ÿÿRevised in June 2020 (25th edition)
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Japan standard product
classification number 871139, 871179

Psychoactive antiepileptic drugs

Manic state treatment drugs

Storage
method: Shade and store at room temperature

Use within
the expiry date indicated on the packaging .

Prescription medicines: Caution - Use only as prescribed by a doctor, etc.

	Tablet 100mg	Tablet 200mg	Fine granules
50% Approval number	22700AMX00174	22700AMX00173	22700AMX00175
Listed in drug price	June 2015	June 2015	June 2015
Sales started in	June 2015	September 1998	June 1978
Indication added in	June 1978 - November 1991	month 1992 February	

カルバマゼピン錠100mg「フジナガ」
カルバマゼピン錠200mg「フジナガ」
カルバマゼピン細粒50%「フジナガ」

CARBAMAZEPINE TABLETS, FINE GRANULES “FUJINAGA”

Carbamazepine preparations

[Contraindications] (Do not administer to the following patients) 1. Patients with a history of hypersensitivity to the components of this drug or tricyclic antidepressants 2. Patients with serious blood disorders [as a side effect Blood disorders have been reported and may worsen blood abnormalities.]

3. Patients with second-degree or higher atrioventricular block or severe bradycardia (less than 50 beats/min) [Stimulus conduction may be suppressed and further severe atrioventricular block may occur.] 4. Patients receiving voriconazole, tadalafil (Adcirca), rilpivirine, macitentan, ticagrelor, grazoprevir, elbasvir, daclatasvir/asunaprevir/beclavir, asunaprevir, dolutegravir/rilpivirine, sofosbuvir/velpatasvir, bictegravir/emtricitabine/tenofovir alafenamide [Blood concentrations of these drugs may decrease.]] (See “Interactions” section) 5. Patients with porphyria [Porphyrin synthesis increases and symptoms The condition may worsen.]

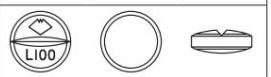
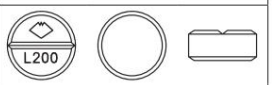
ÿComposition•Characterÿ

1. Composition

Contains the following ingredients in 1 tablet or 1 g of fine granules.

Brand Name	Active Ingredients	Additives
Carbamazepine Tablets 100mg "Fujinaga"	Carbamazepine 100mg	Crystalline Cellulose, Hydroxy Propyl Cellulose, Ste Carbamazepine Propyl Starch, Hydroxy Cypropyl Cellulose, Ste Japanese Pharmacopoeia Magnesium phosphate Japanese Pharmacopoeia
Carbamazepine Tablets 200mg "Fujinaga"	Carbamazepine 200mg	Japanese Pharmacopoeia
Carbamazepine fine grain 50% “Fujinaga”	Carbamazepine 500mg	Corn starch, D-mannitol, hypromellose

2. Properties of the preparation Carbamazepine tablets 100mg "Fujinaga": White plain tablets. Carbamazepine tablets 200mg "Fujinaga": White plain tablets. Carbamazepine fine granules 50% "Fujinaga": White fine granules.

Brand name	Identification code	Appearance, etc.
Carbamazepine tablets 100mg “Fujinaga”	L100	 Weight (mg), diameter (mm), thickness (mm) 140 8.0 3.1
Carbamazepine tablets 200mg "Fujinaga"	L200	 Weight (mg), diameter (mm), thickness (mm) 280 9.0 4.0

[Efficacy or effect] 1. Psychomotor seizures, epileptic personality and mental disorders associated with epilepsy, epileptic convulsive seizures: tonic-clonic seizures (generalized convulsive seizures, grand mal seizures)

2. Mania, manic state in manic-depressive disorder, excited state in schizophrenia

3. Trigeminal neuralgia

[Dosage and dosage] 1.

Psychomotor seizures, epileptic personality and mental disorders associated with epilepsy, epileptic convulsive seizures: For tonic-clonic seizures (generalized convulsive seizures, grand mal seizures), carbamazepine is usually administered to adults . Initially, the daily dose is 200 to 400 mg orally administered in 1 to 2 divided doses, and the dose is gradually increased until the optimal effect is achieved (usually 600 mg per day). The dose can be increased to 1,200mg per day depending on symptoms. For children, the usual daily dose is 100 to 600 mg orally administered in divided doses, depending on age and symptoms.

2. In the case of mania, manic depression (manic depression), or excited state (schizophrenia), the optimal effect is obtained by administering carbamazepine orally to adults at an initial daily dose of 200 to 400 mg in 1 to 2 divided doses. Gradually increase the dose up to (usually 600mg per day). The dose can be increased to 1,200mg per day depending on symptoms. **3. For trigeminal neuralgia**

Carbamazepine is usually administered orally to adults at a daily dose of 200 to 400 mg, usually up to 600 mg per day, but the dose can be increased to 800 mg per day depending on symptoms. For children, reduce the dose as appropriate depending on age and symptoms.

