Patient leaflet insert according to the Pharmacists' Regulations (Preparations) – 1986
This medicine is to be supplied by physician's prescription only

PROTELOS
Granules for oral suspension

Active ingredient:
Each sachet contains:
Strontium ranelate 2g.
Inactive ingredients: see section 6.

Read this package insert carefully in its entirety before using this medicine.
The leaflet contains concise information about PROTELOS. If you have any questions, refer to your physician or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.
PROTELOS is not intended for use in children and adolescents (below the age of 18).

1. What is PROTELOS used for?
Treatment of severe osteoporosis in postmenopausal women, at high risk of fracture, for whom treatment with other medicinal products approved for the treatment of osteoporosis is not possible due to, for example, contraindications or intolerance.

In postmenopausal women, strontium ranelate reduces the risk of fracture at the spine and at the hip.

Therapeutic group: Medicines that affect bone structure and mineralisation.

About osteoporosis
Your body is constantly breaking down old bone and making new bone tissue. If you have osteoporosis, your body breaks down more bone than it forms so that gradually bone loss occurs and your bones become thinner and fragile. This is especially common in women after the menopause. Many people with osteoporosis have no symptoms and you may not even know that you have it. However, osteoporosis makes you more likely to have fractures (break bones), especially in your spine, hips and wrist.

How PROTELOS works?
PROTELOS, which contains the substance strontium ranelate, belongs to a group of medicines used to treat bone diseases.
PROTELOS works by reducing bone fragility and stimulating rebuilding of bone and therefore reduces the risk of fracture. The newly formed bone is of normal quality.

2. Before using PROTELOS

X Do not use PROTELOS:

- If you are allergic to strontium ranelate or any of the other ingredients of PROTELOS (listed in section 6).
- If you have or have had a blood clot (for example, in the blood vessels in your legs or lungs).
- If you are immobilised permanently or for some time such as being wheel-chair bound, or confined to bed or if you are to undergo an operation or recovering from an operation. The risk of vein thrombosis (blood clots in the leg or lungs) may be increased in the event of lengthy immobilisation.
- If you have established ischemic heart disease, or cerebrovascular disease, e.g. you have been diagnosed with a heart attack, stroke, or transient ischemic attack (temporary reduction of blood flow to the brain; also known as "mini-stroke"), angina, or blockages of blood vessels to the heart or brain.
- If you have or have had problems with your blood circulation (peripheral arterial disease) or if you have had surgery on the arteries of your legs.
- If you have high blood pressure not controlled by treatment.

! Special warnings regarding the use of PROTELOS:

Before taking PROTELOS, tell your physician:

- If you are at risk of heart disease, this includes high blood pressure, high cholesterol, diabetes, smoking.
- If you are at risk of blood clots.
- If you have severe kidney disease.

Your physician will evaluate the conditions of your heart and blood vessels regularly, generally every 6 to 12 months for as long you are taking PROTELOS.

Take special care with PROTELOS:

- During treatment if you experience an allergic reaction (such as swelling of the face, tongue or throat, difficulty in breathing or swallowing, skin rash), you must immediately stop taking PROTELOS and seek medical advice (see section 4).
- Potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis and severe hypersensitivity reactions (DRESS)) have been reported with the use of PROTELOS.
  - The highest risk of occurrence of serious skin reactions is within the first weeks of treatment for Stevens-Johnson syndrome and toxic epidermal necrolysis and usually around 3-6 weeks for DRESS.
  - If you develop a rash or these skin symptoms, stop taking PROTELOS, seek urgent advice from a physician and tell him that you are taking this medicine.
  - If you have developed Stevens-Johnson syndrome or toxic epidermal necrolysis or DRESS with the use of PROTELOS, you must not be re-started on PROTELOS at any time.
  - If you are of Asian origin, talk to your physician before taking PROTELOS as you may be at higher risk of skin reactions.

If you are taking, have recently taken or might take any other medicines, including non-prescription medicines or food supplements, tell your physician or pharmacist. Especially inform your physician or pharmacist if you are taking:

- Medicines containing calcium, you should wait at least 2 hours before you take PROTELOS.
- Antacids (medicines to relieve heartburn), you should take them at least 2 hours after PROTELOS. If this is not possible, it is acceptable to take the two medicines at the same time.
- You should stop taking PROTELOS if you have to take oral tetracyclines such as doxycycline or quinolones such as ciprofloxacin (two types of antibiotics). You can take PROTELOS again when you have finished taking these antibiotics. If you are unsure about this ask your physician or pharmacist.

If you need to have blood or urine tests to check your level of calcium, you should tell the laboratory that you are taking PROTELOS as it may interfere with some testing methods.

Using the medicine and food
Food, milk and milk products reduce the absorption of strontium ranelate. It is recommended that you take PROTELOS in-between meals, preferably at bedtime at least two hours after food, milk or milk products or calcium supplements.

Pregnancy and breast-feeding:
PROTELOS is meant for use only in postmenopausal women. Do not take PROTELOS during pregnancy or when you are breastfeeding. If you take it by accident during pregnancy or breastfeeding, stop taking it straight away and talk to your physician.

Driving and using machines
PROTELOS is not expected to have any effect on your ability to drive or use machines.

Important information about some ingredients of the medicine
PROTELOS contains aspartame (E951). If you suffer from phenylketonuria (a rare, hereditary disorder of the metabolism) talk to your physician before you start to take this medicine.

