

Revised: October 2009 (12th version)

Standard Commodity Classification No. of Japan
871145

- Analgesic/anti-inflammatory agent activated in tissues -

**Infree<sup>®</sup> Capsules 100mg**  
**Infree<sup>®</sup> S Capsules 200mg**

&lt;Indometacin farnesil preparation&gt;

Powerful drug and Prescription drug

Storage
INFREE should be stored at room temperature. (See "PRECAUTIONS FOR HANDLING" section.)

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

	Cap. 100 mg	S Cap. 200 mg
Approval No.	20300AMZ00250000	20600AMZ00985000
Date of listing in the NHI reimbursement price	May 1991	Dec 1994
Date of initial marketing in Japan	May 1991	Dec 1994
Date of latest reexamination	Dec 2001	

Caution : Use only as directed by a physician.

**CONTRAINDICATIONS (INFREE is contraindicated in the following patients.)**

1. Patients with peptic ulcer (but, see "Careful Administration" section.)  
[Peptic ulcer may be aggravated.]
2. Patients with serious blood dyscrasia  
[Blood dyscrasia may be aggravated.]
3. Patients with serious hepatic function disorders  
[Hepatic function disorders may be aggravated.]
4. Patients with serious renal function disorders  
[Renal function disorders may be aggravated.]
5. Patients with serious cardiac dysfunction  
[Cardiac dysfunction may be aggravated.]
6. Patients with serious hypertension  
[Hypertension may be aggravated.]
7. Patients with serious pancreatitis  
[It has been reported that acute pancreatitis occurred with the use of indometacin, the active metabolite of INFREE.]
8. Patients with hypersensitivity to INFREE, indometacin or salicylates (e.g. aspirin, etc.)
9. Patients with aspirin-induced asthma (asthma induced by non-steroidal anti-inflammatory analgesics, etc.) or its history  
[A serious aspirin-induced asthma attack may occur.]
10. Pregnant women or women suspected of being pregnant  
[See "Use during Pregnancy, Delivery or Lactation" section.]
11. Patients on triamterene therapy  
[See "Drug Interactions" section.]

**RELATIVE CONTRAINDICATIONS (As a general rule, INFREE is contraindicated in the following patients. If the use of INFREE is considered essential, it should be administered with care.)**

Children

[If it is to be used in patients with rheumatoid arthritis, who show no response or are intolerant to other treatment, INFREE may be used if due caution is exercised. See "Pediatric Use" section.]

**DESCRIPTION****1. Composition****Capsules 100 mg:**

Each white, hard capsule contains 100 mg of indometacin farnesil.



It also contains hydrated silicon dioxide, glycine, light anhydrous silicic acid, microcrystalline cellulose, tartaric acid, gelatin, talc, tocopherol, macrogol 6000, methylcellulose and sodium lauryl sulfate as inactive ingredients.

**S Capsules 200 mg:**

Each light orange, soft capsule contains 200 mg of indometacin farnesil.

It also contains L-aspartic acid, yellow ferric oxide, carnauba wax, hydrogenated oil, titanium oxide, gelatin, D-sorbitol solution, tocopherol, concentrated glycerin, ethyl parahydroxybenzoate, propyl parahydroxybenzoate, propylene glycol esters of fatty acid and polyoxyethylene hydrogenated castor oil 60, glyceryl monooleate as inactive ingredients.

## 2. Product description

Brand name	Dosage form and identification code	Appearance			Description
INFREE Capsules 100 mg	Hard Capsules				Capsules Cap : White Body: White Contents Light yellow granules or powder
	E 235	Length (mm) 16.2	Weight (mg) 236	Size No.3	
INFREE S Capsules 200 mg	Soft Capsules				Capsules Light orange Contents Light yellow, viscous liquid
	—*	Long diameter (mm) 13.1	Short diameter (mm) 8.1	Weight (mg) 525	

\* The term of “インフリー-200” is printed on the surface of each soft capsule.

## INDICATIONS

Anti-inflammation and analgesia in the following diseases and symptoms:

Rheumatoid arthritis, osteoarthritis, low back pain, scapulothoracic periarthritis and neck-shoulder-arm syndrome

## DOSAGE AND ADMINISTRATION

The usual adult dosage for oral use is 200 mg of indometacin farnesil twice daily, in the morning and in the evening after meals.

The dosage may be adjusted depending on patient's age and symptoms.

## PRECAUTIONS

### 1. Careful Administration (INFREE should be administered with care in the following patients.)

- (1) Patients with a history of peptic ulcer  
[Peptic ulcer may recur.]
- (2) Patients with peptic ulcer due to long-term administration of non-steroidal anti-inflammatory analgesics, who need to take INFREE for a long time and are being treated with misoprostol  
[Although an indication of misoprostol is peptic ulcer due to administration of non-steroidal anti-inflammatory analgesics, some peptic ulcers are resistant to misoprostol therapy. Therefore, if INFREE is administered continuously, the patient's condition should be closely observed and INFREE administered with care.]
- (3) Patients with blood dyscrasia or its history  
[Blood dyscrasia may be aggravated or recur.]
- (4) Patients with hepatic function disorder or their history  
[Hepatic function disorder may be aggravated or recur.]
- (5) Patients with renal function disorder or their history  
[Renal function disorder may be aggravated or recur.]
- (6) Patients with cardiac dysfunction  
[Cardiac dysfunction may be aggravated.]
- (7) Patients with hypertension  
[Hypertension may be aggravated.]
- (8) Patients with pancreatitis  
[It has been reported that acute pancreatitis occurred with the use of indometacin, the active metabolite of INFREE.]