[Precautions for use] 1. Careful administration (Administer carefully to the following patients)

(1) Patients with heart disease such as heart failure, myocardial infarction, or first-degree atrioventricular block [stimulus conduction It may inhibit heart function and worsen heart function.]

(2) Patients who have difficulty urinating or increased intraocular pressure [Since it has anticholinergic effects, symptoms may be worsened.]

(3) Elderly patients [See section ``Administration in the Elderly''] (4) Patients with liver or renal impairment [Since metabolic and excretory functions are reduced in these patients, blood concentrations should be monitored. (5) Patients with drug hypersensitivity (6) Patients with hypothyroidism [There are reports that it reduces thyroid hormone concentration.]

2. Important basic precautions

(1)) **Rapid reduction in dosage or discontinuation of administration during prolonged use** may cause status epilepticus, so when discontinuing administration, be careful, such as by gradually reducing the dose. Please be especially careful if you are elderly or infirm. (2) **It is recommended to periodically conduct liver/kidney function and blood tests during prolonged use.** Delicious.

(3) As drowsiness and a decrease in alertness, concentration, and reflex movement ability may occur, patients receiving this drug should be careful not to engage in dangerous activities such as driving a car . (4) When used to treat the excited state of schizophrenia, it should be used when antipsychotic drugs are not sufficiently effective. (5) Seizures may be exacerbated or induced by administration of antiepileptic drugs. When administering this drug to patients with mixed seizure type or small seizures for which this drug is considered ineffective (absence seizures, atypical absence seizures, atonic seizures, myoclonic seizures), pay attention to the condition and prevent seizures. If symptoms worsen or are induced, gradually reduce the dose of this drug and discontinue it.

(6) Symptoms such as drowsiness, nausea/vomiting, dizziness, double vision, and ataxia are often signs of overdosage, so if such symptoms occur, gradually reduce the dose to the optimum effective dose. Lose weight. It is particularly common in the early stages of administration, so it is desirable to start administration at a lower dose.

3. Interactions

Although interactions of this drug with many drugs have been reported, not all possible combinations have been investigated, so it may not be possible to use this drug in combination with other drugs, or to use this drug in combination with other drugs. Be careful when discontinuing the drug. In particular, the main metabolic enzyme of this drug is cytochrome P450 3A4, and it also induces metabolic enzymes including cytochrome P450 3A4, so it should not be used in combination with drugs that affect these activities or are metabolized by them. If so, measure the blood drug concentration and observe clinical symptoms as much as possible, and administer with care, paying attention to the dose. In addition, the enzyme involved in the metabolism of carbamazepine-10,11-epoxide, the main metabolite of carbamazepine, is epoxide hydrolase, and when used together with drugs that inhibit this enzyme, carbamazepine-10,11 -Since the blood concentration of epoxide may increase, clinical symptoms should be observed as much as possible and the dose should be carefully administered. (1) **Concomitant use contraindications (do not use together)**

Drug name, etc.	Clinical symptoms/measures	Mechanism/risk factors
Voriconazole (Vifend) **Tadalafil** (Adcirca) **Rilpivirine** (Ejurant) **Macitentan** (Opsumit) Ticagrelor (Brilinta) ÿ **Grazoprevir** (Gradyna) **Elbasvir** ÿ (Elersa) ÿ **Daclatasvir / Asunaprevir/ Beclabvir** ÿ (Zimency combination ÿ tablets)) **Asunaprevir** (Sunvepra) **Dolutegravir/ Rilpivirine** (Jalka Combination ÿ Tablets) **Sofosbuvir/ Velpatasvir** ÿ (Epclusa Combination Tablets)	There is a risk that the blood concentration of these drugs will decrease and their effects will be weakened.	This drug's hepatic drug-metabolizing enzyme-inducing effect accelerates the metabolism of these drugs.
ÿ		Due to the inducing effects of this drug on P-gp and metabolic enzymes, the plasma concentrations of these drugs may
ÿ **Bictegravir Emtrici Tabin Tenofo Vir Alafenamide** (Bictarvy combination tablets)	decrease. The plasma concentration of Namide is due to the P-gp and metabolic enzyme inducing effects of bictegravir and this drug. This decreases the effectiveness of this drug and may lead to the development of resistance to this drug.	