3. How should you use the medicine?

The treatment should only be started by a physician with experience in treating osteoporosis.
Always use according to the physician's instructions.
You should check with your physician or pharmacist if you are not sure.
The dosage and treatment will be determined only by the physician.
The recommended dosage is one 2g sachet a day.
Do not exceed the recommended dosage.

Instruction for use:
Protelos is intended for oral use.
It is recommended that you take PROTELOS at bedtime, preferably at least 2 hours after dinner. You may lie down immediately after taking PROTELOS if you wish.

PROTELOS can interact with milk and milk products, so it is important that you mix PROTELOS only with water to be sure it works properly.

Take the granules contained in the sachets as a suspension in a glass containing a minimum of 30 ml (approximately one third of a standard glass) of water. See instructions below.

Empty the granules from the sachet into a glass.

Add water.

Stir until the granules are evenly dispersed in the water.

Drink straight away. If for some reason you cannot drink the medicine straight away, make sure you stir it again before drinking. You should not leave more than 24 hours before you drink it.

If you accidently have taken a higher dosage you should consult your physician. The physician might advise you to drink milk or take antacids to reduce the absorption of the active substance.
If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a physician or to the hospital emergency room and bring the package of the medicine with you.

If you forgot to take PROTELOS at the scheduled time, do not take a double dose. Take the next dose at the usual time and consult the physician.

If you stop taking PROTELOS
It is important that you continue taking PROTELOS for as long as your physician prescribes the medicine. PROTELOS can treat your severe osteoporosis only if you continue to take it.
Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting the physician or the pharmacist.

How can you contribute to the success of the treatment?
Osteoporosis-therapy is usually required for a long period.
Your physician may advise you to take calcium and vitamin D supplements in addition to PROTELOS.
Do not take calcium supplements at bedtime, at the same time as PROTELOS.

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

If you have any further questions on the use of this medicine, ask your physician or pharmacist.

4. Side Effects:

As with any medicine, use of PROTELOS may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

If the following happens to you, stop using PROTELOS and talk to your physician immediately:

Common (may affect up to 1 in 10 people):
Heart attack: sudden crushing pain in your chest which may reach your left arm, jaw, stomach, back and/or shoulders. Other symptoms may be nausea/vomiting, sweating, shortness of breath, palpitations, (extreme) tiredness and/or dizziness. Heart attack may occur commonly in patients at high risk for heart disease. Your physician will not prescribe PROTELOS for you if you are at particular risk.
Blood clots in veins: pain, redness, swelling in your leg, sudden chest pain or difficulty breathing.

Rare (may affect up to 1 in 1000 people):
Signs of severe hypersensitivity reactions (DRESS): initially as flu-like symptoms and a rash on the face, than an extended rash with a high temperature (uncommon), increased levels of liver enzymes seen in blood tests (uncommon) an increase in a type of white blood cell (eosinophilia) (rare) and enlarged lymph nodes (uncommon).

Very rare (may affect up to 1 in 10,000 people):
Signs of potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis): initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs may include ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These potentially life-threatening skin rashes are often accompanied by flu-like symptoms. The rash may progress to widespread blistering or peeling of the skin.

Other possible side effects:

Very Common (may affect more than 1 in 10 people):
Itching, hives, skin rash, angioedema (such as swollen face, tongue or throat, difficulty in breathing or swallowing), bone, limb, muscle and/or joint pain, muscle cramps.

Common (may affect up to 1 in 10 people):
Vomiting, abdominal pain, reflux, indigestion, constipation, flatulence, difficulty in sleeping, inflammation of the liver (hepatitis), swelling in limbs, bronchial hypereactivity (symptoms include wheezing and shortness of breath and cough), increased level of a muscle enzyme (Creatine phosphokinase), increased levels of cholesterol.
Nausea, diarrhoea, headache, eczema, fainting fit, memory trouble, pins and needles, dizziness, vertigo.

However, these effects are mild and short-lived and usually do not cause the patients to stop taking their treatment. Talk to your physician if any effects become troublesome or persist.

Uncommon (may affect up to 1 in 100 people):
Seizures, oral irritation (such as mouth ulcers and gum inflammation), hair loss, feeling confused, feeling unwell, dry mouth, skin irritation

Rare (may affect up to 1 in 1,000 people):
Reduction in production of blood cells in the bone marrow.

If you have stopped treatment due to hypersensitivity reactions, do not take PROTELOS again.

If you experience side effect, if any of the side effects gets worse, or when you suffer from side effect not mentioned in the leaflet, you should consult the physician.

5. How to store the medicine?

Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning.
Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
Storage conditions: Store below 30°C.
It is recommended to drink the suspension immediately after preparation.

6. Additional information

In addition to the active ingredient, the medicine also contains:
Aspartame(E951), Maltodextrin, Mannitol(E421).

What does the medicine looks like and what is the content of the pack:
PROTELOS is available in sachets containing yellow granules for oral suspension**.**
PROTELOS is supplied in boxes of 7, 14, 28, 56, 84 or 100 sachets.
Not all pack sizes may be marketed.

Registration Holder: Mediline Ltd., City Gate, 22 Ben Gurion st., Herzlia

Manufacturer: Les Laboratoires Servier Industrie – France, for Les Laboratoires Servier , Neuilly Sur Seine-France.

The leaflet was checked and approved by the Ministry of Health in: 01/2015.

Registration number of the medicine in the National Drug Registry of the Ministry of Health**:**
142-09-31882-00.