CRYSTORVAS TABLET

Atorvastatin (40mg & 20mg)

What is in this leaflet

What Crystorvas is used for

Crystorvas belongs to a group of medicines known as statins, which are lipid (fat) regulating medicines.

Crystorvas is used to lower lipids known as cholesterol (total cholesterol, low-density lipoprotein [LDL] cholesterol) and other fats (triglycerides) in the blood when a low fat diet and lifestyle changes on their own have failed.

Crystorvas can lower the risk for heart attack, stroke, certain types of heart surgery, and chest pain in patients who have heart disease or risk factors for heart disease such as: Age, smoking, high blood pressure, low HDL-C, heart disease in the family.

Crystorvas can lower the risk for heart attack or stroke in patients with diabetes and risk factors such as: Eye problems, kidney problems, smoking, or high blood pressure.

How Crystorvas works

Crystorvas works by reducing the amount of cholesterol made by the liver. In terms of good and bad cholesterol, Crystorvas reduces the bad cholesterol and raises the good cholesterol.

Before you use Crystorvas

- *When you must not use it*

Do not take Crystorvas

- if you are hypersensitive (allergic) to Crystorvas or to any similar medicines used to lower blood lipids or to any of the other ingredients of the medicine;
- if you have or have ever had a disease which affects the liver;
- if you have had any unexplained abnormal blood tests for liver function;
- if you are a woman able to have children and not using reliable contraception;
- if you are pregnant or trying to become pregnant;
- if you are breast-feeding.

Talk to your doctor or pharmacist before taking Crystorvas:

- If you have or have had myasthenia (a disease with general muscle weakness including in some cases muscles used when breathing), or ocular myasthenia (a disease causing eye muscle weakness) as statins may sometimes aggravate the condition.

Pregnancy and lactation

Women of childbearing potential

Women of child-bearing potential should use appropriate contraceptive measures during treatment (see *Contraindications*).

Pregnancy

Crystorvas is contraindicated during pregnancy (see *Contraindications*). Safety in pregnant women has not been established. No controlled clinical trials with atorvastatin have been conducted in pregnant women. Rare reports of congenital anomalies following intrauterine exposure to HMG-CoA reductase inhibitors have been received. Studies in animals have shown toxicity to reproduction.

Maternal treatment with atorvastatin may reduce the foetal levels of mevalonate which is a precursor of cholesterol biosynthesis.

Atherosclerosis is a chronic process, and ordinarily discontinuation of lipid-lowering medicinal products during pregnancy should have little impact on the long-term risk associated with primary hypercholesterolaemia.

For these reasons, Crystorvas should not be used in women who are pregnant, trying to become pregnant or suspect they are pregnant. Treatment with Crystorvas should be suspended for the duration of pregnancy or until it has been determined that the woman is not pregnant (see *Contraindications*).

Breast-feeding

It is unknown whether atorvastatin or its metabolites are excreted in human milk.

In rats, plasma concentrations of atorvastatin and its active metabolites are similar to those in milk. Because of the potential for serious adverse reactions, women taking Crystorvas should not breast-feed their infants (see *Contraindications*). Atorvastatin is contraindicated during breast-feeding (see *Contraindications*).

Fertility

In animal studies atorvastatin had no effect on male or female fertility.

How to use Crystorvas

- *How much to use*
- General

Before instituting therapy with atorvastatin, an attempt should be made to control hypercholesterolemia with appropriate diet, exercise and weight reduction in obese patients, and to treat the underlying medical problems. The patient should continue on a standard cholesterol- lowering diet during treatment with atorvastatin. The dosage range is 10mg to 80mg once daily. Doses may be given any time of the day with or without food. Starting and maintenance dosage should be individualized according to baseline LDL-C levels, the goal of therapy, and patient response. After initiation and/or upon titration of atorvastatin, lipid levels should be analyzed within 2-4 weeks, and dosage adjusted accordingly

- Primary Hypercholesterolemia and Combined (Mixed) Hyperlipidemia

The majority of patients are controlled with 10mg atorvastatin once daily. A therapeutic response is evident within 2 weeks, and the maximum response is usually achieved within 4 weeks. The response is maintained during chronic therapy.

