PRODUCT MONOGRAPH

PreCardix®

Bioactive marine peptide tablets

Shrimp protein hydrolysate (Pandalus borealis – shell)

NPN: 80080580

600mg per tablet

Suggested daily serving: 2 tablets (1200 mg)

"Helps to maintain healthy blood pressure levels and to support cardiovascular health."

Manufactured by:	Pharmaline Inc. 2835 Argentia Road, Mississauga, Ontario L5N 8G6	Date of Issue: May 27, 2020
Distributed by:	Marealis Health Inc.	
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Indications and Clinical Uses

PreCardix® is used in the treatment and prevention of elevated blood pressure. The Health Canada approved claim is: PreCardix® helps to maintain healthy blood pressure and to support cardiovascular health.

PreCardix® is not approved for the treatment of congestive heart failure, left ventricular dysfunction and diabetic neuropathy.

Action and Clinical Pharmacology

PreCardix® is a clinically supported natural treatment for elevated blood pressure. Each tablet contains 600 mg of protein hydrolysate from coldwater shrimp (*Pandalus borealis - shell*).

The mechanism by which PreCardix® lowers blood pressure is primarily through suppression of parts of the renin-angiotensin-aldosterone system and more specifically inhibiting excess levels of the Angiotensin-Converting Enzyme (ACE).

The active ingredient, RSPC (Refined Shrimp Peptide Concentrate), contains thousands of unique peptides. The RSPC contains mainly di-, tri- and tetrapeptides, which are resistant to modification by digestion and able to pass the intestinal wall to enter the bloodstream and reach their target. The peptides work in synergy with some having direct ACE-inhibiting effects. The bioactivity and ACE-inhibiting attributes of each production batch is tested to ensure consistency in the high quality and efficacy parameters of each production batch. Two of the most potent peptides found in PreCardix® have been patented.

In a peer-reviewed, double-blind, placebo-controlled, multicenter clinical trial, 1,200 mg per day of PreCardix® protein hydrolysate was found to have a statistically significant reduction in systolic and diastolic blood pressure on mild to moderate hypertensive subjects[2]. Angiotensin II levels were significantly reduced in the treatment group compared to baseline documenting the ACE-inhibitory effect[2].

Contra-Indications

Patients who have an allergy to shellfish should not take PreCardix®

PreCardix® has not been studied in patients with a history of angioedema related to the previous use of ACE inhibitors and should be avoided in this patient population.

PreCardix® has not been studied in patients who have renal artery stenosis and should be avoided in this patient population based on the known contraindication with pharmaceutical ACE inhibitor medication.

PreCardix® has not been studied in pregnancy and should be avoided throughout the entire gestational period due to the potential teratogen effects of ACE inhibitors. Women who are breastfeeding should not take PreCardix®.

Children under the age of 18 should not take PreCardix®.

Drug Interactions

**PreCardix® has not been directly studied in combination with pharmaceuticals. Drug Interactions are inferred based on ACE inhibitor pharmaceuticals[3].*

The antihypertensive effect of PreCardix® may be augmented by other antihypertensive agents and patients who are combining PreCardix® with antihypertensive pharmaceuticals should be monitored for hypotension. Patients who add alpha-blocking medications to ACE inhibitor pharmaceuticals have experienced increased hypotension after the first dose of alpha-blockers. Patients who are taking PreCardix® and are adding in alpha-blockers should be monitored closely for this potential effect.

PreCardix® has not been found to increase potassium levels. In the clinical trial, serum potassium levels were measured at baseline and at 8 weeks in all study participants. There was no clinically significant difference between potassium levels at both baseline and at 8 weeks between the placebo and treatment group. However, considering PreCardix®s ACE inhibitor action, caution should be taken when using PreCardix® alongside agents that increase serum potassium such as potassium-sparing diuretics, potassium supplements, and potassium-containing salts. Patients using any of these combinations should have serum potassium levels monitored frequently.

A possible causal relationship may exist between ACE inhibitor treatment and allopurinol, predisposing patients to hypersensitivity reactions. PreCardix® should be used cautiously with allopurinol until further research establishes the safety of this combination.

The use of NSAIDs may antagonize the antihypertensive effect of ACE inhibitor medications. Patients who are using NSAIDs regularly along with PreCardix® should be monitored frequently.

Intravenous infusion of iron should be administered cautiously in patients using PreCardix®. ACE inhibitors have been found to augment the systemic effects of I.V iron. Oral iron supplementation is not a concern.

Patients who are taking PreCardix® with lithium should have lithium levels monitored frequently. ACE inhibitor medication may decrease renal elimination of lithium leading to lithium toxicity (CNS symptoms, ECG changes, renal failure). PreCardix® has not been

studied alongside lithium medication however considering its ACE inhibitor mechanism caution should be taken.

Adverse Reactions

PreCardix® has no documented major side effects. Clinical research found no occurrences of dry cough, itching, edema, hypotension, hyperkalemia or kidney impairment.

PreCardix® may cause moderate nausea in some individuals. Adverse reactions found to be possibly related to PreCardix® from the clinical trial included 1 case each of euphoric mood, fatigue, upper abdominal pain, and headache. All of these symptoms were rated as mild in intensity.

Dosage and Administration

2 tablets (1,200 mg of the active ingredient) should be taken together orally daily as per the dose and protocol found to be effective in the clinical trial. PreCardix® should be taken a few hours away from medication or natural health care products, between meals and before noon.

Patients should take PreCardix® for a minimum of 8 weeks to determine the effectiveness of treatment. In the clinical study, 31% of patients saw a significant reduction in blood pressure after just 2 weeks, however, 89% of patients saw a significant reduction in blood pressure after 8 weeks compared to baseline.

It is recommended that PreCardix® be taken on an ongoing basis to maintain results. Blood pressure levels can rise to pre-treatment levels if discontinued prematurely.

Expected effect

Individual variations in the magnitude of blood pressure lowering effects from PreCardix® may be seen. Case reports suggest that higher baseline blood pressure levels correlate with greater drops in blood pressure.

The blood pressure lowering effect seen in study participants varied from 0 to 38 mmHg for systolic and from 0 to 28.7 mmHg for diastolic blood pressure after the 8-week trial period compared to baseline. The average reduction after the 8 weeks was 9.5 mmHg for systolic and 4.2 mmHg for diastolic, and 43% of the study participants saw a reduction higher than 10 mmHg in systolic blood pressure compared to baseline.

Overdosage

Marealis Health recommends a maximum intake of two tablets (1,200mg) of PreCardix® per day. An overdose leading to serious bodily injury is considered unlikely to occur. This was tested in pre-clinical toxicity trials where subjects were given a daily dosage 100 times higher than the recommended dosage with no resulting safety issues or hypotension. In the full-scale clinical trial, no safety issues or hypotension were documented. PreCardix®'s reduced potential for toxicity or negative side effects is due to
it's rapid clearance from the blood[4]. In the unlikely event of an overdose, patients should be monitored closely.

Storage and Stability

PreCardix® should be stored at room temperature (15 - 30°C) and in a dry place. Keep out of reach and sight of children. PreCardix® should be used within the date of expiration.

Reporting Suspected Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

· Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhpmps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or

· Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

More Information

For more information, please contact your health professional or pharmacist first, or Marealis Health Inc. at support@marealishealth.com.

This leaflet was prepared by:

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