(2) **Caution when used together (Be careful when using together)**

Drug name, etc.	Clinical symptoms/measures	Mechanism/risk factors
MAO inhibitors may cause	symptoms such as sweating, restlessness, general convulsions, abnormally high fever, and coma.	This drug has a similar structure to tricyclic antidepressants, so similar symptoms may occur.
There have been reports of	psychoneurological symptoms (confusion, gross tremor, disorientation, etc.) occurring with **lithium carbonate .**	Although the exact mechanism is unknown, it is thought that the additive effects of both drugs on sodium metabolism and nerve conduction velocity may be related.
There have been reports that	neurological symptoms (gait disturbance, ataxia, nystagmus, diplopia, hyperreflexia in the lower	Mechanism unknown
limbs) have appeared with	**metoclopramide .** There is a possibility that the interaction with **alcohol** may be enhanced. Avoid excessive alcohol consumption.	Both drugs have central nervous system depressant effects.
central nervous system depressant Haloperidol Thioridazine	Mutual effects may be enhanced.	
Diuretics (sodium-losing)	Hyponatremia/ SIADH may appear. Consider using diuretics other than sodium-wasting diuretics.	Both may lower serum sodium.
Isoniazid May enhance the hepatotoxicity of isoniazid.	Additionally, the blood concentration of this drug may rise rapidly, and symptoms of toxicity (drowsiness, nausea/ vomiting, dizziness, etc.) may occur.	The hepatic drug-metabolizing enzyme-inducing effect of this drug increases the metabolism of isoniazid, promoting the production of isoniazid metabolites that are hepatotoxic. Additionally, isoniazid inhibits the metabolism of this drug.
Fluvoxamine **Verapamil** **Diltiazem** **Cimetidine** **Omeprazole** **Danazol** **Bicalutamide** **Quinupristin/ Dalfopristin Macrolide antibiotics** **Erythromycin ,** Clarithromycin, etc. **Ritonavir** **Darunavir** **Azole antifungal agents** Miconazole, Fluconazole, etc. **Ciprofloxacin**	The blood concentration of this drug may rise rapidly, and symptoms of toxicity (drowsiness, nausea/vomiting, dizziness, etc.) may occur.	These drugs inhibit the metabolism of this drug.
Acetazolamide		Mechanism unknown
Quetiapine	The blood concentration of quetiapine may decrease. Additionally, the blood concentration of this drug's metabolites may increase.	The metabolism of quetiapine is promoted by the hepatic drug-metabolizing enzyme-inducing effect of this drug. Additionally, quetiapine inhibits the metabolism of this drug's
itraconazole telaprevir	Blood levels of these drugs may decrease. Additionally, the blood concentration of this drug may increase.	metabolites. This drug's hepatic drug-metabolizing enzyme-inducing effect accelerates the metabolism of these drugs. Additionally, these drugs inhibit the metabolism of this drug.
clobazam **paroxetine**	Blood levels of these drugs may decrease. Additionally, the blood concentration of this drug may increase.	This drug's hepatic drug-metabolizing enzyme-inducing effect accelerates the metabolism of these drugs. Furthermore, the mechanism by which the blood concentration of this drug increases due to concomitant use is unknown.
Phenobarbital **Rifampicin**	The blood concentration of this drug may decrease.	The metabolism of this drug is accelerated by the hepatic drug-metabolizing enzyme-inducing effects
The blood concentration of **phenytoin** may decrease. It may also increase or decrease the blood concentration of phenytoin.		of these drugs. Both drugs have hepatic drug-metabolizing enzyme-inducing effects, so they mutually promote metabolism. Additionally, phenytoin metabolism is inhibited due to metabolic competition.

Valproic acid May decrease the blood concentration of valproic acid. Additionally, the blood concentration of this drug and its metabolites may increase or the blood concentration of this drug may decrease.		The metabolism of valproic acid is promoted by the hepatic drug-metabolizing enzyme-inducing effect of this drug. Additionally, valproic acid inhibits the metabolism of this drug's metabolites. There are reports that the blood concentration of this drug increases or decreases when used in combination with valproic acid, but the mechanism is unknown.
Blood concentrations of primidone and **primidone** may decrease. Additionally, the blood concentration of this drug's metabolites may increase.		Metabolism is thought to be mutually promoted by the hepatic drug-metabolizing enzyme-inducing effects of both drugs. Primidone also inhibits the metabolism of this drug's metabolites.
Blood concentrations of **efavirenz** may decrease.		Metabolism is thought to be mutually promoted by the hepatic drug-metabolizing enzyme-inducing effects of both drugs.
Theophylline aminophylline hydrate		This drug promotes theophylline metabolism by inducing hepatic drug-metabolizing enzymes. Furthermore, the mechanism by which the blood concentration of this drug decreases due to concomitant use
Anti-anxiety/sleep-inducing agent Alprazolam Midazolam **Antiepileptic agent** Zonisamide Clonazepam Ethosuximide ÿ Topiramate Perampanel **Tramadol Buprenorphine Anti-parkinsonian drug** * Istradefi **Lin Butyrophenone drug Tricyclic antidepressants** such as haloperidol Imipramine, amitriptyline, nortriptyline, etc. Trazodone Mianserine Sertraline Mirtazapine **Neuropsychiatric drug** Olanzapine Aripiprazole Risperidone Blonanserin Clozapine Paliperidone Donepezil **Flecainide Eletri Putan Dihydropyridine calcium antagonists such as** nifedipine, felodipine, nilvadipine, etc. **Ondansetron Corticosteroids such as** prednisolone, dexamethasone, etc. **Luteal and follicular hormones such as** drospirenone, ethinyl estradiol, etc. ÿ	It may reduce the effects of these drugs.	is unknown. The metabolism of these drugs is promoted by the hepatic drug-metabolizing enzyme-inducing effect of this drug.
	There is a risk of decreased efficacy and increased incidence of abnormal vaginal bleeding.	

