

Revised: December 2011 (12th version)

Standard Commodity Classification No. of Japan
872119

- Metabolic cardiogenic -

Neuquinon[®] Tablets 5mg
Neuquinon[®] Tablets 10mg
Neuquinon[®] Sugar Coated Tablets 10mg
Neuquinon[®] Capsules 5mg
Neuquinon[®] Granules 1%

<Ubidecarenone preparation>

	Tablets 5mg	Tablets 10mg	Sugar coated Tablets 10 mg	Capsules 5mg	Granules 1%
Approval No.	15200AMZ00880000	15100AMZ00371000	15400AMZ01434000	21800AMX10306000	21800AMX10422000
Date of listing in the NHI reimbursement price	Apr 1978	Apr 1978	Sep 1981	Jun 2006	Dec 2006
Date of initial marketing in Japan	Apr 1978	Apr 1978	Sep 1981	Apr 1974	Oct 1976
Date of latest reevaluation	Jan 1988				

Storage

NEUQUINON should be stored at room temperature. [NEUQUINON may become spotted if stored above melting point (about 48°C) of ubidecarenone.] [See "PRECAUTIONS FOR HANDLING" section.]

Expiration date

NEUQUINON should be used before the expiration date indicated on the package or label.

DESCRIPTION**1. Composition****Tablets 5 mg:**

Each yellow to orange-yellow plain tablet contains 5 mg of ubidecarenone.

It also contains carnauba wax, carmellose calcium, hydrated silicon dioxide, microcrystalline cellulose, stearic acid, cornstarch, lactose hydrate and hydroxypropylcellulose as inactive ingredients.

Tablets 10 mg:

Each yellow to orange-yellow plain tablet contains 10 mg of ubidecarenone.

It also contains carnauba wax, carmellose calcium, hydrated silicon dioxide, microcrystalline cellulose, stearic acid, cornstarch, lactose hydrate and hydroxypropylcellulose as inactive ingredients.

Sugar coated Tablets 10 mg:

Each orange sugar coated tablet contains 10 mg of ubidecarenone.

It also contains FD & C Yellow No. 6 (Sunset Yellow FCF), carnauba wax, hydrated silicon dioxide, microcrystalline cellulose, titanium oxide, stearic acid, calcium stearate, talc, precipitated calcium carbonate, cornstarch, lactose hydrate, white shellac, hydroxypropylcellulose, pullulan, povidone and macrogol 6000 as inactive ingredients.

Capsules 5mg:

Each orange and pale brown hard capsule contains 5 mg of ubidecarenone.

It also contains FD & C Yellow No. 6 (Sunset Yellow FCF), microcrystalline cellulose, gelatin, cornstarch, hydroxypropylcellulose and sodium lauryl sulfate as inactive ingredients.

Granules 1%:

Each gram of yellow to orange-yellow granules contains 10 mg of ubidecarenone.

It also contains lactose hydrate, hydroxypropylcellulose and D-mannitol as inactive ingredients.

2. Product description

Brand name	Dosage form and identification code	Appearance			Description
		Face	Reverse	Lateral	
NEUQUINON Tablets 5 mg	Plain tablets				Yellow to orange-yellow
	EISAI NQ005	Diameter (mm) 5.1	Weight (mg) 50	Thickness (mm) 2.5	
NEUQUINON Tablets 10 mg	Plain tablets				Yellow to orange-yellow
	EISAI NQ010	Diameter (mm) 6.1	Weight (mg) 100	Thickness (mm) 3.4	
NEUQUINON Sugar coated Tablets 10 mg	Sugar coated tablets				Orange
	E224	Diameter (mm) 7.5	Weight (mg) 170	Thickness (mm) 4.2	
NEUQUINON Capsules 5mg	Hard capsules				Cap: Orange Body: Pale brown Contents: Yellow
	NQ005E	Length (mm) 14.3	Weight (mg) 170	Size No.4	
NEUQUINON Granules 1%	Granules				Yellow to orange-yellow, slightly sweet taste

INDICATIONS

Mild to moderate symptom of congestive heart failure during basic therapy

DOSAGE AND ADMINISTRATION

The usual adult dosage for oral use is 10 mg of ubidecarenone, three times daily after meals.

Tablets 5 mg:

The usual adult dosage for oral use is two tablets three times daily after meals.

Tablets 10 mg:

The usual adult dosage for oral use is one tablet three times daily after meals.

Sugar coated Tablets 10 mg:

The usual adult dosage for oral use is one tablet three times daily after meals.

Capsules 5 mg:

The usual adult dosage for oral use is two capsules three times daily after meals.

Granules 1%:

The usual adult dosage for oral use is 1 g three times daily after meals.

