**2. DRUG PROFILE**

**2.1.ROSUVASTATIN**

**Drug :** *Rosuvastatin*

**Molecular formula :** C22H28FN3O6S

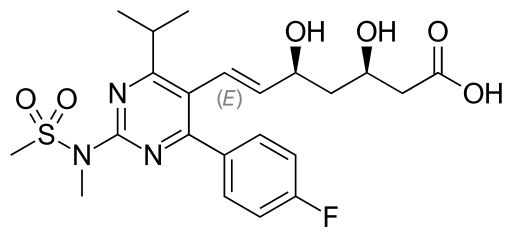
**Molecular weight :** 481.539 g/mol

##### **Solubility :** Water Solubility

**pKa value** **:** 3.8, 4.9, 5.5 and 14.65.

##### **PH :** 7.2

**Structural formula :**



**Chemical name :** Rosuvastatin; (3R,5S,E)-7-(4-(4-Fluorophenyl)-6-

isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-

5-yl)-3,5-dihydroxyhept-6-enoic acid;[Provisacor](https://www.ncbi.nlm.nih.gov/pcsubstance/?term=%22Provisacor%22%5BCompleteSynonym%5D%20AND%20446157%5BStandardizedCID%5D)

Rosuvastatin calcium, [Crestor](https://www.ncbi.nlm.nih.gov/pcsubstance/?term=%22Crestor%22%5BCompleteSynonym%5D%20AND%20446157%5BStandardizedCID%5D)

## Precautions : Patients w/ predisposing factors for myopathy (e.g. untreated hypothyroidism, renal impairment), history of chronic liver disease and alcoholism. *Monitoring Parameters* Monitor creatine kinase (CK) periodically and LFT. Discontinue treatment if there is significant or persistent increase in CK levels,

## serum aminotransferase levels or evidence of myopathy.

**Description :** Rosuvastatin is used together with a proper diet to lower cholesterol and triglycerides (fats) in the blood. This medicine may help prevent or slow down medical problems, like atherosclerosis (hardening of the arteries), that are caused by fats clogging the blood vessels. It may also be used to prevent certain types of heart and blood vessel problems in patients with risk factors for heart problems.

**Stability :** The solutions were stored at 5º and at ambient temperature without protection of light and tested after 12, 24, 36 and 48 h.

**Mechanism of action:**

Rosuvastatin is a [competitive inhibitor](https://en.wikipedia.org/wiki/Competitive_inhibition) of the enzyme [HMG-CoA reductase](https://en.wikipedia.org/wiki/HMG-CoA_reductase), having a mechanism of action similar to that of other statins.[[15]](https://en.wikipedia.org/wiki/Rosuvastatin#cite_note-ASTEROID-15)

Putative beneficial effects of rosuvastatin therapy on chronic heart failure may be negated by increases in collagen turnover markers as well as a reduction in plasma [coenzyme Q10](https://en.wikipedia.org/wiki/Coenzyme_Q10) levels in patients with chronic heart failure.[[16]](https://en.wikipedia.org/wiki/Rosuvastatin#cite_note-16)

**Pharmacokinetics:**

Absolute [bioavailability](https://en.wikipedia.org/wiki/Bioavailability) of rosuvastatin is about 20% and [Cmax](https://en.wikipedia.org/wiki/Cmax_(pharmacology)) is reached in 3 to 5 hours; administration with food did not affect the [AUC](https://en.wikipedia.org/wiki/Area_under_the_curve_(pharmacokinetics)) according to the original sponsor submitted clinical study and as per product label.[[2]](https://en.wikipedia.org/wiki/Rosuvastatin#cite_note-PI-2) However, a subsequent clinical study has shown a marked reduction in rosuvastatin exposure when administered with food.[[17]](https://en.wikipedia.org/wiki/Rosuvastatin#cite_note-17)It is 88% [protein bound](https://en.wikipedia.org/wiki/Plasma_protein_binding), mainly to [albumin](https://en.wikipedia.org/wiki/Albumin).[[18]](https://en.wikipedia.org/wiki/Rosuvastatin#cite_note-drugs_com-18) Fraction absorbed of rosuvastatin is frequently misquoted in the literature as approximately 0.5 (50%)[[19]](https://en.wikipedia.org/wiki/Rosuvastatin#cite_note-19) due to a miscalculated hepatic extraction ratio in the original submission package subsequently corrected by the FDA reviewer.[[20]](https://en.wikipedia.org/wiki/Rosuvastatin#cite_note-20) It is likely that closer to 0.25 (25%) of the administered dose is absorbed.

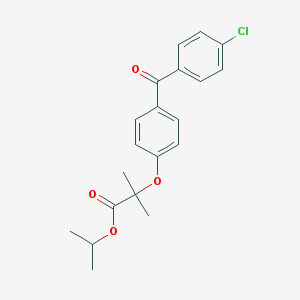
Rosuvastatin is metabolized mainly by [CYP2C9](https://en.wikipedia.org/wiki/CYP2C9) and not extensively metabolized; approximately 10% is recovered as [metabolite](https://en.wikipedia.org/wiki/Metabolite) *N*-desmethyl rosuvastatin. It is excreted in [feces](https://en.wikipedia.org/wiki/Feces) (90%) primarily and the [elimination half-life](https://en.wikipedia.org/wiki/Biological_half-life) is approximately 19 hours.