solifenacin coumarin anticoagulant warfarin **immunosuppressant** cyclosporin tacrolimus everolimus **antineoplastic agent** irinotecan imatinib gefitinib sorafenib sunitinib dasatinib nilotinib lapatinib toremifene tamibarotene temsirolimus axitinib ceritinib ÿ osimertinib ÿ palbociclib ibrutinib ÿ po natinib ÿ ÿ	It may reduce the effects of these drugs.	The metabolism of these drugs is promoted by the hepatic drug-metabolizing enzyme-inducing effect of this drug.
ÿ **Anti-cancer agent** lenvatinib		Due to the inducing effect of this drug on P-gp and metabolic enzymes, the blood concentration of lenvatinib may decrease.
ÿ **Doxycycline Antiviral agents (HIV** infection treatment drugs) Saquinavir, indinavir, nelfinavir, lopinavir, dolutegravir, abacavir, lamivudine, etc. Maraviroc Delavirdine Etravirine Praziquantel Eplerenone Sildenafil Tadalafil **(Cialis) Dienogest Aprepitant Rivaroxaban Simvastatin**		The metabolism of these drugs is promoted by the hepatic drug-metabolizing enzyme-inducing effect of this drug.
fosaprepitan tomeglumine		The hepatic drug-metabolizing enzyme-inducing effect of this drug promotes the metabolism of aprepitant, the active substance of fosaprepitant meglumine, and lowers its blood concentration.
Nondepolarizing muscle relaxants Pancuronium, Digoxin, **Albendazole**		Mechanism unknown
ÿ **Hydroxychloroquine**	The effect of this drug may be reduced.	
Mirabegron The action of mirabegron may be attenuated.		The hepatic drug-metabolizing enzyme inducing effect and P-glycoprotein inducing effect of this drug accelerates the metabolism of mirabegron and lowers its blood concentration.
Cyclophosphamide	May enhance the effects of cyclophosphamide.	The concentration of active metabolites of cyclophosphamide increases due to the hepatic drug-metabolizing enzyme-inducing effect of this drug.
Caspofungin Blood concentration of caspofungin may decrease.		This drug affects the uptake and transport process of caspofungin, leading to the induction of caspofungin clearance.

Acetaminophen	May reduce the effect of acetaminophen. There are also reports that it increases the likelihood of liver damage.	The hepatic drug metabolism enzyme-inducing effect of this drug accelerates the metabolism of acetaminophen, reducing its blood concentration. It also accelerates the metabolism of acetaminophen to N-acetyl-p-benzoquinoneimine, which is hepatotoxic.
Lamotrigine	May decrease the blood concentration of lamotrigine.	Glucuronidation of lamotrigine in the liver is promoted.
dabigatran etexilate	It may reduce the effect of dabigatran.	Due to the P-glycoprotein inducing effect of this drug, the blood concentration of dabigatran may decrease.
St. John's Wort (St. John's Wort)-containing foods	Be careful not to ingest foods containing St. John's wort when administering this drug, as the metabolism of this drug may be accelerated and the blood concentration may decrease. Be careful not to ingest grapefruit juice when administering this drug, as the metabolism of this drug may be suppressed and the blood concentration may increase.	It is thought that St. John's wort induces hepatic drug metabolism enzymes.
grapefruit juice		It is thought that the ingredients contained in grapefruit juice inhibit enzymes that metabolize this drug in the small intestine.

4. Side effects: No studies have been conducted on this drug to clarify the frequency of side effects, such as use results surveys. **(1)**

Serious side effects 1) **Aplastic anemia, pancytopenia, leukopenia, agranulocytosis, anemia, hemolytic anemia, erythroblastic aplasia, thrombocytopenia** (incidence unknown): Serious blood disorders. Patients should be carefully monitored by regularly conducting blood tests, and if any abnormalities are observed, administration should be discontinued and appropriate measures should be taken.

