality of the blood vessels in the brain, e.g., weakening of blood vessel (aneurysm), stroke or inflammation of blood vessels (vasculitis)
 - severe depression, bipolar disorder or other mental illnesses
 - suicidal thoughts or behavior
 - epilepsy (seizures, convulsions or fits)
 - high blood pressure
 - history of addiction to alcohol, drugs or drug dependence
 - acute mental disorders that cause abnormal thinking and perceptions (psychosis) or an unusual feeling of excitement, hyperactivity and disinhibition (acute mania) - the doctor will tell you if you have these conditions
 - psychotic symptoms such as seeing or feeling things that are not really there (hallucinations)
 - aggressive behavior
- If you have any of the conditions listed above, the doctor may want to take special precautionary measures.

Additional warnings

- **Rephenidate LA** may give a false-positive result in tests for drug use, including tests used in sports
- Some children receiving long-term **Rephenidate LA** may have slower growth, but, will usually catch up once the treatment is discontinued (also see sections: "Duration of treatment" and "Tests and follow-up")
- In some patients, **Rephenidate LA** may cause abdominal discomfort, loss of appetite and sleeping difficulties, especially at the beginning of treatment. The doctor can help reduce these symptoms by lowering

Rephenidate LA dose or by changing the time of administration of the medicine

- If you experience abnormally sustained or frequent and painful erections of the penis on **Rephenidate LA** treatment or after treatment discontinuation, you may need urgent medical treatment. This can occur in any age group. **If this happens, refer to a doctor immediately**
- If you are taking **Rephenidate LA** with medicines that raise the serotonin level in the body (serotonergic medicines such as sertraline and venlafaxine, used to treat depression), and you experience a combination of the following symptoms: restlessness, tremors, sudden muscle contractions, abnormally high fever, nausea and vomiting, stop treatment with **Rephenidate LA** and these medicines and refer to your doctor immediately
- If you are due to undergo surgery, inform the doctor that you are taking **Rephenidate LA**. Do not take **Rephenidate LA** on the day of surgery in case a certain type of anesthetic is used, since there is a chance of a sudden increase in blood pressure during surgery

Children and adolescents

The medicine is not intended for children under 6 years of age.

Tests and follow-up

Be sure to come to follow-up visits to the doctor so that treatment progress can be monitored. The doctor will periodically measure blood pressure, and perform blood tests, to prevent side effects.

If your child is not growing in height or gaining weight as expected, breaks in the **Rephenidate LA** administration may be necessary.

Drug interactions

If you are taking or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Some medicines and **Rephenidate LA** that are taken together may interfere with each other.

These medicines include:

- medicines that increase blood pressure
- oral anticoagulants or warfarin (medicines used to prevent blood clots)
- alpha-2 receptor agonists like clonidine (used to treat high blood pressure)
- medicines to treat depression, such as tricyclic antidepressants and monoamine oxidase (MAO) inhibitors. See also section "Do not use the medicine"
- certain anticonvulsants (to treat epilepsy or convulsions)
- phenylbutazone (to treat pain or fever)
- guanethidine
- anesthetics

• medicines that influence the level of dopamine in the body (dopaminergic medicines used to treat Parkinson's disease or psychosis)

• medicines that raise the serotonin level in the body (serotonergic medicines, e.g., those used to treat depression, like sertraline and venlafaxine)

It may be necessary to change the dosage of your medicines or you may have to take other medicines. Consult the doctor.

If you did not inform the doctor of the other medicines you are taking, consult him before taking **Rephenidate LA**.

If you are about to start treatment with a new medicine, remind your doctor, dentist, or pharmacist that you are being treated with **Rephenidate LA**.

Use of the medicine and food

Rephenidate LA capsules may be taken with or without food.

Use of the medicine and alcohol consumption

Do not consume alcohol during the course of treatment with **Rephenidate LA**. Remember that certain foods and medicines contain alcohol.

Alcohol consumption may exacerbate some of the side effects of **Rephenidate LA**, such as dizziness and drowsiness.

Pregnancy and Breastfeeding

Pregnancy

Do not use **Rephenidate LA** during pregnancy, unless the doctor explicitly prescribed it. This medicine may affect the unborn baby if you take it during pregnancy.

If you became pregnant while being treated with **Rephenidate LA**, consult the doctor. The doctor will discuss with you the risks and benefit of taking the medicine during pregnancy.

Breastfeeding

Do not breast-feed during the course of treatment with **Rephenidate LA**. The active ingredient in **Rephenidate LA** can pass into breast milk.

Driving and using machines

Exercise caution when driving, operating machines or performing activities that require alertness during the course of treatment with **Rephenidate LA**, until you know how this medicine affects you. This medicine may cause hallucinations, dizziness, drowsiness, blurred vision or other central nervous system side effects that may impair some people's ability to concentrate. If you experience any of these symptoms, do not drive a car, operate machines or perform activities that require rapid reactions or that may be dangerous.

As for children, they should be warned about riding a bicycle or playing near roads etc.

Important information about some of the ingredients of the medicine

This medicine contains sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How should you use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

Dosage:

The dosage and treatment regimen will be determined by the doctor only, according to the patient's needs and response to treatment.

