Patient leaflet in accordance with the Pharmacists' Regulations (preparations) - 1986
The medicine is dispensed according to a doctor's prescription only

Sifrol® ER 0.375
Sifrol® ER 0.75
Sifrol® ER 1.5
Extended-release tablets

Each tablet of Sifrol ER 0.375 contains pramipexole dihydrochloride monohydrate 0.375 mg
Each tablet of Sifrol ER 0.75 contains pramipexole dihydrochloride monohydrate 0.75 mg
Each tablet of Sifrol ER 1.5 contains pramipexole dihydrochloride monohydrate 1.5 mg

Inactive ingredients and allergens in the medicine - see section 6 'Additional information'.

Read the entire leaflet carefully before you start using the medicine. This leaflet contains concise information about the medicine. If you have further questions, contact your doctor or pharmacist.

Keep the leaflet. You may need to read it again.

This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is the medicine intended for?

The medicine is intended for the treatment of signs and symptoms of Parkinson's disease, as monotherapy or in combination with levodopa (an additional medicine intended for treatment of Parkinson's disease).

Therapeutic group: medicines that activate the dopamine receptor (dopaminergic medicines).

Sifrol ER contains the active ingredient pramipexole and belongs to a group of medicines known as dopaminergic medicines, which stimulate dopamine receptors in the brain, thereby triggering nerve impulses in the brain that help to control body movements.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient pramipexole or to any of the additional ingredients that the medicine contains (for the list of inactive ingredients, see section 6 'Additional information').
- You are breastfeeding.

Special warnings about using the medicine
Before treatment with Sifrol ER, tell your doctor if you have (or had) or if you develop symptoms or medical conditions, especially any of the following:

- Kidney disease.
- Hallucinations (seeing, hearing or feeling things that are not there). Most hallucinations are visual.

- Dyskinesia (e.g. abnormal, uncontrolled movements of the limbs). If you suffer from advanced Parkinson's disease and are also taking levodopa, you might develop dyskinesia during the up-titration of Sifrol ER.
- Dystonia [inability of keeping the body and neck straight and upright (axial dystonia)]. In particular, you may experience forward flexion of the head and neck, forward bending of the lower back, or sideward bending of the back.
- Sleepiness and episodes of suddenly falling asleep.
- Psychosis (e.g. resembles with symptoms of schizophrenia).
- Vision impairment. Regular periodic eye examinations should be performed during the treatment with Sifrol ER.
- Severe heart or blood vessels disease. You will need to have your blood pressure monitored regularly, especially at the beginning of treatment. This is to avoid postural hypotension (a fall in blood pressure on standing up).

Tell the doctor if you or your family/carer notices that you are developing urges or cravings to behave in a way that is unusual for you, and you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include behaviours such as addictive gambling, excessive eating or spending, an abnormally high sex drive or increased frequency of sexual thoughts or feelings. Your doctor may need to adjust the dosage or stop the treatment.

Tell the doctor if you or your family/carer notices that you are developing mania (agitation, elated mood or over-excitement) or delirium (decreased awareness, confusion, loss of contact with reality). Your doctor may need to adjust your dosage or stop the treatment.

Tell the doctor if you experience symptoms such as depression, apathy, anxiety, tiredness, sweating or pain after stopping treatment or reducing your Sifrol ER dosage. If the symptoms persist throughout more than a few weeks, the doctor may need to adjust your treatment.

Tell your doctor if you are developing an inability of keeping the body and neck straight and upright (axial dystonia). In such situation, your doctor may want to adjust your dosage or change the treatment.

Sifrol ER tablets have been specially designed to enable gradual release of the active ingredient once the tablet has been ingested. Parts of the tablets may occasionally pass and appear in your stool (faeces) and may look like whole tablets. Tell your doctor if you notice tablet parts in the stool.

Children and adolescents
Sifrol ER is not intended for use in children and adolescents under the age of 18 years.

Tests and follow-up
Use of the medicine may cause vision impairment. Regular periodic eye examinations should be performed during the treatment with Sifrol ER. You will also need to have your blood pressure monitored regularly, especially at the beginning of treatment with the medicine (see section 2 'Special warnings about using the medicine').

Drug interactions
If you are taking or have recently taken or may take other medicines, including non-prescription medicines and dietary supplements, tell the doctor or pharmacist.

Avoid taking Sifrol ER together with antipsychotic medicines.

Particularly inform the doctor or pharmacist if you are taking:
- cimetidine (to treat excess stomach acid and stomach ulcers)
- amantadine (can be used to treat Parkinson's disease)
- mexiletine (to treat irregular heartbeats, a condition called ventricular arrhythmia)
- zidovudine (can be used to treat AIDS, acquired immune deficiency syndrome, which is a disease of the human immune system)
- cisplatin (to treat various types of cancer)
- quinine [can be used for the prevention of painful night-time leg cramps and for the treatment of a type of malaria known as falciparum malaria (malignant malaria)]
- procainamide (to treat irregular heart beat).