2) **Toxic Epidermal Necrolysis** * **Necrolysis (TEN), mucocutaneous oculomucocutaneous syndrome (Stevens Johnson syndrome), erythema multiforme, acute generalized rash, pustulosis, erythroderma (exfoliative dermatitis) (incidence unknown): Severe skin symptoms may appear .** Therefore, the patient should be carefully observed for symptoms such as fever, red eyes, swelling of the face, erosion of the lips, oral mucosa, and genitals, blisters on the skin and mucous membranes, numerous small pustules, erythema, sore throat, itching, and general malaise. If any abnormalities are observed, administration should be discontinued immediately and appropriate measures should be taken. Furthermore, since most of these symptoms develop within 3 months of starting administration of this drug, patients should be carefully monitored, especially during the early stages of administration. 3) SLE-like symptoms (incidence unknown): SLE-like symptoms (skin symptoms such as butterfly erythema, fever, arthralgia, white blood cell count, thrombocytopenia, antinuclear antibody positivity, etc.) may occur, so careful observation is required. If any abnormalities are observed, administration should be discontinued and appropriate measures should be taken. 4) Hypersensitivity syndrome (incidence unknown): Fever and rash are seen as initial symptoms, followed by lymphadenopathy, arthralgia, increased white blood cells, increased eosinophilia, appearance of atypical lymphocytes, hepatosplenomegaly, and liver dysfunction. Delayed and serious hypersensitivity symptoms may occur, accompanied by organ damage. Also, be aware that symptoms such as rash, fever, and liver dysfunction may flare up or become prolonged. Furthermore, it is often accompanied by reactivation of viruses such as human herpesvirus 6 (HHV-6). If such symptoms occur, administration should be discontinued and appropriate measures should be taken.

5) Hepatic dysfunction, jaundice (incidence unknown): Cholestatic, **hepatocellular, mixed, or granulomatous liver dysfunction and jaundice may occur, which may lead to fulminant hepatitis, etc.,** so Patients should be carefully monitored, including liver function tests. If any abnormalities are observed, administration should be discontinued and appropriate measures should be taken. 6) **Acute kidney injury (interstitial nephritis, etc.) (incidence unknown): Severe** * serious kidney injury may occur, so monitor the patient thoroughly by regularly conducting kidney function tests, and check if any abnormalities are detected. If this occurs, discontinue administration and take appropriate measures. 7) **PIE syndrome, interstitial pneumonia (incidence unknown):** PIE syndrome and interstitial pneumonia accompanied by fever, cough, dyspnea, sputum, eosinophilia, and infiltrative shadows in the lung fields may occur. If such symptoms occur, discontinue administration and take appropriate measures. 8) Thromboembolism (incidence unknown):

Thromboembolism such as pulmonary embolism, deep vein thrombosis, and thrombophlebitis may occur, so carefully observe the patient and take appropriate action if any abnormalities are observed. Discontinue administration and take appropriate measures. 9) Anaphylaxis (incidence unknown): Anaphylaxis accompanied by hives, angioedema, circulatory failure, hypotension, difficulty breathing, etc. may occur. If such symptoms occur, administration should be discontinued. Appropriate measures should be taken. 10) **Congestive heart failure, atrioventricular block, sinus insufficiency,** bradycardia (incidence unknown): Congestive heart failure, atrioventricular block, sinus insufficiency, bradycardia may occur, so carefully monitor the patient and check for abnormalities. If this is observed, administration should be discontinued and appropriate measures should be taken. 11) **Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)** (incidence unknown): Inappropriate secretion of antidiuretic hormone accompanied by hyponatremia, hypoosmolarity, increased urinary sodium excretion, hypertonic urine, convulsions, disturbance of consciousness, etc. If such symptoms occur, administration should be discontinued and appropriate measures such as restricting fluid intake should be taken. 12) Aseptic meningitis (incidence unknown): Aseptic meningitis may occur with nuchal stiffness, fever, headache, nausea/vomiting, or clouded consciousness, so if such symptoms occur, If so, administration should be discontinued and appropriate measures should be taken. 13) Malignant syndrome (incidence unknown): Administration of this drug may cause fever, impaired consciousness, akinesia, severe muscle stiffness, difficulty swallowing, tachycardia, fluctuations in blood pressure, sweating, etc. In such cases, administration should be discontinued and appropriate measures should be taken along with systemic management such as body cooling and hydration. This may occur if the drug is suddenly discontinued, so do not suddenly stop administering this drug. In addition, special care should be taken as malignant syndrome is more likely to occur during concomitant use with antipsychotics. Furthermore, at the onset of this disease, an increase in white blood cells and serum CK (CPK) is often observed, and a decline in renal function accompanied by myoglobinuria may be observed. **(2) Other side effects**

