1. NAME OF THE MEDICINAL PRODUCT

Myoqinon 100 mg soft capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 100 mg ubidecarenone.

Excipient with known effect
Each soft capsule contains 297 mg refined soybean oil.

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Soft capsule.

Oval, brown, opaque, soft capsule filled with 462-537 mg of orange paste.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

In case of proven coenzyme Q_{10} deficiency, as adjuvant therapy to alleviate the symptoms of chronic heart failure.

4.2 Posology and method of administration

Posology

The soft capsules should only be taken orally.
The usual dose is 100-200 mg daily. If the recommended daily dose is 200 mg, this should be divided into two parts, 100 mg in the morning and 100 mg in the evening. This is necessary because of the saturation effect, as the absorption efficiency of ubidecarenone decreases when increasing the dose.

A starting dose of 200 mg/day may be used as adjuvant therapy alongside standard-of-care treatment. After six months, it can be decreased to a maintenance dose of 100 mg daily based on changes in the patient's symptoms and their monitoring.
It is recommended to take the capsule with food (to optimise absorption and minimise the likelihood of undesirable gastrointestinal effects) and an ample quantity of water. If swallowing Myoqinon 100 mg soft capsule is difficult, the soft capsule can be cut open and its contents squeezed onto a spoon and swallowed on their own or with food.

Paediatric population
Not recommended for children and adolescents due to a lack of experience.

Elderly
No dose adjustment is required.

Use in patients with kidney or liver damage
No dose adjustment is required.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Do not use this preparation in case of a known allergy to peanuts or soya.

4.4 Special warnings and precautions for use

Ubidecarenone may reduce blood pressure in patients with hypertension; the decrease observed in untreated hypertensive patients and in patients taking antihypertensive drugs was similar (see section 4.5). No major antihypertensive effect has been observed.

Paediatric population
Taking Myoqinon 100 mg is not recommended for children and adolescents due to a lack of experience.

Soya oil
The preparation contains 297 mg refined soybean oil per soft capsule.
Use of this preparation is contraindicated in case of peanut or soya allergy (see section 4.3).

4.5 Interaction with other medicinal products and other forms of interaction

Some case reports suggest that in some patients, ubidecarenone may reduce the effect of coumarin-type (vitamin K antagonist) anticoagulant drugs (warfarin, phenprocoumon, acenocoumarol). It is recommended to check coagulation time (INR) a few weeks after the start and end of therapy with Myoqinon 100 mg soft capsules to determine if an adjustment to the dose of anticoagulant is necessary. A clinical study involving 21 patients on stable warfarin therapy showed that 1×100 mg of Myoqinon soft capsules taken daily for 4 weeks had no effect on INR values.

Ubidecarenone may reduce blood pressure in patients with hypertension. It is recommended to monitor blood pressure in patients taking antihypertensive drugs during therapy with ubidecarenone.

Concomitant administration of high doses of vitamin E (350 mg) reduces the expected increase in ubidecarenone blood levels.

In clinical studies, 34 insulin-treated type I diabetics received 1×100 mg Myoqinon soft capsules or placebo daily for 3 months; and 24 type II diabetics on diet alone or diet plus a sulphonylurea-type medicinal product received 2×100 mg Myoqinon soft capsules daily for 6 months, and this had no effect on their glycaemic control.

4.6 Pregnancy and lactation

Pregnancy
There are limited amounts of data from the use of ubidecarenone in pregnant women.

Use of Myoqinon during pregnancy is not recommended

Breastfeeding
Limited information is available on the excretion of ubidecarenone into human breast milk.
Use of Myoqinon during breast-feeding is not recommended.

4.7 Effects on ability to drive and use machines

Myoqinon 100 mg soft capsule is not expected to influence the ability to drive and use machines. The effects of this medicinal product on the ability to drive and use machines has not been studied.

4.8 Undesirable effects

Ubiodecarenone is generally well tolerated. Undesirable effects reported with ubidecarenone include gastrointestinal symptoms, headache, dizziness and cutaneous reactions. The symptoms are usually mild and often subside with continued treatment. A temporary or permanent dose reduction may be considered if the undesirable effects do not resolve. Occasional irritability and dizziness have been reported, but their association with ubidecarenone use has not been confirmed.
A slight increase in serum aminotransferase levels has occasionally been observed with high doses of ubidecarenone, but no liver toxicity has been reported.

The following (MedDRA) terminologies have been used in order to classify the occurrence of undesirable effects:

- very common: ≥ 1/10;
- common: ≥ 1/100 – < 1/10;
- uncommon: ≥ 1/1000 – < 1/100;
- rare: ≥ 1/10,000 – < 1/1000;
- very rare: < 1/10,000;
- not known frequency cannot be estimated from the available data.

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

MedDRA frequency categories **MedDRA System Organ Class**	**Rare**	**Not known**
Nervous System Disorders	headache dizziness	-
Gastrointestinal Disorders	nausea constipation diarrhoea pain in the stomach area indigestion	-
Skin and Subcutaneous Tissue Disorders	-	rash itching

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important, because it allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected side effects via the national reporting system listed in Appendix V.

