Patient Package Insert in Accordance With the Pharmacists' Regulations (Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

Crestor® 5 mg **Crestor® 10 mg**
Film-coated tablets Film-coated tablets

Composition:
Each tablet contains:

Rosuvastatin 5 mg	Rosuvastatin 10 mg
(as rosuvastatin calcium)	(as rosuvastatin calcium)

Crestor® 20 mg **Crestor® 40 mg**
Film-coated tablets Film-coated tablets

Composition:
Each tablet contains:

Rosuvastatin 20 mg	Rosuvastatin 40 mg
(as rosuvastatin calcium)	(as rosuvastatin calcium)

For inactive ingredients and allergens please refer to Section 2 - "Important information about some of the ingredients in this medicine" and Section 6 - "Further Information".

Read this leaflet carefully in its entirety before using the medicine.
This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.
Crestor is not intended for children and adolescents under the age of 18.

1. What is this medicine intended for?

Crestor is indicated for treatment of Adults with:

- primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) (conditions when the blood cholesterol level is high) or mixed dyslipidaemia from type IIb (disorder in the level of different blood lipids). The medicine is given as an adjunct to diet when response to diet and other non-pharmacological treatments (e.g. exercise weight reduction) is inadequate.
- homozygous familial hypercholesterolaemia (conditions when the blood cholesterol level is high) as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate.

Therapeutic group

HMG-CoA reductase enzyme inhibitor

Crestor belongs to a group of medicines called statins, works by reducing fat levels in the blood, the most common of which is called cholesterol. There are several types of cholesterol in the blood, 'bad cholesterol' and 'good cholesterol'.
Crestor works by helping the body block the production of 'bad cholesterol' and clearing it from the body and helping to increase the "good cholesterol" levels.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive to the active ingredient or to any of the other ingredients contained in the medicine (please see section 6 - "Further Information").
- You are pregnant or breastfeeding. If you become pregnant while using Crestor, stop taking Crestor immediately and inform your doctor. Avoid becoming pregnant by using suitable contraceptives.
- You have a liver disease.
- You have severe kidney problems.
- You have repeated or unexplained muscle aches or pains.
- You are taking a drug combination of sofosbuvir/velpatasvir/voxilaprevir (used for viral infection of the liver called hepatitis C).

- You are taking ciclosporin (ciclosporin is used for instance following organ transplantation).
- You are under 18 years old.

If any of the above applies to you (or you are in doubt), please refer to your doctor.

In addition, do not use the 40 mg tablets (the highest dosage) if:

- You have moderate problems with kidney function (if in doubt, please ask your doctor).
- Your thyroid gland is not working properly.
- You have repeated unexplained muscle aches or pains; if you have a family or personal history of muscle problems, or have had muscle problems in the past while taking other cholesterol-lowering medicines.
- You regularly consume large amounts of alcohol.
- You are of Asian origin (Chinese, Filipino, Indian, Korean, Vietnamese, Japanese).
- You take other cholesterol-lowering medicines known as fibrates.

If any of the above applies to you (or you are in doubt), please refer to your doctor.

Special warnings regarding the use of Crestor

Before treatment with Crestor, tell the doctor if:

- **You have impaired liver, kidney, or thyroid function.**
- **You have repeated or unexplained muscle aches or pains,** or if you or a family member have had muscle problems, or if you have a history of muscle problems when taking other cholesterol-lowering agents. Inform the attending doctor immediately if you experience unexplained muscle aches or pains, especially if these are accompanied by a general unwell feeling or a fever. Also, tell your doctor if you have a muscle weakness that is constant.
- **You suffer or have suffered in the past from myasthenia gravis** (a disease causing general muscle weakness including in some cases muscles used when breathing), or Ocular myasthenia (a disease causing eye muscle weakness), since statins can sometimes aggravate the disease or cause it to occur (see section 4).