- Homozygous Familial Hypercholesterolemia

In a compassionate-use study of patients with homozygous familial hypercholesterolemia, most patients responded to 80mg atorvastatin with a greater than 15% reduction in LDL- C (18%-45%)

- Heterozygous Famililal Hypercholesterolemia in Pediatric Patients (10-17 years of age)

The recommended starting dose of atorvastatin is 10mg/day; the usual dose range is 10 to 20mg orally once daily. Doses should be individualized according to the recommended goal of therapy. Adjustments should be made at intervals of 4 weeks or more

- Severe Dyslipidemias in Pediatric Patients

For patients aged 10 years and above, the

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recommended starting dose is 10mg atorvastatin once daily. The dose may be increased to 80mg daily, according to the response and tolerability. Doses should be individualized according to the recommended goal of therapy.
Adjustment should be made at intervals of 4 weeks or more

- Use in Patients with Renal Insufficiency

Renal disease has no influence on plasma concentration or on LDL-C reduction with atorvastatin. Thus, no dose adjustment is required.

- Use in Elderly

No differences in safety, efficacy or lipid treatment goal attainment were observed between elderly patients and the overall population.

- Dosage in Patients taking Cyclosporine, Clarithromycin, Itraconazole, or Certain Protein Inhibitors

In patients taking cyclosporine or the human immunodeficiency virus (HIV) protease inhibitors (tipanivir plus ritonavir) or the hepatitis C protease inhibitor (telaprevir), therapy with atorvastatin should be avoided. In patients with HIV taking lopinavir plus ritonavir, caution should be used when prescribing atorvastatin and the lowest dose necessary is employed. In patients taking clarithromycin, itraconazole, or in patients with HIV taking a combination of saquinavir plus ritonavir, darunavir plus ritonavir, fosamprenavir, or fosamprenavir plus ritonavir, therapy with atorvastatin should be limit to 20mg, and appropriate clinical assessment is recommended to ensure that the lowest dose necessary of atorvastatin is employed. In patients taking the HIV protease inhibitor nelfinavir or the hepatitis C protease inhibitor boceprevir, therapy with atorvastatin should be limited to 40mg, and appropriate clinical assessment is recommended to ensure that the lowest dose necessary of atorvastatin is employed.

- Use in Children (Homozygous Familial Hypercholesterolemia)

Treatment experience in a pediatric population is limited to doses of atorvastatin up to 80mg/day for one year in 8 patients with homozygous FH. No clinical or biochemical abnormalities were reported in these patients.

- *When to use it*

Use as directed by your doctor or pharmacist.
Crystorvas tablets should be swallowed whole with a drink of water, and can be taken at any time of day, with or without food. However, try to take your tablet at the same time every day.

- *How long to use it*

Continue taking Crystorvas for as long as your doctor recommends.

- *If you forget to use it*

Consult your doctor or pharmacist on what you should do if you forget to use it. Take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose. Do not take a double dose to make up for the missed dose.

- *If you use too much (overdose)*

Contact your doctor immediately or go to the Emergency Department of your nearest hospital, if you think you or anyone else may have taken too much of this medicine. Do this even if there are no signs of discomfort or poisoning.
You may need urgent medical attention.

While you are using it

- *Things you must do*

Take your medicine exactly as your doctor has told you.
Tell all the doctors, dentists and pharmacists treating you that you are taking Crystorvas
Tell your doctor immediately if you become pregnant while taking this medication.
You should avoid alcohol while you are taking Crystorvas.

- *Things you must not do*

- Do not stop taking the medicine unless advised by your doctor.
- Do not take any new medicines therapy without consulting your doctor.
- Do not give Crystorvas to anyone else, even if they have the same symptoms or condition as you.
- Do not take more than one or two small glasses of grapefruit juice per day because large quantities of grapefruit juice can change the effects of Crystorvas
- Do not drink too much alcohol while taking Crystorvas.

- *Things to be careful of*

Driving and using machines
This medicine may affect your ability to drive or use machines. If the tablets make you feel sick, dizzy or tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

Side effects
Following table presents the adverse reaction profile for Crystorvas.

Infections and infestations
Common: nasopharyngitis.

Blood and lymphatic system disorders
Rare: thrombocytopenia.

Immune system disorders
Common: allergic reactions.
Very rare: anaphylaxis.

Metabolism and nutrition disorders
Common: hyperglycaemia.
Uncommon: hypoglycaemia, weight gain, anorexia.

Psychiatric disorders
Uncommon: nightmare, insomnia.

Nervous system disorders
Common: headache.
Uncommon: dizziness, paraesthesia, hypoesthesia, dysgeusia, amnesia.
Rare: peripheral neuropathy.
Unknown frequency: Myasthenia gravis (a disease causing general muscle weakness including in some cases muscle used when breathing)

Eye disorders
Uncommon: vision blurred.
Rare: visual disturbance.
Unknown frequency: Ocular myasthenia (a disease causing eye muscle weakness)

Ear and labyrinth disorders
Uncommon: tinnitus.
Very rare: hearing loss.