If you are treated with levodopa - the dosage of levodopa is recommended to be reduced when you start treatment with Sifrol ER.

Take care if you are taking any sedatives (have a sedative effect) or if you are drinking alcohol. In these cases, Sifrol ER may affect your ability to drive and operate machines.

Using the medicine and food
Sifrol ER can be taken with or without food.

Using the medicine and alcohol consumption
Be cautious while drinking alcohol during the period of treatment with Sifrol ER.

Pregnancy and breastfeeding
If you are pregnant, think that you are pregnant, planning a pregnancy or are breastfeeding, consult the doctor before using the medicine. The doctor will discuss with you if you should continue taking Sifrol ER.
The effect of Sifrol ER on the unborn child is not known. Therefore, do not use Sifrol ER if you are pregnant, unless instructed otherwise by the doctor.

Do not use the medicine during breastfeeding. Sifrol ER may reduce the production of breast milk. Also, the medicine can pass into the breast milk and may reach your baby. If the use of Sifrol ER is unavoidable, breastfeeding should be stopped.

Consult the doctor or pharmacist before taking any medicine.

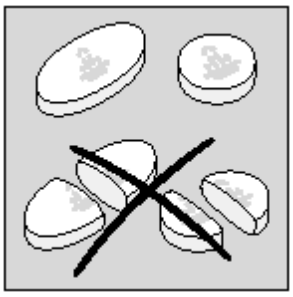
Driving and using machines
Sifrol ER may cause hallucinations (seeing, hearing or feeling things that are not there). If affected by the medicine in this manner, do not drive or operate machines.
Sifrol ER has been associated with sleepiness and episodes of suddenly falling asleep, particularly with Parkinson's disease patients. If you experience these side effects, you must not drive or operate machines. You should tell your doctor if these effects happen to you.

3. How to 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 how to take the medicine.
Only the doctor will determine the dosage and how to take the medicine.

The usual dosage is usually: Take the medicine once a day, at about the same time every day.

Do not exceed the usual dose.
Sifrol ER can be taken with or without food. Swallow the tablets whole with water.
Do not chew, divide or crush the extended-release tablets. Chewing, dividing or crushing the tablet may cause an overdose, because the medicine may be released into the body too quickly.



During the first week, the usual daily dose is 0.375 mg Sifrol ER. The dose will be increased every 5-7 days as directed by your doctor until your symptoms are controlled (maintenance dose).

Ascending dose schedule of Sifrol ER		
Week	Daily dose (mg)	Number of tablets
1	0.375	one Sifrol ER 0.375 mg tablet
2	0.75	one Sifrol ER 0.75 mg tablet OR two Sifrol ER 0.375 mg tablets
3	1.5	one Sifrol ER 1.5 mg tablet OR two Sifrol ER 0.75 mg tablets OR four Sifrol ER 0.375 mg tablets

The usual maintenance dose is 1.5 mg per day. However, your dose may be increased even further. If necessary, the doctor can increase your dose up to a maximum dose of 4.5 mg of pramipexole (the active ingredient in the salt formulation) per day. A lower maintenance dose of one Sifrol ER 0.375 mg tablet per day is also possible.

<u>Patients with kidney disease:</u>
If you suffer from kidney disease, your doctor may advise you to take the starting dosage of 0.375 mg Sifrol ER not every day, but only every other day during the first week. After that, the doctor may increase the dosing frequency to one Sifrol ER 0.375 mg tablet every day. If a further dosage increase is necessary, the doctor can increase the dosage by adding 0.375 mg Sifrol ER at a time.

If you suffer from serious kidney problems, your doctor may change the medicine to a different medicine. If during treatment the kidney problems get worse, contact the doctor as soon as possible.

<u>If you are switching from Sifrol immediate release tablets:</u>
Your doctor will base the dosage of Sifrol ER extended-release tablets on the dosage of Sifrol immediate release tablets you were taking.

Take your Sifrol (immediate release) tablets as normal the day before switching. Then take your Sifrol ER extended-release tablets next morning and stop taking Sifrol (immediate release) tablets.

If you have accidentally taken a higher dosage or if a child has accidentally swallowed some medicine, immediately see a doctor or go to the nearest hospital emergency room and bring the medicine package with you.
Taking an overdose may cause vomiting, restlessness, or other side effects described in section 4, 'Side effects'.

If you forget to take the medicine
If you forget to take the medicine, but less than 12 hours have passed from the usual intake time, take the forgotten dose immediately once you remember and the next dose at the usual time.
If you forget to take the medicine, and more than 12 hours have passed, skip the forgotten dose and take the next dose at the usual time.
Do not take a double dose in order to make up for a forgotten dose.
Adhere to the treatment as recommended by the doctor.
Even if your health status improves, do not stop taking the medicine without consulting the doctor.

If you stop taking the medicine
Do not stop taking Sifrol ER prior to consulting your doctor. If you have to stop taking the medicine, your doctor will reduce the dosage gradually in order to reduce the risk of worsening symptoms.