- **If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking Crestor or other related medicines.**
- **You regularly consume large amounts of alcohol.**
- **You take other cholesterol-lowering medicines known as fibrates.** Please read this leaflet carefully, even if you have taken other medicines for lowering cholesterol before.
- **You are taking medicines to treat HIV** (such as ritonavir with lopinavir and/or atazanavir). **Please refer to section "Drug interactions".**
- **You are taking or have taken in the last 7 days antibiotics containing fusidic acid** (a medicine for bacterial infection, orally or by injection). The combination of fusidic acid and Crestor can lead to serious muscle problems (rhabdomyolysis), please refer to section "Drug interactions".
- **You are over 70 years of age** (Your doctor needs to choose the right start dose of Crestor to suit you).
- **You have severe impairment of the respiratory system.**
- **You are of Asian origin** (Chinese, Filipino, Indian, Korean, Vietnamese, Japanese). Your doctor needs to choose the right start dose of Crestor to suit you.

If any of the above applies to you (or if you are not sure):
Do not take Crestor 40 mg (the highest dose) and check with your doctor or pharmacist before you actually start taking any dose of Crestor.

Serious skin reactions including Stevens-Johnson syndrome and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with Crestor treatment. Stop using Crestor and seek medical attention immediately if you notice any of the symptoms described in section 4.

In a small number of patients, statins may affect the liver; this is identified by a simple blood test that checks for a rise in liver enzyme levels. Your doctor will therefore ask you to do liver-function blood tests before and during treatment with Crestor.

During treatment with this medicine, your doctor will monitor you closely to see if you have diabetes or are at risk of developing diabetes. You may be at risk of developing diabetes if you have high levels of sugars and fats in your blood, or are overweight, and have high blood pressure.

Children and adolescents:
Crestor is not intended for children and adolescents under the age of 18.

Drug interactions:
If you are taking, or have recently taken any other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:

- Ciclosporin (used following organ transplantation)
- Warfarin, clopidogrel or ticagrelor (or any other drug used for thinning the blood)
- Fibrates (such as gemfibrozil or fenofibrate) or any other cholesterol-lowering medicine (such as ezetimibe)
- indigestion remedies (used to neutralize acid in your stomach)
- Erythromycin (an antibiotic), Fusidic acid (antibiotics – see below and also in section “Special warnings regarding use of Crestor”)
- Contraceptive pills
- regorafenib (used to treat cancer)
- darolutamide (used to treat cancer)
- capmatinib (used to treat cancer)
- Hormone replacement therapy
- fostamatinib (used to treat low platelet counts)
- febuxostat (used to treat and prevent high blood levels of uric acid)
- teriflunomide (used to treat multiple sclerosis)
- Medicines used to treat viral infections, including HIV or hepatitis C infection, alone or in combination with (please see section "Special warnings regarding use of Crestor"): ritonavir, lopinavir, atazanavir, sofosbuvir, voxilaprevir, ombitasvir, paritaprevir, dasabuvir, velpatasvir, grazoprevir, elbasvir, glecaprevir, pibrentasvir.

The effect of these medicines could be changed by concomitantly use with Crestor or they could change the effect of Crestor.

- Fusidic acid (antibiotic) - If you need to take oral fusidic acid to treat a bacterial infection you will need to temporarily stop using Crestor. Your doctor will tell you when it is safe to restart Crestor. Taking Crestor with fusidic acid may rarely lead

to weakness, tenderness or pain in muscles (rhabdomyolysis). Please see further information regarding rhabdomyolysis in section 4.

Use of the medicine and food:
Crestor can be taken regardless to food.

Pregnancy and breastfeeding:
Do not take Crestor if you are pregnant or breastfeeding.
If you become pregnant while using Crestor, **stop taking Crestor immediately** and inform your doctor. Avoid becoming pregnant during treatment with this medicine by using suitable contraceptives.
Consult your doctor or pharmacist before taking any medicine.

Driving and operating machinery:
Most patients are able to drive a car and operate machinery while using Crestor - the medicine does not impair their ability to perform these actions. However, some patients may feel dizzy during treatment with Crestor. If you feel dizzy, you must refer to the doctor before operating machinery or driving a car.

Important information about some of the ingredients in this medicine:
The medicine contains lactose. If your doctor has told you that you have an intolerance to some sugars (lactose or milk sugar), contact your doctor before taking this medicine. Please see section 6 – "Further information".