PRECAUTIONS

1. Adverse Reactions

Adverse reactions were reported in 78 of 5,350 patients (1.46%). (At the end of the investigation for incidence of adverse reactions.)

	5% > ≥0.1%
Gastrointestinal	Stomach discomfort, anorexia, nausea and diarrhea
Hypersensitivity ^{note)}	Rash

Note) In the event of such symptoms, appropriate measures such as discontinuation of the medication should be taken.

2. Precautions concerning Use

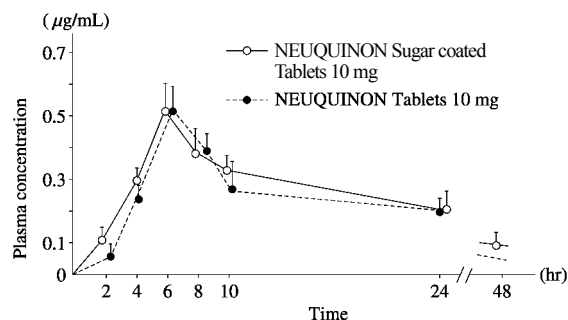
Caution in handing over drug (tablets, Sugar coated tablets and capsules)

For drugs that are dispensed in a press-through package (PTP), instruct the patient to remove the drug from the package prior to use. [It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, causing perforation and resulting in serious complications such as mediastinitis.]

PHARMACOKINETICS

1. Blood concentration of NEUQUINON Tablets 10 mg and NEUQUINON Sugar coated Tablets 10 mg

10 tablets of NEUQUINON Tablets 10 mg or 10 tablets of NEUQUINON Sugar coated Tablets 10 mg were administered orally to healthy adult male volunteers at a single dose (100 mg ^{note)} of ubidecarenone) in a cross-over design, and changes in the plasma concentration were compared. For both dosage forms the time to reach peak plasma concentration (about 0.5 µg/mL of exogenous CoQ₁₀) was 6 hr after administration, and thereafter, the plasma concentration gradually declined. There was no statistically significant difference between the two different dosage forms.



Plasma exogenous CoQ₁₀ concentrations after oral administration at a single dose of 100 mg ^{note)} of ubidecarenone

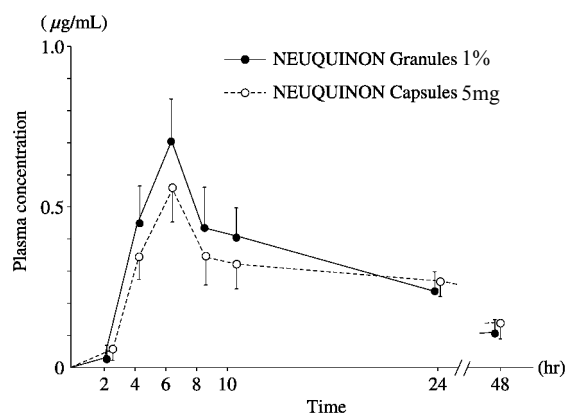
Pharmacokinetic parameters of NEUQUINON Tablets 10mg and NEUQUINON Sugar coated Tablets 10mg

	t _{max} (hr)	C _{max} (µg/mL)	AUC (µg · hr/mL)	t _{1/2} (hr)
NEUQUINON Sugar coated Tablets 10mg	6	0.51	10.5	25.0
NEUQUINON Tablets 10mg	6	0.52	9.5	19.2

Note) A single oral dose of 100 mg is unapproved.

2. Blood concentration of NEUQUINON Capsules 5mg and NEUQUINON Granules 1%

20 capsules of NEUQUINON Capsules 5mg or 10 g of NEUQUINON Granules were administered orally to healthy adult male volunteers at a single dose (100 mg ^{note)} of ubidecarenone) in a cross-over design, and changes in the plasma concentration were compared. For both dosage forms, the time to reach peak plasma concentration (0.55-0.7 µg/mL of exogenous CoQ₁₀) was 6 hr after administration, and thereafter, the plasma concentration gradually declined. Although the plasma concentration of capsules tended to be lower than for granules, there was no statistically significant difference between the two different dosage forms.



Plasma exogenous CoQ₁₀ concentrations after oral administration at a single dose of 100 ^{note)} mg of ubidecarenone

Pharmacokinetic parameters of NEUQUINON Capsules and NEUQUINON Granules

	t_{\max} (hr)	C_{\max} ($\mu\text{g}/\text{mL}$)	AUC ($\mu\text{g} \cdot \text{hr}/\text{mL}$)	$t_{1/2}$ (hr)
NEUQUINON Capsules 5mg	6	0.55	11.7	32.2
NEUQUINON Granules 1%	6	0.70	12.1	20.7

Note) A single oral dose of 100 mg is unapproved.