	Hypersensitivity note 1)
Scarlet fever-like rash, measles-like rash, poison eruption-like rash, photosensitivity, vasculitis, angioedema, pruritus, urticaria, dyspnea, flushing, pigmentation, acne, papules, polymorphism	
skin	Erythema nodosum, purpura, hirsutism, lichenoid keratosis, nail disorders (onycholysis, nail deformation, nail discoloration, etc.)
Musculoskeletal muscle spasms, muscle weakness, joint pain, muscle pain	

Blood Note 1)	Porphyria, megaloblastic anemia, leukocytosis, eosinophilia, reticulocytosis, lymphadenopathy
Liver Note 1)	Increased AST (GOT), increased ALT (GPT), increased Al-P, increased ÿ-GTP Proteinuria, increased
kidney	BUN, increased creatinine, oliguria, urinary retention, frequent urination, hematuria
Decreased **mental and nervous system**	attention/concentration/reflex motor ability, etc., lightheadedness, depression, headache/dull head, weakness, fatigue, excitement, ataxia, involuntary movements (tremor, asterixis, etc.), speech disorders, Confusion, drowsiness, dizziness, hallucinations (visual, auditory), light-headedness, delirium, paresthesia, impotence, peripheral neuritis, orofacial dyskinesia, chorea athetosis, paralytic symptoms, aggressive behavior, agitation, disturbance of consciousness, Sedation, memory impairment Double vision,
Eye Note 2)	blurred vision, accommodative disorders, nystagmus, abnormal eye movements (eye rotation attacks), lens opacity, conjunctivitis,
increased intraocular pressure, decreased cardiovascular blood pressure, increased blood pressure, arrhythmia, impulse **conduction** disorders	
Gastrointestinal anorexia, nausea/vomiting, constipation, diarrhea, dry mouth, pancreatitis Note 1), stomatitis, glossitis, abdominal pain, colitis Vitamin	
Department of Endocrinology and Metabolism	D/calcium metabolism abnormalities (lower serum calcium, etc.), thyroid function test values Abnormalities (low T4 level, etc.), low serum folate level, gynecomastia, galactorrhea, increased prolactin, hyponatremia, osteomalacia, osteoporosis, hyperglycemia
Other symptoms include fever, taste abnormalities, hearing abnormalities (tinnitus, hyperacusis, hearing loss, changes in pitch, etc.), hair loss, edema, sweating, increased cholesterol, increased CK (CPK) levels, increased triglycerides, fluid retention, and immunoglobulin. decrease (IgA, IgG, etc.), weight gain, CRP rise, cold symptoms (nasopharyngitis, cough, etc.)	

Note 1) Administration should be discontinued. Note 2) It is desirable to conduct visual acuity tests regularly. **5. Administration to the elderly**

Take precautions such as reducing weight [Physiological functions generally decline in the elderly.] (See section ``Important basic notes").

6. Administration to pregnant women, parturient women, lactating women, etc. (1) The drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are judged to outweigh the risks. If it is unavoidable to administer this drug during pregnancy, it is desirable to avoid concomitant use with other anti-epileptic drugs as much as possible. Epidemiological research reports indicate that there are many cases of children giving birth to children with abnormalities (including those in the vertebrae) or children with developmental disabilities. Additionally, compared to administering this drug alone, the combination of this drug and other antiepileptic drugs (particularly sodium valproate) may result in more babies being born with malformations such as cleft palate, cleft lip, and ventricular septal defect. There are epidemiological investigation reports. There have also been reports of hypospadias.].

(2) It has been reported that if this drug is used in combination with this drug or other antiepileptic drugs before delivery, withdrawal symptoms (convulsions, breathing problems, vomiting, diarrhea, eating disorders, etc.) may occur in the newborn after delivery.

be. (3) Administration during pregnancy may cause bleeding tendency in newborns. (4) There are reports that administration during pregnancy causes a decrease in folic acid.

(5) It should be administered to lactating women only when the therapeutic benefits are judged to outweigh the risks [It has been reported that it passes into breast milk.].

