

# Consumer Information

## RyChol™

### What does RyChol™ do?

RyChol™ is a botanical compound that helps lower your total cholesterol and LDL ('bad' cholesterol) levels, thereby reducing your risk of heart disease and stroke.

### What is cholesterol?

Cholesterol is a fat-like substance, naturally found in the bodies of all humans and animals. It has many important functions that are essential to the body and forms part of the basic structure of some hormones, all cell membranes and the insulation layer around nerves. Too much cholesterol, however, causes hardening of the arteries, a degenerative medical condition that leads to heart attacks and strokes. The good news is that by proactively managing your cholesterol levels, you can dramatically reduce your risk of heart disease and premature death and live a longer, healthier and more productive life.

### What is the difference between 'good' and 'bad' cholesterol?

Although a portion of cholesterol is found on its own in the blood stream, most cholesterol molecules are bonded to specialised proteins, called lipoproteins, that transport cholesterol through the body. Cholesterol bonded to *low-density lipoprotein* or LDL, tends to accumulate inside arteries, and is therefore detrimental or 'bad' for the body. Cholesterol bonded to *high-density lipoprotein* or HDL, on the other hand, gets transported to the liver where it is naturally expelled from the system as a component of bile. It is therefore 'good' to have high levels of HDL.

### How does cholesterol cause disease?

Hardening of the arteries is a complex process whereby a layer or crust accumulates within the artery. As this layer increases in thickness, the inner passage of the artery, called the lumen, becomes progressively obstructed, leading to the diminished flow of blood through the artery. A clot may easily form inside this narrowed and diseased artery, sealing it off entirely and blocking the flow of blood. This occurrence causes heart attacks and strokes.

### Why do cholesterol levels increase?

Besides consuming a diet containing too much saturated fat, many inherit certain genetic abnormalities from their parents, making them abnormally prone to elevated cholesterol levels.

### What is saturated fat?

All fats are formed out of smaller components called fatty acids. These are molecules made up from carbon and hydrogen atoms. A saturated fat contains all the hydrogen atoms it can potentially accommodate and is therefore "saturated" with hydrogen, whilst an "unsaturated" fat has some unoccupied space left. Saturated fat is for various medical reasons worse for the body than unsaturated fat. The mixture of fats consumed by most people, usually contain three times more saturated than unsaturated fat. Saturated fat increases blood cholesterol levels to a greater degree than the actual cholesterol content of food. Because cholesterol is produced through a biochemical process taking place inside the liver, only food from animal origin (creatures with livers) contains cholesterol. Saturated fat, however, is produced via a different biochemical process. Many plant-derived products therefore contain high levels.

### Which foods are high in saturated fat?

Food from animal origin is often high in saturated fat as well as cholesterol. This includes red meat, organ meat, full cream milk and yoghurt, cream, cream-cheese, cheese, butter, lard and eggs. Lean poultry, lean pork and lean bacon also contain saturated fat, but to a lesser degree than red meat. There are many other miscellaneous sources of food that do not necessarily come from animal origin, but also contain large quantities of saturated fat. Examples are hardened vegetable oil including many margarines, biscuits, cakes, tarts, pie crusts, pastries, rusks, chocolate, coffee creamers, ice cream, chips/crisps and non-dairy cream substitutes. Coconut oil and palm kernel oil are also high in fat.

### How must I alter my diet to help me reduce my cholesterol levels?

Try and eat fish and soya most often, as well as reduced fat and dairy products like skim milk or fat free milk, fat free yoghurt, fat free or low fat cottage cheese, fat free cream cheese and egg whites. Eat moderate amounts of lean red meat, skinless chicken, lean bacon and game, as well as low fat milk, low fat yoghurt, low fat buttermilk, low fat cheese (less than 15g per 100g), low fat processed cheese, creamed cottage cheese and sorbet. Eat minimal amounts of fatty red meat, processed meat, organ meat, sausages, shellfish, beef biltong, droe wors, full cream milk, full cream yoghurt, cream and cream substitutes, coffee creamers, dairy blends, cream cheese, most cheese, ice cream, eggs. This includes vegetables prepared in butter and cream (usually in restaurants) and commercially baked products such as pies, cakes, tarts, croissants, doughnuts, high fat refined biscuits or crackers and buttered popcorn. In addition, avoid

muesli containing coconut shavings, butter, hard margarine, coconut milk, French fries, chocolate and soups containing cream (read the nutrition labels).