3. How should you use the medicine?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and manner of treatment. The dosage and manner of treatment will be determined by the doctor only. The recommended dosage is usually:
Treatment with Crestor starts with one 5 mg or 10 mg tablet once a day, even if you have previously taken other statins in higher dosages. The choice of your start dose will depend upon:

- Your cholesterol levels.
- The level of risk you have of experiencing a heart attack or stroke.

- Whether you have a factor that may make you more sensitive to possible side effects.

Please consult your doctor or pharmacist about the dosage that is most suitable for you.

Your doctor may decide to give you the lowest dose, 5 mg, if:
- You are of **Asian** origin (Chinese, Filipino, Indian, Korean, Vietnamese, Japanese).
- You are **over 70 years** of age.
- You have moderate kidney problems.
- You are at risk of muscle aches and pains (myopathy).

Increasing the dose and maximum daily dose
Your doctor may decide to increase your dose, so that you are taking the amount that is right for you. If you started with Crestor 5 mg dose, your doctor may decide to double this to Crestor 10 mg, then 20 mg and then 40 mg if necessary. If you started on Crestor 10 mg, your doctor may decide to double this to 20 mg and then 40 mg if necessary. There will be a gap of four weeks between every dose adjustment.

The maximum daily dose is 40 mg. It is usually for patients with very high cholesterol levels and a high risk of heart attacks or stroke whose cholesterol levels are not lowered enough with 20 mg.

Do not exceed the recommended dose.

If you take an antacid of the aluminum or magnesium salt type, you must take Crestor at least two hours before taking the aluminum/magnesium salt antacid.
Regularly check cholesterol levels to confirm that your cholesterol has reached and is maintained at the desired level.
It is possible that the doctor will decide to increase the dose of the medicne so that you take the amount of Crestor that suits you.

You can take the medicine at any time of day, with or without food. In order to remember to take the medicine, it is recommended to take the tablet at the same time every day.
Swallow the tablets whole with water.
There is no data regarding crushing or halving the tablet.

If you mistakenly take higher dose, contact your doctor or refer to a hospital emergency room.
If you take an overdose or if a child has accidentally swallowed the medicine, refer to a doctor immediately or proceed to a hospital emergency room, and bring the package of the medicine with you.

If you forget to take the medicine, skip the forgotten dose and take the next dose according to the usual schedule. Never take two doses together to compensate for a missed one.

Adhere to treatment as recommended by your doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting with the doctor.

If you stop treatment with the medicine your cholesterol levels might increase again.

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

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

4. Side effects

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

Effects that require special attention, stop treatment with Crestor and refer to the doctor immediately if:

- You experience any of the following hypersensitive reaction (allergy):
  - difficulty breathing with or without swelling of the face, lips, tongue and/or throat.
  - swelling of the face, lips, tongue and/or throat, which may cause difficulty in swallowing.
  - severe itching of the skin (with raised blisters).
  - Reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome).

- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).
- **You have unusual muscle aches or pains,** which go on for longer than you might expect. As with other statins, a small number of patients have experienced an unpleasant muscle effect and, rarely, this effect can become life threatening, damaging muscles - a condition known as rhabdomyolysis.
- **you experience muscle rupture.**
- **you have lupus-like disease syndrome** (including rash, joint disorders and effects on blood cells).

Common side effects (effects occurring in 1-10 of 100 users):

- Headaches,
- Abdominal pain,
- Constipation,
- Feeling ill,
- Muscle pain,
- Weakness,
- Dizziness,
- A rise in urine protein levels; these usually return to normal without the need to discontinue the use of the medication (only for Crestor 40 mg).
- Diabetes: the risk of developing diabetes is more likely if you have high levels of fats and sugar in your blood, are overweight, and have high blood pressure. You must be under medical supervision during the course of treatment.

Uncommon side effects (effects occurring in 1-10 of 1,000 users):

- Skin rash,
- Itching or other skin reactions.
- A rise in urine protein levels; these usually return to normal without the need to discontinue the use of the medication (only for Crestor 5 mg, 10 mg, and 20 mg).