Do not change the dosage without consulting the doctor. If you think that the effect of the medicine is too strong or too weak, consult the attending doctor.

Do not exceed the recommended dose.

Duration of treatment:

Continue taking **Rephenidate LA** for the duration of time instructed by the doctor.

This medicine helps regulate the symptoms, but does not cure. The doctor will check the improvement in your condition in order to confirm that the medicine is working properly and discuss with you the question of how long to continue treatment.

Treatment for ADHD varies in length from patient to patient. During the course of treatment of ADHD, the doctor may tell you to stop taking **Rephenidate LA** for certain periods of time (e.g., over weekends or school vacations) to see if it is still necessary to take it. These treatment breaks also help to prevent a slowdown in growth that sometimes occurs when children take this medicine for a long time.

Method of administration:

Rephenidate LA can be taken with or without food. Swallow the capsule whole, once daily in the morning, with a full glass of water. Do not crush, chew or divide the capsules, since it can damage the drug release mechanism.

If the patient is unable to swallow the capsule, the

capsule can be carefully opened and its content (small beads) sprinkled on a small amount of soft food (e.g., applesauce):

- Make sure the food is not hot because this could affect the special properties of the beads inside the capsule
- Immediately eat all of the medicine/food mixture
- Do not store the mixture for future use

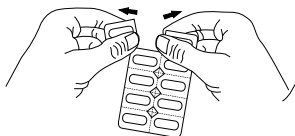
If the capsules cause you abdominal discomfort, they can be taken with food, but make sure to always take them the same way (i.e., always with food or always without food). In this way, the effect will always be the same.

Opening instructions for the blister

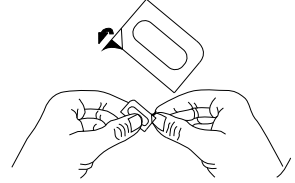
This medicine is available in peelable, child resistant blisters. Please observe the following opening instruction for the blister:

- Do not push the capsule out of the blister, as this will crush it.

- Take the blister with the printed foil up and bend it backwards along the perforated line. Bend the blister in the opposite direction and tear along the cross-perforation.



- Pull off a single dose by tearing along the perforated line on the blister and peel back the foil on the blister to expose the capsule.



If you have accidentally taken a higher dosage

Some of the symptoms of overdose are: vomiting, agitation, headache, tremors, muscle twitching, irregular heartbeat, flushing, fever, sweating, dilated pupils, breathing difficulties, confusion, seizures and muscle spasms accompanied by fever and red-brown urine.

If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room, and bring the package of the medicine with you. Do this even if you do not experience any signs of poisoning or discomfort.

If you forgot to take the medicine

If you forgot to take this medicine at the designated time, and you remembered before mid-day, take a dose as soon as you remember and go back to your usual schedule the following day.

If you did not remember to take it before mid-day, skip the missed dose and take the next dose the next morning, as usual. Do not take two doses together to compensate for the missed dose. If you do so, you may increase the chance of side effects.

If it is hard for you to remember when to take your medicine, consult the pharmacist.

Continue with the treatment as recommended by the doctor.

As with all stimulants, **this medicine can be addictive and abused by certain people**. If you take it properly, as instructed by the doctor, abuse or dependence should not be a problem, neither now nor in the future.

If you stop taking the medicine

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor. If you stop the treatment suddenly, your medical condition may return to its pretreatment state or side effects, such as depression, may occur. In order to avoid this, the doctor may tell you to reduce the daily dose gradually before stopping treatment completely. Medical supervision after stopping treatment is necessary.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Tell the doctor as soon as possible, if you do not feel well while you are taking Rephenidate LA.

Like any medicine, the use of **Rephenidate LA** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Report to the doctor immediately or proceed to an emergency room in the following cases:

- signs of an allergy, such as: swelling of face, lips or tongue, shortness of breath, wheezing or breathing difficulties. These are signs of a severe allergic reaction
 - weakness or paralysis of the limbs or face, difficulty speaking or unexplained fainting
 - skin rash, itching, red blotches on the skin, blisters or peeling of the skin
 - sudden increase in body temperature, sweating, fast heartbeat, chest pain, muscle stiffness and blood pressure fluctuations, which may lead to coma
 - constant "flu-like" symptoms such as chills, fever, sore throat and runny nose, swollen glands, aching muscles or joints
 - unusual bleeding or skin bruising
 - unusual tiredness, shortness of breath when exercising, dizziness, pale skin
 - involuntary shaking of the body (signs of tremor), such as uncontrollable twitching, jerking or writhing movements
 - seizures (fits) or unexplained fainting
 - pain or tightness in the chest
 - fast or irregular heartbeat
 - yellowing of the skin or eyes, dark-colored urine or light-colored stools
 - confusion, hallucinations or delusions (seeing or feeling things that are not really there)
 - excitement, hyperactivity and uninhibited behavior
 - severe or persistent headache
 - uncontrolled speech and body movements (Tourette's syndrome)
 - prolonged erection, causing discomfort of the penis (sign of priapism)
 - thoughts or attempts of killing yourself (suicidal ideation or attempt, including completed suicide)
 - fingers and toes feeling numb, feeling cold, tingling and changing color (from white to blue, and then red) when cold (Raynaud's phenomenon, peripheral coldness)
- The side effects listed above may be serious. Urgent medical attention may be necessary.