### **Are raised blood cholesterol levels always caused by bad diets?**

Although diet plays an important role, many cases of high cholesterol is caused by certain genetic disadvantages that you inherit from your parents. These cause elevated cholesterol levels, even when your diet does not contain all that much saturated fat.

### **Can you lower your cholesterol levels just by following a low fat diet?**

Some people can achieve this goal, but for those with a genetic tendency towards high cholesterol, it is usually not possible to lower your cholesterol levels sufficiently. This is because the majority of your body's total cholesterol content is produced in your own liver. For obvious reasons, it is not possible to evade this source, since the cholesterol manufacturing process is controlled and determined by your genetic makeup.

### **If diet alone is often not sufficient, does it mean that you should take medication?**

Yes, if your intention is to increase your life expectancy and decrease your risk of stroke and heart attacks. **RyChol™**, however, offers you a safe yet effective alternative to prescription medication.

### **When should you use RyChol™?**

If you have a mild to moderately elevated cholesterol level.  
If you are prone to the side effects of the statins.

### **Can you use RyChol™ in conjunction with prescription medication?**

Yes, there are no documented reports of any drug interactions. **RyChol™** can therefore safely be taken with most prescription drugs, including cardiac, blood pressure and schedule 4 cholesterol lowering drugs.

### **What dosage must I take?**

Use the following guideline according to your cholesterol level: (Cholesterol levels in mmol/dl)

Cholesterol level above 5: take 2 tablets per day

Cholesterol level above 6: take 3 tablets per day

Cholesterol level above 7: take 4 tablets per day

### **What if my results are not satisfactory?**

Some people with a certain genetic predisposition to high cholesterol may be resistant. In these cases, better results will be achieved by doubling your dosage of **RyChol™**.

### **Will everybody respond to RyChol?**

No, our trials at the Medical Nutritional Institute have shown that approximately 6% of the population will not have an adequate response to RyChol and will require one of the more potent cholesterol lowering prescription drugs.

### **What do other people say about RyChol™?**

*"I have a high risk factor profile for heart disease which includes raised cholesterol. I tried all the different statins but could not tolerate the muscle cramps they gave me. RyChol lowered my cholesterol from 8.4 to 3.8 mmol/L in 9 months without any side-effects, and the results that I achieved were comparable to the statins."*

*Colin – Sandton*

*"RyChol lowered my 14 year old daughter's cholesterol from 6.7 to 5.1 in just 3 weeks. I was so relieved that I did not have to start her on a drug at such a young age."*

*Ingrid - Fourways*

# Technical information

## RyChol™

### PHARMACOLOGICAL CLASSIFICATION:

Complementary medicine

### COMPOSITION:

Two tablets contain:

TrimoStat™ (Contains Berberine)	60 mg
Red yeast rice extract	1000 mg
Coenzyme Q10	30 mg

### INDICATIONS:

**RyChol™** is a non-prescription medication that consists of a combination of natural compounds that display different but synergistic cholesterol lowering effects. It's unique dual-action mechanism simultaneously targets two separate cholesterol producing pathways, thereby increasing its efficacy. **RyChol™** may assist with the lowering of total cholesterol, LDL and triglyceride levels, thereby helping you to reduce your risk of heart disease and stroke. Due to its low documented side-effect profile, **RyChol™** may be taken by both adults and children over age 10.

### DOSAGE AND DIRECTIONS FOR USE:

Cholesterol levels in mmol/dl

Above 5: take 2 tablets per day

Above 6: take 3 tablets per day

Above 7: take 4 tablets per day (Take with any meal as a single dosage)

### PHARMACOLOGICAL ACTION

**RyChol™** consists of a combination of natural compounds that display different but synergistic cholesterol lowering and cardio-protective effects. These are TrimoStat™, a patented compound containing berberine, red yeast rice extract and Coenzyme Q10. **RyChol's™** unique dual-action mechanism simultaneously targets two separate cholesterol producing pathways, thereby increasing its cholesterol lowering efficacy.

**TrimoStat™** is a patented Berberine extract containing berberine, a quaternary ammonium salt from the group of isoquinoline alkaloids found in plants such as Berberis, Hydrastis canadensis and Coptis chinenses. Berberine has been identified as an unique cholesterol-lowering agent with the ability to lower total cholesterol and LDL<sup>[1-20]</sup>, as well as triglycerides<sup>[1,2,6,10,11,16,19,20]</sup>. Research has shown that this mechanism of action is distinctly different from that of the statins<sup>[2,3,6]</sup> and involves the up-regulation of hepatic low density lipoprotein receptor (LDLR) expression via mRNA stabilization<sup>[2-7,9,12,18]</sup>. Research has also shown that a combination of berberine with simvastatin increased the LDLR gene expression to a level significantly higher than monotherapies<sup>[5]</sup>. More effective reduction of serum triglycerides was also achieved with the combination as compared with either monotherapy<sup>[5]</sup>.