Rare side effects (effects occurring in 1-10 of 10,000 users):

- Severe allergic reaction – signs include: swelling of the face, lips, tongue and/or throat, difficulty in swallowing and breathing, a severe itching of the skin (with

raised lumps). If you think you are having an allergic reaction, then stop taking Crestor and seek medical help immediately.

- Muscle damage in adults – as a precaution, stop taking Crestor and talk to your doctor immediately if you have any unusual aches or pains in your muscles which go on for longer than expected.
- Severe abdominal pain (pancreatitis).
- Increase in liver enzymes in the blood.
- Bleeding or bruising more easily than normal due to low level of blood platelets.
- Lupus-like disease syndrome (including rash, joint disorders and effects on blood cells).

Very rare side effects (effects occurring in less than 1 of 10,000 users):

- Jaundice (yellowing of the skin and eyes).
- Hepatitis (an inflamed liver).
- Traces of blood in your urine.
- Damage to the nerves of your legs and arms (such as numbness or tingling sensation).
- joint pain.
- Memory loss.
- Breast enlargement in men (gynaecomastia).

Other side effects (effects the incidence of which has not yet been determined):

- Diarrhea.
- Cough.
- Shortness of breath.
- Edema (swelling as a result of fluid buildup).
- Sleep disturbances, including insomnia and nightmares.
- Problems with sexual function.
- Depression.
- Breathing problems including a persistent cough and/or shortness of breath or fever.
- Tendon injury

- Constant muscle weakness
- Myasthenia gravis (a disease causing general muscle weakness and including in some cases muscles used when breathing.
- Ocular myasthenia (a disease causing eye muscle weakness)
  Consult your doctor if you experience weakness in your arms or legs that worsens after periods of activity, double vision or drooping of your eyelids, difficulty swallowing, or shortness of breath.

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, you must consult the doctor.

Side effects can be reported to the Ministry of Health by clicking on the "Report on side effects due to medication therapy" link on the Ministry of Health home page (www.health.gov.il) which refers to the online form for side effects reporting, or by entering the link:
https://sideeffects.health.gov.il

5. How should the medicine be stored?

- Do not store above 30°C.
- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order 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) appearing on the package. The expiry date refers to the last day of that month.
  Please note the medication's expiry date! In case of doubt, consult the pharmacist who dispensed the medicine to you.
- Do not store different medications in the same package.

6. Further information

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

Lactose monohydrate, microcrystalline cellulose, calcium phosphate, crospovidone, magnesium stearate, hypromellose, glycerol triacetate, titanium dioxide.
ferric oxide yellow - 5 mg tablets
ferric oxide red - 10, 20, and 40 mg tablets

Each Crestor 5 mg tablet also contains 94.88 mg lactose monohydrate.
Each Crestor 10 mg tablet also contains 91.3 mg lactose monohydrate.
Each Crestor 20 mg tablet also contains 182.6 mg lactose monohydrate.
Each Crestor 40 mg tablet also contains 168.32 mg lactose monohydrate.

What does the medicine look like and contents of the pack:
Crestor 5 mg tablets: round, film-coated, bi-convex, yellow tablets, engraved with "ZD4522 5" on one side.
Crestor 10 mg tablets: round, film-coated, bi-convex, pink tablets, engraved with "ZD4522 10" on one side.
Crestor 20 mg tablets: round, film-coated, bi-convex, pink tablets, engraved with "ZD4522 20" on one side.
Crestor 40 mg tablets: oval, film-coated, bi-convex, pink tablets, engraved with "40" on one side and "ZD4522" on the other side.
The package contains 7 or 28 tablets in a blister pack. Not all pack sizes may be marketed.

Manufactured by:
IPR Pharmaceuticals Inc., Puerto Rico
For AstraZeneca UK Ltd.,
Macclesfield, UK.

Registration holder and importer:
AstraZeneca (Israel) Ltd.,
1 Atirei Yeda St.,
Kfar Saba 4464301.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:

Crestor 5 mg: 139 22 31615 00

Crestor 10 mg: 129 74 30798 00

Crestor 20 mg: 129 75 30799 00

Crestor 40 mg: 129 76 30800 00

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