**Adverse effects:**

S[constipation](https://en.wikipedia.org/wiki/Constipation), [heartburn](https://en.wikipedia.org/wiki/Heartburn), [dizziness](https://en.wikipedia.org/wiki/Dizziness), [sleeplessness](https://en.wikipedia.org/wiki/Insomnia), [depression](https://en.wikipedia.org/wiki/Depression_(mood)), [joint pain](https://en.wikipedia.org/wiki/Arthralgia), [cough](https://en.wikipedia.org/wiki/Cough), [memory loss](https://en.wikipedia.org/wiki/Memory_loss) or [forgetfulness](https://en.wikipedia.org/wiki/Forgetting), [confusion](https://en.wikipedia.org/wiki/Confusion)

**2.2**. FENOFIBRATE **:**

**Structure:**



structure of Fenofibrate

**Chemical Name :** Fenofibrate; Lipanthyl; Procetofen; Antara;

Lipidil

**Synonyms :** Antara Micronized Procetofen, Apo Feno Micro, Apo

Fenofibrate, Apo-Feno-Micro, Apo-Fenofibrate, AZU,

Fenofibrat, CiL, Controlip,Debat, Fénofibrate,durafenat

**Appearance :** Solid  
**Molecular formula :** C20H21ClO4 **Density :** 1.18 g/cm3  
**Boiling Point :**469.8 °C at 760 mmHg   
**Melting Point :** 80-81 deg C   
**Flash Point :** 165.4 °C

**PH :**6.8 **Refractive index :** 1.617  
**Solubility :** **Solubility** in water   
**Stability :**Stable at normal temperatures and pressures.

**Description**  **:**An antilipidemic agent which reduces both cholesterol and

triglycerides in the blood.

**Moleculr weight :** 360.831 g/mol.

**CLINICAL PHARMACOLOGY**

**Mechanism Of Action**.

The active moiety of TRICOR is fenofibric acid. Through this **mechanism**, **fenofibrate** increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity).

**Pharmacokinetic data:**

Fenofibrate is a [pro](http://www.rxlist.com/script/main/art.asp?articlekey=22849)-drug of the active chemical moiety fenofibric acid. Fenofibrate is converted by ester hydrolysis in the body to fenofibric acid which is the active constituent measurable in the [circulation](http://www.rxlist.com/script/main/art.asp?articlekey=2735).

##### ***Absorption***

The absolute bioavailability of fenofibrate cannot be determined as the compound is virtually insoluble in aqueous media suitable for injection. However, fenofibrate is well absorbed from the [gastrointestinal tract](http://www.rxlist.com/script/main/art.asp?articlekey=25976). Following oral administration in healthy volunteers, approximately 60% of a single dose of radiolabelled fenofibrate appeared in urine, primarily as fenofibric acid and its glucuronate conjugate, and 25% was excreted in the feces. Peak plasma levels of fenofibric acid occur within 6 to 8 hours after administration.

The absorption of fenofibrate is increased when administered with food. With fenofibrate tablets, the extent of absorption is increased by approximately 35% under fed as compared to fasting conditions.

##### ***Distribution***

Upon multiple dosing of fenofibrate, fenofibric acid steady state is achieved within 5 days. Plasma concentrations of fenofibric acid at steady state are approximately double of those following a single dose. Serum protein binding was approximately 99% in normal and hyperlipidemic subjects.

##### ***Metabolism***

Following oral administration, fenofibrate is rapidly hydrolyzed by esterases to the active metabolite, fenofibric acid; no unchanged fenofibrate is detected in plasma.Fenofibric acid is primarily conjugated with glucuronic acid and then excreted in urine. A small amount of fenofibric acid is reduced at the carbonyl moiety to a benzhydrol metabolite which is, in turn, conjugated with glucuronic acid and excreted in urine.

*In vivo* [metabolism](http://www.rxlist.com/script/main/art.asp?articlekey=4359) data indicate that neither fenofibrate nor fenofibric acid undergo oxidative metabolism (e.g., cytochrome P450) to a significant extent.

##### ***Elimination***

After absorption, fenofibrate is mainly excreted in the urine in the form of metabolites, primarily fenofibric acid and fenofibric acid glucuronide. After administration of radiolabelled fenofibrate, approximately 60% of the dose appeared in the urine and 25% was excreted in the feces.

Fenofibric acid is eliminated with a half-life of 20 hours, allowing once daily dosing.

**Over dosage**

**Fenofibrate** is a prescription medication used to lower cholesterol and triglycerides (a type of fat) and to increase HDL ("good") cholesterol in the blood. It may be used alone or with other cholesterol-lowering medications. ... Common side effects of fenofibrate include headaches, heartburn, nausea, and muscle aches

**Adverse effects**

* Tongue swelling or other mouth.
* Throat problems.
* Yellow appearance of the skin,nails,or whites of the eye(this could be jaundice,a sign of serious effects on the liver).
* Pain in the upper area your back.
* Stomach or digestion problems such as pain bloating,heart burn,nausea,more gas than usual or vomiting.