**Red yeast rice extract** is a traditional Chinese spice that has been used as a food colorant for the last seven centuries. It is produced with the aid of the yeast *Monascus purpureus*, grown on rice. Red yeast rice is a rich source of monacolins, known to inhibit the activity of the cholesterol producing enzyme HMG-CoA reductase, as well as other natural cholesterol lowering agents including certain sterols (sitosterol, campesterol, and stigmasterol), isoflavones and unsaturated fatty acids. Numerous trials have demonstrated its ability to lower total cholesterol and LDL<sup>[20 - 31]</sup>, as well as its ability to increase HDL<sup>[25,27]</sup>.

The lipid-lowering effects of red yeast rice in a population known to be intolerant to the side effects of statins has been tested. During this trial it was concluded that red yeast rice decreased total cholesterol and LDL cholesterol, was well-tolerated, and that it was an acceptable alternative to patients intolerant of other lipid-lowering medications<sup>[21]</sup>. A study also examined the effects of red yeast rice extract on hypercholesterolaemic children<sup>[22]</sup>. Results indicate that it was effective, safe and well tolerated, especially when compared to the statins<sup>[27,31]</sup>. Studies have also compared the efficacy of red yeast rice to the efficacy of simvastatin and pravastatin<sup>[22,27,29]</sup> regarding cholesterol lowering potency. It was found that the efficacy was comparable, with one trial demonstrating that red yeast rice achieved superior LDL

cholesterol reduction than pravastatin<sup>[23]</sup>. One of the largest placebo controlled trials conducted on red yeast rice is the China Coronary Secondary Prevention Study (CCSPS). Close to 5000 post-heart attack patients were enrolled for an average of 4.5 years to either receive a placebo or red yeast rice. In the treated group risk of subsequent heart attacks was reduced by 45%, cardio deaths by 31%, and all-cause deaths by 33%<sup>[32]</sup>.

**Coenzyme Q10** is an organic, fat-soluble antioxidant naturally manufactured in the liver where it plays a critical role in ATP production, the body's most basic energy unit. As a powerful antioxidant, coenzyme Q10 has the ability to protect the body and heart by neutralising toxic free radical molecules that may damage our bodily tissues. Since coenzyme Q10 and cholesterol are both synthesized from the same substrate, namely mevalonate, any product that targets cholesterol synthesis may also potentially inhibit the body's own production of coenzyme Q10. To prevent a shortage from developing, as well as protect your heart and arteries, coenzyme Q10 has therefore been added to **RyChol™** as a supplement.

#### **SIDE-EFFECTS AND SPECIAL PRECAUTIONS:**

##### **TrimoStat™**

Rare adverse effects that have been reported include headaches, skin irritations and facial flushing. Berberine must also be used with caution by individuals with low blood pressure, as it may display antihypertensive effects.

##### **Red yeast rice extract**

Mild headache and abdominal discomfort have been reported. Due to a similarity in biochemical action, individuals with a previous episode of a severe statin related side effect should be cautious, as similar side effects may theoretically be possible. However, trials have examined the lipid-lowering effects of red yeast rice in a population known to be intolerant to the side effects of statins. During this trial it was concluded that red yeast rice was well-tolerated and that it was an acceptable alternative to patients intolerant of other cholesterol-lowering medications, including the statins<sup>[21]</sup>. Other studies have also examined the benefit versus side effect profile of red yeast rice extract on children with elevated cholesterol levels<sup>[22]</sup>. The results achieved indicated that it was effective, safe and well tolerated, especially when compared to the statins<sup>[27,31]</sup>. Due to the likely mechanism of action of the monacolins in the liver, individuals with known liver disease should consult their doctor before using **RyChol™**.

##### **Coenzyme Q10**

Trials have shown that coenzyme Q10 has a low side effect profile. Mild gastro-intestinal irritation and nausea has been reported when taken on an empty stomach.

#### **CONTRA-INDICATIONS:**

Known hypersensitivity to any of the ingredients. Liver disease. Pregnancy and lactation.