Additional side effects

Tell the doctor if you notice any of the following effects and it worries you:

Very common side effects (effects that occur in more than 1 in 10 users):

- nausea
- loss of appetite
- sore throat and runny nose
- nervousness
- inability to sleep
- dry mouth

Common side effects (effects that occur in 1-10 out of 100 users):

- vomiting or abdominal pain
- upset stomach or indigestion
- feeling anxious or agitated
- feeling jittery
- restlessness
- sleep disorders
- headache
- cough
- drowsiness
- dizziness
- irritability
- hair loss
- hives (urticaria)
- joint pain
- toothache
- excessive sweating
- abnormal heart rate
- palpitations
- excessive emotional distress or excitement
- decreased weight
- feeling depressed
- feeling aggressive
- excessive teeth grinding

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

- trismus - spasm of the jaw muscles that makes it difficult to open the mouth

Rare side effects (effects that occur in 1-10 out of 10,000 users):

- weight loss and slowed growth in children
- blurred vision or visual focus disturbances

Very rare side effects (effects that occur in less than 1 in 10,000 users):

- transient depressed mood
- muscle cramps
- anemia (a reduction in the number of red blood cells), leukopenia (a reduction in the number of white blood cells), thrombocytopenia (a reduction in the number of platelets)

Side effects with unknown frequency (effects for which a frequency has not yet been determined):

- stuttering
- bed wetting in children at night

Additional side effects that occurred with other medicines that contain the same active ingredient as Rephenidate LA:

- inflammation of the nasal passages and throat
- a reduction in the number of blood cells (red blood cells, white blood cells and platelets) at once
- swelling of the ears (a sign of an allergic reaction)
- irritability, aggression, mood changes, abnormal behavior or thinking, anger, excessive awareness of surroundings, feeling unusually excited, over-active and uninhibited (mania), disorientation, change in sex drive, lack of feeling or emotion, doing things over and over again, being obsessed with one thing, confusion, addiction
- temporary muscle weakness, loss of skin sensation or other functions of the body due to a temporary lack of blood supply to the brain (reversible ischemic neurological deficit), migraine
- double vision, dilated pupils, trouble seeing
- stopped heartbeat, heart attack
- sore throat, shortness of breath
- diarrhea, constipation
- swelling of face and throat, reddening of the skin, large red blotches on the skin appearing within a few hours of taking the medicine
- muscle pain, muscle twitching
- blood in the urine
- swelling of the breasts in men
- chest pain, tiredness, sudden death
- abnormal sounds from the heart

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult the doctor.

Reporting side effects:

Side effects can be reported to the Ministry of Health by clicking the link "דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health (www.health.gov.il) directing to the online form for reporting side effects or via the link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

• Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

• Do not use the medicine after the expiry date (EXP DATE) stated on the package. The expiry date refers to the last day of that month.

• Storage conditions: Store below 25°C.

6. Additional information

In addition to the active ingredient, the medicine also contains:

Sugar spheres, methacrylic acid-methyl methacrylate copolymer (1:1), ammonio methacrylate copolymer (type B), povidone, talc, triethyl citrate, gelatin, titanium dioxide (E171), red ink (shellac glaze, propylene glycol, red iron oxide (E172), strong ammonia solution, potassium hydroxide)

In addition, **Rephenidate LA** 10mg, 30mg, 40mg and 60mg contain: iron oxide yellow (E172).

What the medicine looks like and what the package contains:

Rephenidate LA 10mg, 20mg, 30mg, 40mg and 60mg capsules contain white and whitish pellets.

Rephenidate LA 10mg: A capsule with dark yellow opaque cap and a white opaque body, imprinted with "RUB" in red on the cap and "M10" in red on the body.

Rephenidate LA 20mg: A white opaque capsule, imprinted with "RUB" in red on the cap and "M20" in red on the body.

Rephenidate LA 30mg: An ivory opaque capsule, imprinted with "RUB" in red on the cap and "M30" in red on the body.

Rephenidate LA 40mg: A dark yellow opaque capsule, imprinted with "RUB" in red on the cap and "M40" in red on the body.

Rephenidate LA 60mg: A capsule with dark yellow opaque cap and an ivory opaque body, imprinted with "RUB" in red on the cap and "M60" in red on the body.

Each package of **Rephenidate LA** contains 30 capsules.

Manufacturer and address: Laboratorios Rubio S.A., Barcelona, Spain
Revised in September 2022 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health:

Rephenidate LA 10mg capsules: 170-55-37007-99

Rephenidate LA 20mg capsules: 170-56-37008-99

Rephenidate LA 30mg capsules: 170-57-37009-99

Rephenidate LA 40mg capsules: 170-58-37010-99

Rephenidate LA 60mg capsules: 170-59-37011-99

Registration holder:

Dexcel® Ltd.

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