- (9) Patients with a history of hypersensitivity to any drug
- (10) Patients with a central nervous system diseases, such as epilepsy or parkinsonism  
[It has been reported that indometacin, the active metabolite of INFREE, aggravates these diseases.]
- (11) Patients with bronchial asthma  
[Asthmatic attacks may occur.]
- (12) Patients with SLE (systemic lupus erythematosus)  
[It has been reported that an analogue compound (phenylbutazone) aggravated SLE. In addition, acute renal failure has been reported in patients with SLE given indometacin, the active metabolite of INFREE.]
- (13) Patients with ulcerative colitis  
[It has been reported that indometacin, the active metabolite of INFREE, aggravated this disease.]
- (14) Patients with Crohn's disease  
[It has been reported that indometacin, the active metabolite of INFREE, aggravated this disease.]
- (15) Elderly patients  
[See “Use in the Elderly” section.]

### 2. Important Precautions

- (1) Treatment with anti-inflammatory analgesics is generally not causal therapy, but symptomatic therapy.
- (2) The patient should be carefully observed for adverse reactions. Symptoms such as an excessive decrease in body temperature, collapse, and coldness of limbs have been reported in patients receiving indometacin, the active metabolite of INFREE; hence, INFREE should be administered with great care in the elderly with fever or patients with degenerative diseases.
- (3) When INFREE is used for the treatment of a chronic disease (rheumatoid arthritis, osteoarthritis, etc.), the following should be considered.
  - 1) When INFREE must be used in long-term therapy, laboratory tests (e.g. urinalysis, hematological test, hepatic function tests, and ophthalmologic examination, etc.) should be performed periodically during treatment. If abnormal findings are observed, appropriate measures, such as reduction in dosage or temporary discontinuation of the medication, should be taken.
  - 2) Alternatives to drug therapy should also be considered.
- (4) INFREE may mask the signs and symptoms of infections. Therefore, an appropriate antibiotic should be used in combination to treat inflammation, and the patient should be closely monitored and INFREE administered with care.
- (5) It is recommended to avoid the concomitant use of other anti-inflammatory analgesics with INFREE.
- (6) Since drowsiness and dizziness may occur with the use of INFREE, patients should be cautioned against engaging in potentially hazardous activities requiring alertness, such as operating machinery or driving a car.

### 3. Drug Interactions

#### (1) Contraindications for coadministration (INFREE should not be coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Triamterene (Triteren)	It has been reported that acute renal failure occurs in patients concomitantly administered indometacin, the active metabolite of INFREE, and triamterene.	Prostaglandin synthesis increases to compensate for renal function disorder brought about by decrease in renal blood flow due to triamterene. Indometacin inhibits prostaglandin synthesis, resulting in a decrease in renal function.

#### (2) Precautions for coadministration (INFREE should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Anticoagulants, and antiplatelet agents Warfarin potassium Reviparin sodium Clopidogrel sulfate, etc.	The risk of bleeding may increase, because the effects of these agents are enhanced by the concomitant use with indometacin (the active metabolite of INFREE). It has also been reported that the effect of warfarin may be enhanced by combined use with INFREE. INFREE should be used with thorough hemorrhage control such as blood coagulation tests or other means.	Platelet aggregation is suppressed due to the inhibition of prostaglandin biosynthesis by indometacin. It is also considered that INFREE enhances the anti-coagulation effect of warfarin by extrication of warfarin from the binding site of plasma proteins.
Lithium preparation Lithium carbonate	It has been reported that when concomitantly administered with these products, indometacin, the active metabolite of INFREE, potentiates their effects. If coadministration is necessary, caution should be exercised, such as reducing the dosage of the lithium preparation or methotrexate.	Renal clearance of lithium is reduced by indometacin, and the blood lithium concentration is increased as a result.
Methotrexate		Renal excretion of methotrexate is inhibited by indometacin, and the blood methotrexate concentration is increased as a result.
Probenecid	When concomitantly administered with indometacin, the active metabolite of INFREE, probenecid may potentiate the effect of indometacin. If coadministration is necessary, caution should be exercised, such as reducing the dosage of INFREE.	Urineriferous tubule excretion of indometacin is inhibited by probenecid, and the blood indometacin concentration is increased as a result.
Calcium channel blockers	When concomitantly administered with INFREE, calcium channel blockers may have a diminished effect.	It is considered that the efficacy of such hypotensive agents is reduced due to the inhibition of prostaglandin biosynthesis in the kidney by indometacin. This results in water and sodium retention which causes an increase in the humoral circulatory volume.
β-Blockers ACE inhibitors A-II receptor antagonists Thiazides, and other hypotensive diuretics in this class Hydrochlorothiazide, etc. Loop diuretics Furosemide, etc.	When concomitantly administered with indometacin, the active metabolite of INFREE, these products may have a diminished effect.	
Potassium-sparing diuretics Spironolactone, etc. Eplerenone	Concomitant use with indometacin (the active metabolite of INFREE) may cause a decrease in the hypotensive effects of these agents, and may induce serious hyperkalemia in patients with renal function disorders.	The inhibition of prostaglandin biosynthesis in kidneys by indometacin is thought to be a contributing factor.