#### **IDENTIFICATION:**

**RyChol™**: terracotta brown oval tablet with no distinctive markings.

#### **PRESENTATION:**

60 tablets contained in a white plastic container.

#### **STORAGE INSTRUCTIONS:**

Store below 25° C. Keep out of reach of children.

#### **NAPPI CODE:**

706139-001

#### **SCIENTIFIC REFERENCES**

1. Doggrell SA. Berberine—a novel approach to cholesterol lowering. *Expert Opin Investig Drugs*. 2005 May;14(5):683-5.
2. Kong W, Wei J, Abidi P, Lin M, Inaba S, Li C, Wang Y. Berberine is a novel cholesterol-lowering drug working through a unique mechanism distinct from statins. *JOURNAL: Nat Med*. 2004 Dec;10(12):1344-51.
3. Abidi P, Chen W, Kraemer FB, Li H, Liu J. The medicinal plant goldenseal is a natural LDL-lowering agent with multiple bioactive components and new action mechanisms. *J Lipid Res*. 2006 Oct;47(10):2134-47.
4. Abidi P, Zhou Y, Jiang JD, Liu J. Berberine, a novel cholesterol-lowering agent, upregulates low-density lipoprotein (LDL) receptor expression through mRNA stabilization. *Arterioscler Thromb Vasc Biol*. 2005 Oct;25(10):2170-6.
5. Kong WJ, Wei J, Zuo ZY, Wang YM, Song DQ, You XF, Zhao LX, Pan HN, Jiang JD. Combination of simvastatin with berberine improves the lipid-lowering efficacy. *Metabolism*. 2008 Aug;57(8):1029-37.
6. Brusq JM, Ancellin N, Grondin P, Guillard R, Martin S, Saintillan Y, Issandou M. Inhibition of lipid synthesis through activation of AMP kinase: an additional mechanism for the hypolipidemic effects of berberine. *J Lipid Res*. 2006 Jun;47(6):1281-8.
7. Li YH, Yang P, Kong WJ, Wang YX, Hu CQ, Zuo ZY. Berberine analogues as a novel class of the low-density-lipoprotein receptor up-regulators: synthesis, structure-activity relationships, and cholesterol-lowering efficacy. *J Med Chem*. 2009 Jan 22;52(2):492-501.
8. Hu YS, Davies GE. Berberine inhibits adipogenesis in high-fat diet-induced obesity mice. *Fitoterapia*. 2009 Oct 25.
9. Wang YX, Wang YP, Zhang H, Kong WJ, Li YH, Liu F, Gao RM, Liu T, Jiang JD, Song DQ. Synthesis and biological evaluation of berberine analogues as novel up-regulators for both low-density-lipoprotein receptor and insulin receptor. *Bioorg Med Chem Lett*. 2009 Nov 1;19(21):6004-8.
10. Wang Y, Jia X, Ghanam K, Beaupaire C, Zidichouski J, Miller L. Berberine and plant stanols synergistically inhibit cholesterol absorption in hamsters. *Atherosclerosis*. 2009 Sep 4.