7. Overdose1) (1)

Symptoms: The first signs and symptoms usually appear 1 to 3 hours after taking the drug (see ``Important Precautions'' section). Central nervous system disorders (tremors, excitement, convulsions, disturbances of consciousness, coma, electroencephalogram changes, etc.) are the most obvious, and cardiovascular disorders (blood pressure changes, electrocardiogram changes, etc.) are usually mild. Additionally, rhabdomyolysis may occur. (2) Treatment: No specific antidote is known. Typically, the following actions are taken: - Emesis, aspiration of gastric contents, gastric lavage, hemodialysis. Administer activated charcoal if necessary.•Secure the airway. Endotracheal intubation, artificial respiration, and oxygen inhalation as necessary. - Elevate both legs and administer plasma volume expanders for hypotension. Administer vasopressors as necessary. - Inject diazepam intravenously for convulsions (however, be careful of respiratory depression, hypotension, and worsening of coma due to diazepam). After taking appropriate measures, continue to monitor breathing, cardiac function, blood pressure, body temperature, etc. for several days. **8. Precautions for application When** delivering the drug: Instruct patients to take the PTP packaged drug out of the PTP sheet before taking it. (If the PTP sheet is swallowed accidentally, the hard sharp edges may penetrate the esophageal mucosa and even cause perforation. It has been reported that this can cause serious complications such as mediastinal sinusitis.) **9.**

Other precautions (1)

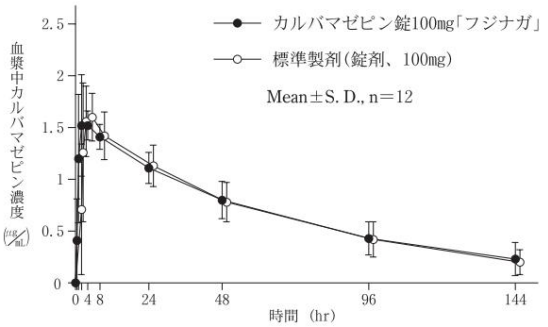
When switching to another antiepileptic drug, it is usually recommended to use diazepam or a barbiturate compound in combination to prevent exacerbation. (2) It has been reported that in experiments in which carbamazepine was orally administered to rats over a long period of time (25, 75, and 250 mg/kg for 2 years), the occurrence of liver tumors in females was significantly observed in a dose-dependent manner. (3) Abnormalities in serum immunoglobulin (IgA, IgG, etc.) may occur. (4) There are reports of male fertility impairment and abnormal spermatogenesis. (5) There have been reports of cross-sensitivity (skin hypersensitivity including hypersensitivity syndrome) occurring between this drug and other antiepileptic drugs (phenytoin, phenobarbital). (6) In a retrospective genome-wide association analysis in Japanese subjects, HLA-A It has been reported that 58% (45/77) were carriers of 3101, and 13% (54/420) were carriers of HLA-A*3101 in the group that did not develop severe drug eruption. Furthermore, the frequency of the HLA-A* 3101 allele is reported to be 0.071-0.120 in Japanese people. In a study on patients of Han-Chinese ancestry, almost all of the cases of oculomucocutaneous syndrome and toxic epidermal necrolysis caused by this drug were HLA-B*1502 carriers . There are reports that there was. On the other hand, studies in Japanese subjects have not suggested a clear relationship between cases of severe drug eruption caused by this drug and HLA-B*1502 possession . It has been reported that the frequency of the HLA-B*1502 allele is 0.019-0.124 in Han Chinese and 0.001 in Japanese. (7) The results of 199 placebo-controlled clinical trials of multiple antiepileptic drugs, including this drug, conducted overseas for epilepsy, psychiatric disorders, etc., show that the risk of suicidal thoughts and attempts is Approximately twice as high in the antiepileptic drug group compared to the placebo group (antiepileptic drug group: 0.43%, placebo group: 0.24%); (95% confidence interval: 0.6-3.9). It was also calculated that in the subgroup of epilepsy patients, there were 2.4 more patients per 1000 compared to the placebo group.

[Drug kinetics] 1. Bioequivalence

study 2) One tablet each (100 mg of carbamazepine) of carbamazepine tablets 100 mg "Fujinaga" and the standard preparation were administered to 12 healthy adult males once on an empty stomach using a crossover method. The bioequivalence of both drugs was confirmed as a result of oral administration, measurement of plasma concentrations, and statistical analysis of the obtained pharmacokinetic parameters.

	AUCÿ0-144hrÿ ÿhr•ÿg/mLÿ	Cmax ÿÿg/mLÿ	Tmax ÿhrÿ	T1/2 ÿhrÿ
Carbamazepine tablet 100mg "Fujinaga"	98.9±21.2	1.72±0.18	2.3±2.0	51.9±17.0
standard formulation (tablet, 100mg)	98.6±23.4	1.68±0.29	2.6±1.3	49.6±13.4

ÿMean±S.D.,nÿ12ÿ



Plasma concentrations and parameters such as AUC and Cmax may vary depending on test conditions such as subject selection and number and time of body fluid collection. **2.**

Effective blood concentration3) The effective blood carbamazepine concentration is said to be 4 to 12 ÿg/mL (for epilepsy). **3.**

Dissolution behavior 4) Carbamazepine tablets 100 mg “Fujinaga”, carbamazepine tablets 200 mg “Fujinaga” and carbamazepine fine granules 50% “Fujinaga” are carbamazepine tablets and carbamazepine fine grains specified in Part 3 of the Japanese Pharmacopoeia Non-Japanese Pharmaceutical Standards. It has been confirmed that it complies with the grain elution standards.