If you suffer from Parkinson's disease, do not stop treatment with this medicine abruptly. A sudden stop could cause you to develop a medical condition called neuroleptic malignant syndrome, which may represent a major health risk. The symptoms include:

- akinesia (loss of muscle movement)
- rigid muscles
- fever
- unstable blood pressure
- tachycardia (increased heart rate)
- confusion
- depressed level of consciousness (e.g. coma).

If you stop the treatment or reduce your Sifrol ER dosage, you may develop a medical condition called dopamine agonist withdrawal syndrome (DAWS). The symptoms include depression, apathy, anxiety, tiredness, sweating or pain. If you suffer from these symptoms, you should contact your doctor.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them.
If you have further questions about using the medicine, consult the doctor or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using Sifrol ER may cause side effects in some users. Do not be alarmed by the list of side effects; you may not suffer from any of them.

Very common side effects (occur in more than 1 in 10 users):
- Dyskinesia (e.g. abnormal, uncontrolled movements of the limbs).
- Sleepiness
- Dizziness
- Nausea

Common side effects (occur in 1-10 in 100 users):
- Urge to behave in an unusual way
- Hallucinations (seeing, hearing or feeling things that are not there)
- Confusion
- Tiredness (fatigue)
- Sleeplessness (insomnia)
- Accumulation of fluid, usually in the legs (peripheral oedema)
- Headache
- Low blood pressure (hypotension)
- Abnormal dreams
- Constipation
- Visual impairment
- Vomiting
- Weight loss including decreased appetite

Uncommon side effects (occur in 1-10 in 1,000 users):
- Paranoia (e.g. excessive fear for one's own wellbeing)
- Delusions
- Excessive daytime sleepiness or suddenly falling asleep
- Amnesia (memory disturbance)
- Excessive movements and inability to keep without movement (hyperkinesia)
- Weight increase
- Allergic reactions (e.g. rash, itching, hypersensitivity)
- Fainting
- *Cardiac failure (heart problems which may cause shortness of breath or ankle swelling)
- *Syndrome of inappropriate antidiuretic hormone (ADH) secretion
- Restlessness
- Difficulties to breathe (dyspnoea)
- Hiccups
- infection of the lungs (pneumonia)
- Inability to resist the impulse, drive or temptation to perform an action that could be harmful to you or others, these actions may include:
    - Strong impulse to gamble excessively despite serious personal or family consequences
    - Altered or increased sexual interest and behavior of significant concern to you or to others, for example, an increased sexual drive
    - Uncontrollable excessive shopping or spending
    - *Binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy the hunger)
- Delirium (decreased awareness, confusion, loss of contact with reality)

Rare side effects (occur in 1-10 in 10,000 users):
- Mania (agitation, elated mood or over-excitement)
- Spontaneous penile erection

Side effects of unknown frequency (the frequency of these effects has not been established yet):

- After stopping treatment or reducing your Sifrol ER dosage: Depression, apathy, anxiety, tiredness, sweating or pain may occur (also known as dopamine agonist withdrawal syndrome or DAWS).

Tell your doctor if you experience any of these behaviours; he will discuss with you ways of managing or reducing the symptoms.

For the side effects marked with - * a precise frequency estimation is not possible, since these side effects were not observed in clinical studies among 2,762 patients treated with pramipexole. The frequency category for these side effects is probably not greater than “uncommon side effects" category.

If you experience any side effect, if any side effect gets worse, or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Reporting side effects
You can report side effects to the Ministry of Health by following the link ‘Reporting Side Effects of Drug Treatment’ on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use the link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store in the original package to protect from moisture, at a temperature below 25°C.
- Do not throw away medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

- In addition to the active ingredient, the medicine also contains:
  maize starch, hypromellose 2208, carbomer 941, colloidal anhydrous silica, magnesium stearate
- What the medicine looks like and contents of the pack:
  Sifrol ER 0.375 and Sifrol ER 0.75 are white to off-white tablets of round shape, convex on both sides with bevelled edges. One side of the tablet is debossed with the Boehringer Ingelheim logo, "BI"; and the other side is debossed with "P1" (Sifrol ER 0.375) and "P2" (Sifrol ER 0.75).
  Sifrol ER 1.5 are white to off-white tablets of oval shape, convex on both sides. One side of the tablet is debossed with the Boehringer Ingelheim logo, "BI"; and the other side is debossed with "P3".
  The tablets are packed in blister strips. Each package contains 10 or 30 extended-release tablets. Not all pack sizes may be marketed.

- Registration holder's, importer's name and address: Boehringer Ingelheim Israel Ltd., 89 Medinat Ha-Yehudim, P.O. Box 4124, Herzliya Pituach 4676672.
- This leaflet was revised in October 2024.
- Registration number of the medicine in the Ministry of Health's National Drug Registry:
  Sifrol ER 0.375 - 144-95-33088-00
  Sifrol ER 0.75 - 144-96-33089-00
  Sifrol ER 1.5 - 144-97-33090-00