CLINICAL STUDIES

Clinical efficacy

In double blind clinical trials and open labeled clinical trials, NEUQUINON has been demonstrated to be useful for treating objective and subjective symptoms (edema, pulmonary congestion, hepatic enlargement and anginal symptoms, etc.) associated with congestive heart failure due to ischemic heart disease, hypertension or rheumatic heart disease, etc. ¹⁻⁴⁾

PHARMACOLOGY

1. Improvement of oxygen utilization efficiency in ischemic myocardium

In an experiment using guinea pig ventricular papillary muscle, ubidecarenone improved impaired myocardial contractility which occurred under hypoxic perfusion. ⁵⁾

2. Stimulation of ATP production in heart muscle

In rabbits heart muscle pretreated with ubidecarenone intraperitoneally, the decrease in ATP production in heart muscle seen after postischemic reperfusion was inhibited, so that postischemic reperfusion-induced myocardial cell injury was only slight. ^{6,7)}

3. Improvement of diminished cardiac function

When ubidecarenone was administered orally from the stage of myocardial injury to the stage of cardiac hypertrophy in models of cardiomyopathy (hamsters with cardiomyopathy), diminished myocardial contractility and expansibility were a lesser extent in the treated animals than in the untreated group or digoxin-treated group. ⁸⁾

In the rat models of myocardial infarction, ubidecarenone slightly inhibited a post-infarction decrease in cardiac function. When the effect of ubidecarenone on the post-infarction prognosis was determined in rat models of myocardial infarction, the long-term survival rate was higher for the treated group than for the untreated group. ⁹⁻¹⁰⁾

4. Anti-aldosterone effect

Ubidecarenone inhibited the secretion of aldosterone and antagonized Na^+ retention brought about by the aldosterone in rats, resulting in the acceleration of Na^+ diuresis. However, ubidecarenone has no effect on K^+ excretion. ¹¹⁾

PHYSICOCHEMISTRY

Nonproprietary name:

Ubidecarenone (JAN, INN)

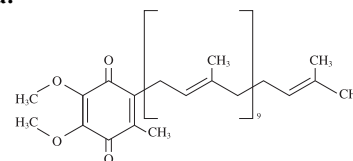
Chemical name:

(2*E*, 6*E*, 10*E*, 14*E*, 18*E*, 22*E*, 26*E*, 30*E*, 34*E*, 38*E*)-2-(3, 7, 11, 15, 19, 23, 27, 31, 35, 39-Decamethyltetraconta-2, 6, 10, 14, 18, 22, 26, 30, 34, 38-decaen-1-yl)-5, 6-dimethoxy-3-methyl-1, 4-benzoquinone

Molecular formula: $\text{C}_{59}\text{H}_{90}\text{O}_4$

Molecular weight: 863.34

Structural formula:



Description:

Ubidecarenone occurs as a yellow to orange, crystalline powder. It is odorless, and tasteless. It is freely soluble in diethylether, very slightly soluble in ethanol (99.5), and practically insoluble in water.

It is gradually decomposed by light, and darkens.

Melting point: about 48°C

PRECAUTIONS FOR HANDLING

- 5 mg and 10 mg tablets: Store away from light after opening outer box of press through packages or cap of bottle package (tablets may become discolored and the content may be decreased).
- Granules: After opening bottle, store away from light (granules may become discolored and the content may be decreased).

PACKAGING

NEUQUINON Tablets 5 mg:

Boxes of 100 and 1,000 in press-through packages

NEUQUINON Tablets 10 mg:

Boxes of 100, 210 (21Tabs. \times 10), 1,000 and 3,150 (21Tabs. \times 150) in press-through packages, and bottles of 500

NEUQUINON Sugar coated Tablets 10 mg:

Boxes of 100 and 1,000 in press-through packages

NEUQUINON Capsules 5mg:

Boxes of 100 and 1,000 in press-through packages, and bottles of 500

NEUQUINON Granules 1%:

Bottles of 100 g

REFERENCES

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- 11) Igarashi T. et al.: Proc. West. Pharmacol. Soc., **18**, 399, 1975.

**REQUESTS FOR LITERATURE AND PRODUCT
INFORMATION SHOULD BE MADE TO:**

Customer Information Service
Toll-free number: 0120-419-497
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Manufactured and marketed by:

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BRAND NAMES IN OTHER COUNTRIES

Decaquinon (Korea, Thailand, Myanmar, Vietnam, Cambodia)
Eiquinon (Hong Kong)
Neuquinon (Malaysia, Taiwan, Philippines, Dominican Republic)
Coenzyme Q10 (China)