Respiratory, thoracic and mediastinal disorders
Common: pharyngolaryngeal pain, epistaxis.

Gastrointestinal disorders
Common: constipation, flatulence, dyspepsia, nausea, diarrhoea.
Uncommon: vomiting, abdominal pain upper and lower, eructation, pancreatitis.

Hepatobiliary disorders
Uncommon: hepatitis.
Rare: cholestasis.
Very rare: hepatic failure.

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Skin and subcutaneous tissue disorders
Uncommon: urticaria, skin rash, pruritus, alopecia.
Rare: angioneurotic oedema, dermatitis bullous including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis.

Musculoskeletal and connective tissue disorders
Common: myalgia, arthralgia, pain in extremity, muscle spasms, joint swelling, back pain.
Uncommon: neck pain, muscle fatigue.
Rare: myopathy, myositis, rhabdomyolysis, tendonopathy, sometimes complicated by rupture.
Very rare: lupus-like syndrome.
Frequency not known: immune mediated necrotizing myopathy (see *Warnings and Precautions*).

Reproductive system and breast disorders
Very rare: gynecomastia.

General disorders and administration site conditions
Uncommon: malaise, asthenia, chest pain, peripheral oedema, fatigue, pyrexia.

Investigations
Common: liver function test abnormal, blood creatine kinase increased.
Uncommon: white blood cells urine positive.

As with other HMG-CoA reductase inhibitors elevated serum transaminases have been reported in patients receiving Atorvastatin. These changes were usually mild, transient, and did not require interruption of treatment. These elevations were dose related and were reversible in all patients.

Paediatric population
The safety and tolerability profile in paediatric patients was similar to the known safety profile of atorvastatin in adult patients.
Based on the data available, the frequency, type and severity of adverse reactions in children is similar to adults.

The following adverse events have been reported with some statins:
- Sexual dysfunction.
- Depression.
- Exceptional cases of interstitial lung disease, especially with long term therapy (see section Warning and Precautions).
- Diabetes Mellitus: Frequency will depend on the presence or absence of risk factors (fasting blood glucose ≥ 5.6 mmol/L, BMI>30kg/m^2, raised triglycerides, history of hypertension).

There have been rare post-marketing reports of cognitive impairment (e.g. memory loss, forgetfulness, amnesia, memory impairment, confusion) associated with statin use. These cognitive issues have been reported for all statins. The reports are generally non-serious and reversible upon statin discontinuation, with variable times to symptom onset (1 day to years) and symptom resolution (median 3 weeks).

Increases in HbA1c and fasting blood glucose have been reported with statins. The risk of hyperglycemia, however, is outweighed by the reduction in vascular risk with statins.

Talk to your doctor if you experience weakness in your arms or legs that worsens after periods of activity, double vision or dropping of your eyelids, difficulty swallowing, or shortness of breath.

If you have muscle problems that do not go away even after your doctor has told you to stop taking Crystorvas Tablet, please refer to your doctor. Your doctor may do further tests to diagnose the cause of your muscle problems.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)]

Storage and Disposal of Crystorvas
- *Storage*
Keep out of the reach and sight of children.
Store below 30°C. Protected from moisture

- *Disposal*
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product Description
- *What it looks like*
Crystorvas Tablet 40mg:
White to off-white, 10 mm round, biconvex, with "40" marking on one side and plain on the other side, film- coated tablet.

Crystorvas Tablet 20mg:
White to off-white, 7 mm round, biconvex, with "20" marking on one side and plain on the other side, film- coated tablet.

Ingredients
- Active ingredient
Crystorvas Tablet 40mg: Each tablet contains 40mg of atorvastatin.
Crystorvas Tablet 20mg: Each tablet contains 20mg of atorvastatin.

- Inactive ingredients
- Polysorbate 80
- Purified Water
- Lactose Monohydrate 200 Mesh
- Calcium Carbonate Fine
- Hydroxypropyl Cellulose (HPC-L Fine)
- Croscarmellose Sodium
- Microcrystalline Cellulose 101
- Croscarmellose Sodium
- Magnesium Stearate
- Opadry II White 32F38977

- *MAL number):*
Crystorvas Tablet 40mg MAL 20046120AZ
Crystorvas Tablet 20mg MAL 20046121AZ

PRODUCT REGISTRATION HOLDER
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DATE OF REVISION
22 Dec 2025

SERIAL NUMBER
NPRA (R2/1) 251216/01586