11. Affuso F, Ruvolo A, Micillo F, Saccà L, Fazio S. Effects of a nutraceutical combination (berberine, red yeast rice and policosanols) on lipid levels and endothelial function randomized, double-blind, placebo-controlled study. *Nutr Metab Cardiovasc Dis.* 2009 Aug 19.
12. Li H, Dong B, Park SW, Lee HS, Chen W, Liu J. Hepatocyte nuclear factor 1alpha plays a critical role in PCSK9 gene transcription and regulation by the natural hypocholesterolemic compound berberine. *J Biol Chem.* 2009 Oct 16;284(42):28885-95.
13. Wang C, Li J, Lv X, Zhang M, Song Y, Chen L, Liu Y. Ameliorative effect of berberine on endothelial dysfunction in diabetic rats induced by high-fat diet and streptozotocin. *Eur J Pharmacol.* 2009 Oct 12;620(1-3):131-7.
14. Jung HA, Min BS, Yokozawa T, Lee JH, Kim YS, Choi JS. Anti-Alzheimer and antioxidant activities of Coptidis Rhizoma alkaloids. *Biol Pharm Bull.* 2009 Aug;32(8):1433-8.
15. Jia X, Chen Y, Zidichouski J, Zhang J, Sun C, Wang Y. Co-administration of berberine and plant stanols synergistically reduces plasma cholesterol in rats. *Atherosclerosis.* 2008 Nov;201(1):101-7.
16. Zhang Y, Li X, Zou D, Liu W, Yang J, Zhu N, Huo L, Wang M, Hong J, Wu P, Ren G, Ning G. Treatment of type 2 diabetes and dyslipidemia with the natural plant alkaloid berberine. *J Clin Endocrinol Metab.* 2008 Jul;93(7):2559-65.
17. Hsieh YS, Kuo WH, Lin TW, Chang HR, Lin TH, Chen PN, Chu SC. Protective effects of berberine against low-density lipoprotein (LDL) oxidation and oxidized LDL-induced cytotoxicity on endothelial cells. *J Agric Food Chem.* 2007 Dec 12;55(25):10437-45.
18. Lee S, Lim HJ, Park JH, Lee KS, Jang Y, Park HY. Berberine-induced LDLR up-regulation involves JNK pathway. *Biochem Biophys Res Commun.* 2007 Nov 3;362(4):853-7.
19. Cicero AF, Rovati LC, Setnikar I. Eulipidemic effects of berberine administered alone or in combination with other natural cholesterol-lowering agents. A single-blind clinical investigation. *Arzneimittelforschung.* 2007;57(1):26-30.
20. Tang LQ, Wei W, Chen LM, Liu S. Effects of berberine on diabetes induced by alloxan and a high-fat/high-cholesterol diet in rats. *J Ethnopharmacol.* 2006 Nov 3;108(1):109-15.
21. Venero CV, Venero JV, Wortham DC, Thompson PD. Lipid-lowering efficacy of red yeast rice in a population intolerant to statins. *Am J Cardiol.* 2010 Mar 1;105(5):664-6.
22. Guardamagna O, Abello F, Baracco V, Stasłowska B, Martino F. The treatment of hypercholesterolemic children: Efficacy and safety of a combination of red yeast rice extract and policosanols. *Nutr Metab Cardiovasc Dis.* 2010 Feb 10.
23. Halbert SC, French B, Gordon RY, Farrar JT, Schmitz K, Morris PB, Thompson PD, Rader DJ, Becker DJ. Tolerability of red yeast rice (2,400 mg twice daily) versus pravastatin (20 mg twice daily) in patients with previous statin intolerance. *Am J Cardiol.* 2010 Jan 15;105(2):198-204.
24. McGowan MP, Proulx S. Nutritional supplements and serum lipids: does anything work? *Curr Atheroscler Rep.* 2009 Nov;11(6):470-6.
25. Yang NC, Chou CW, Chen CY, Hwang KL, Yang YC. Combined nattokinase with red yeast rice but not nattokinase alone has potent effects on blood lipids in human subjects with hyperlipidemia. *Asia Pac J Clin Nutr.* 2009;18(3):310-7.
26. Affuso F, Ruvolo A, Micillo F, Saccà L, Fazio S. Effects of a nutraceutical combination (berberine, red yeast rice and policosanols) on lipid levels and endothelial function randomized, double-blind, placebo-controlled study. *Nutr Metab Cardiovasc Dis.* 2009 Aug 19.
27. Becker DJ, Gordon RY, Halbert SC, French B, Morris PB, Rader DJ. Red yeast rice for dyslipidemia in statin-intolerant patients: a randomized trial. *Ann Intern Med.* 2009 Jun 16;150(12):830-9, W147-9.
28. Lu Z, Kou W, Du B, Wu Y, Zhao S, Brusco OA, Morgan JM, Capuzzi DM. Effect of Xuezhikang, an extract from red yeast Chinese rice, on coronary events in a Chinese population with previous myocardial infarction. *Am J Cardiol.* 2008 Jun 15;101(12):1689-93.
29. Lin JS. An alternative treatment of hyperlipidemia with red yeast rice: a case report. *J Med Case Reports.* 2010 Jan 8;4:4.
30. Huang CF, Li TC, Lin CC, Liu CS, Shih HC, Lai MM. Efficacy of *Monascus purpureus* Went rice on lowering lipid ratios in hypercholesterolemic patients. *Eur J Cardiovasc Prev Rehabil.* 2007 Jun;14(3):438-40.
31. Liu J, Zhang J, Shi Y, Grimsgaard S, Alraek T, Førnnebo V. Chinese red yeast rice (*Monascus purpureus*) for primary hyperlipidemia: a meta-analysis of randomized controlled trials. *Chin Med.* 2006 Nov 23;1:4.
32. Lu ZL. China coronary secondary prevention study (CCSPS) *Zhonghua Xin Xue Guan Bing Za Zhi.* 2005 Feb;33(2):109-15.