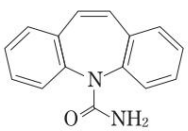
[Drug efficacy/pharmacology] 1.

Anticonvulsant action5) Carbamazepine exhibits almost the same suppressive effect as phenobarbital on electric shock convulsions in rats, and has a sufficient suppressive effect on strychnine convulsions in mice. However, carbamazepine 100 mg/kg (orally) clearly delays the onset of convulsions compared to phenytoin and mephenesin. **2. Antiexcitatory effects5-7)** In behavioral pharmacological tests using mice, carbamazepine exhibits effects of suppressing combative behavior, suppressing stereotypic behavior, and enhancing anesthesia. In electrophysiological tests using rabbits, carbamazepine has been shown to suppress evoked potentials in the emotional pathway from the olfactory bulb to the limbic system (olfactory bulb-amygdaloid nucleus, olfactory bulb-hippocampus). **3. Effect on trigeminal neuralgia8)**

Carbamazepine prolongs the latency of the trigeminospinal tract response to electrical stimulation of the maxillary nerve in cats.

[Physical and chemical knowledge regarding active ingredients]

Common name: Carbamazepine Chemical name: 5H-Dibenzo[b,f]azepine-5-carboxamide Molecular formula: C15H12N2O
Molecular weight: 236.27
Structural formula:



Appearance: White to slightly yellowish white powder, odorless and tasteless at first, but then slightly bitter. Easily soluble in chloroform, slightly soluble in ethanol (95) or acetone, very sparingly soluble in water or diethyl ether. Melting point: 189-193ÿ

[Handling Precautions]

Stability test 9)

Carbamazepine tablets 100mg "Fujinaga" (PTP): The results of a long-term storage test (room temperature, 3 years) using the final packaged product showed that it was within the specification range and was stable for 3 years under normal market distribution. It was confirmed that there is. **Carbamazepine tablets 100mg "Fujinaga" (plastic bottle):** As a result of a relative comparison test using the final packaged product (40ÿ, relative humidity 75%, 6 months), it is estimated that it is stable for 3 years under normal market distribution. It was done. **Carbamazepine Tablets 200mg "Fujinaga" (PTP): The results of a long-term storage test (room temperature, 5 years) using the final packaged product** confirmed that it was within the specifications and stable for 5 years under normal market distribution. Ta. **Carbamazepine tablets 200mg "Fujinaga" (plastic bottle):** As a result of a relative comparison test using the final packaged product (40ÿ, relative humidity 75%, 6 months), it is estimated that it is stable for 5 years under normal market distribution. It was done. **Carbamazepine fine granules 50% "Fujinaga": This drug is** estimated to be stable for 5 years under normal market distribution as a result of a relative comparison test (40ÿ, 75% relative humidity, 6 months) at the time of formulation change. It was done.

[Packaging] Carbamazepine tablets

100 mg "Fujinaga" 100 tablets (PTP) 1,000 tablets (PTP) 500 tablets (plastic bottle)

Carbamazepine tablets 200 mg "Fujinaga" 100 tablets (PTP) 1,000 tablets (PTP) 500 tablets (plastic bottle) 500g

Carbamazepine fine granules 50% "Fujinaga" 100g

[Major documents] 1) JPDI 2011 Japanese Pharmacopoeia Drug Information Jiho 2011; 472-479 2) Fujinaga Pharmaceutical internal materials: Materials regarding bioequivalence 3) Tatsuji Iga et al.: Practical TDM for drug administration design Drugs Gyojihosha 1993; 126-149 4) Fujinaga Pharmaceutical internal materials: Materials related to dissolution 5) Theobald W, et al.: Arzneimittelforschung 1963; 13 (2): 122-125 6) Kenzo Nakao et al.: Pharmacology and treatment 1988; 16 (3): 1189-1190 7) Kenzo Nakao et al.: Pharmacology and Treatment 1988; 16 (3): 1191-1206 8) Fromm GH, et al.: Neurology 1967; 17: 275-280 9) Fujinaga Pharmaceutical internal materials: Stability documentation

[Request for literature/Inquiry for product information] ÿÿ Please contact the following for in-house materials listed in the main literature.

Fujinaga Pharmaceutical Co., Ltd. Medicine Counseling Office Front Place Nihonbashi, 2-14-1 Nihonbashi, Chuo-ku, Tokyo 103-0027 TEL: 03-6327-2478 FAX: 03-6327-2479

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