4.9 Overdose

No overdose has been reported as yet. In clinical studies, no serious undesirable effects were reported with administration of ubidecarenone at a dose of 600 mg/day for several months.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other cardiovascular agents, ATC code: C01EB09

Coenzyme Q_{10} is a vitamin-like substance that plays an essential role in the transport of electrons along the respiratory chain in mitochondria. It also has an antioxidant role, protecting molecules and cells from oxidative stress. Coenzyme Q_{10} is present in all living cells of the body; its concentration is highest in the heart, liver, kidneys and muscle tissue. Decreased levels of coenzyme Q_{10} have been found in chronic heart failure, and myocardial coenzyme Q_{10} levels correlated with heart failure severity. Relatively low serum coenzyme Q_{10} levels could be compensated by orally administered ubidecarenone.

Patients with chronic heart failure on standard-of-care medication have improved with ubidecarenone as an adjuvant treatment, especially in those with relatively low levels of coenzyme Q_{10}. Stroke volume index showed a significant improvement both at rest and on exertion; pulmonary arterial blood pressure at rest and pulmonary capillary wedge pressure at 1 minute of exercise decreased. Coenzyme Q_{10} has been attributed to enhanced ATP synthesis resulting in improved myocardial function. The antioxidant property of coenzyme Q_{10} shows in the reduction of lipid peroxidation and oxidative stress, a general phenomenon in heart failure.

5.2 Pharmacokinetic properties

Absorption
Coenzyme Q_{10} is synthesised in the body, but we also get some (3-5 mg per day on average) from food. In the body, the ring structure of coenzyme Q_{10} is derived from tyrosine, and the carbon backbone is formed via the mevalonate pathway. The synthesis of coenzyme Q_{10} involves numerous enzyme systems, including hydroxymethylglutaryl coenzyme A reductase (HMG-Co-A reductase).

Absorption
The absorption of externally ingested ubidecarenone from the digestive tract is not perfect. Absorption can be improved with simultaneous intake of food. In 10 healthy volunteers, a single intake of 1×100 mg Myoqinon soft capsule with a standardised meal resulted in a two-peaked plasma concentration curve. The first peak was observed 6 hours after taking the medicinal product, with a C_{max} value of 135% of the baseline value of 0.95 mg/l. The relatively slow absorption is attributable to the high molecular weight and fat solubility of ubidecarenone. The second peak in coenzyme Q_{10} concentration occurs approximately 24 hours after taking the medicinal product. This is thought to suggest redistribution from the liver via VLDL cholesterol, but enterohepatic recirculation is also probable. The absorption efficiency of ubidecarenone decreases as the dose increases. The amount of ubidecarenone absorbed depends on the frequency of administration. The administration of 1×100 mg, 2×100 mg or 1×200 mg resulted in equilibrium serum coenzyme Q_{10} concentrations of 2.3 mg/l, 3.4 mg/l and 2.2 mg/l, respectively. Equilibrium serum coenzyme Q_{10} concentrations were reached after 2 weeks of taking 100-200 mg of ubidecarenone daily.

Distribution
After absorption, coenzyme Q_{10} is taken up by the liver, from where it is transported to various organs and tissues, specifically the heart, kidneys and muscles.

Elimination
The terminal elimination half-life of Q_{10} is approximately 35 hours, suggesting low plasma clearance. The rate of metabolism in the liver is not fully known. Coenzyme Q_{10} is mainly secreted via bile and excreted via faeces.

Deuterium labelling studies suggest that long-term ubidecarenone supplementation does not affect endogenous coenzyme Q_{10} production.

5.3 Preclinical safety data

Studies in rodents show that ubidecarenone is not toxic even when used acutely and for long periods. In two studies conducted on pigs, ubidecarenone (as Myoqinon 100 mg soft capsules) maintained cardiac function after ischaemia and reperfusion, significantly inhibited platelet aggregation and reduced levels of fibronectin, thromboxane B_2, prostacyclin and endothelin-1. No undesirable effects were observed in the two studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule filling:
RRR-α-tocopherol (vitamin E),
hydrogenated vegetable oil,
refined soybean oil.

Capsule shell:
red iron oxide (E172),
black iron oxide (E172),
glycerol,
gelatine.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30 ºC, store in the original package.
Do not refrigerate. Do not freeze.

6.5 Nature and contents of container

30, 60 or 90 soft capsules in a transparent PVC/PVdC//Al blister and a box.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Note:(no cross marking)
Classification: Group II
Medicinal product strictly subject to medical prescription (Rx).

7. MARKETING AUTHORISATION HOLDER

Pharma Nord ApS
Tinglykke 4-6
6500 Vojens
Denmark

8. MARKETING AUTHORISATION NUMBER(S)

OGYI-T-10011/04	Myoqinon 100 mg soft capsule (30 capsules)
OGYI-T-10011/05	Myoqinon 100 mg soft capsule (60 capsules)
OGYI-T-10011/06	Myoqinon 100 mg soft capsule (90 capsules)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 January 2005
Date of latest renewal: 19 November 2009

10. DATE OF REVISION OF THE TEXT

22 December 2022