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Aspirin	When concomitantly administered with indometacin, the active metabolite of INFREE, aspirin may diminish the action of indometacin.	Mechanism unknown
Digoxin	It has been reported that when concomitantly administered with digoxin, indometacin, the active metabolite of INFREE, increases the blood digoxin concentration, and potentiates its effect. Caution should be exercised, such as monitoring the increase in the blood digoxin concentration.	It is considered that the renal excretion of digoxin is decreased due to a reduction in renal blood flow due to the inhibition of prostaglandin biosynthesis by indometacin.
Ciclosporin	Attention should be paid to renal function because when concomitantly administered with cyclosporin, indometacin, the active metabolite of INFREE, may cause an increase in renal toxicity due to ciclosporin.	The inhibition of prostaglandin biosynthesis in the kidneys by indometacin is thought to be a contributing factor.

### 4. Adverse Reactions

Adverse reactions were reported in 682 of 13,564 patients (5.03%). (At the end of the reexamination period)

#### (1) Clinically significant adverse reactions

##### 1) Shock and anaphylactoid reaction

Shock (incidence unknown) may occur. Patients should be carefully observed, treatment should be discontinued and appropriate measures taken in the event of symptoms such as cold sweat, facial pallor, dyspnea or decrease in blood pressure, etc.

##### 2) Perforation of the digestive tract, hemorrhage of the digestive tract, ulcer of the digestive tract, hemorrhagic colitis, constriction and obstruction of the intestinal tract, and ulcerative colitis

Perforation of the digestive tract, hemorrhage of the digestive tract, ulcer of the digestive tract, hemorrhagic colitis, constriction and obstruction of the intestinal tract (incidence unknown) may occur. In the event of such symptoms, treatment should be discontinued and appropriate measures taken. It also has been reported that ulcerative colitis (incidence unknown) occurred with the use of indometacin which is the active metabolite of INFREE.

##### 3) Blood dyscrasia

Symptoms of hematological dyscrasia such as aplastic anemia (incidence unknown), hemolytic anemia (incidence unknown), leucocytopenia (<0.1%) or thrombocytopenia (incidence unknown) may occur. Patients should be carefully monitored through blood examinations. In the event of such abnormal findings, treatment should be discontinued and appropriate measures taken.

##### 4) Dermatologic disorders

Oculo-muco-cutaneous syndrome (Stevens-Johnson syndrome) (incidence unknown) or toxic epidermal necrolysis (Lyell syndrome) (incidence unknown) may occur. In the event of such symptoms, treatment should be discontinued and appropriate measures taken.

**5) Asthmatic attack**

Acute respiratory disorders such as asthmatic attack (incidence unknown) may occur. In the event of such symptoms, treatment should be discontinued and appropriate measures taken.

**6) Renal function disorders**

Renal function disorders such as acute renal failure (incidence unknown) or nephrotic syndrome (incidence unknown), or hyperkalemia (<0.1%) may occur. In the event of such symptoms, treatment should be discontinued and appropriate measures taken. It also has been reported that hypoalbuminemia (incidence unknown) occurred with the use of indometacin, the active metabolite of INFREE.

**7) Hepatic function disorders and jaundice**

Hepatic function disorders (5% > ≥0.1%) or jaundice (incidence unknown) may occur. In the event of such symptoms, treatment should be discontinued and appropriate measures taken.

**8) Coma and confusion**

It has been reported that coma (incidence unknown) and confusion (incidence unknown) occurred with the use of indometacin, the active metabolite of INFREE.

**9) Genital bleeding**

It has been reported that genital bleeding (incidence unknown) occurred with the use of indometacin, the active metabolite of INFREE.

**(2) Other adverse reactions**

	5% > ≥0.1%	<0.1%	Incidence unknown
Gastrointestinal	Stomach discomfort, stomachache, diarrhea, abdominal pain, anorexia, stomatitis, heartburn, stomach heaviness, constipation, gastrointestinal symptoms, gastritis and vomiting	Thirst, feeling of enlarged abdomen, glossitis, eructation and cheilitis	Tongue coat
Hematologic		Anemia and eosinophilia, etc.	Subcutaneous hemorrhage
Dermatologic			Alopecia
Hypersensitivity <sup>note 1)</sup>	Rash and itching	Erythema	Angioedema <sup>note 2)</sup>
Sensory organs <sup>note 3)</sup>		Tinnitus, taste abnormality, ocular congestion and photophobia	
Renal	Elevation of BUN	Elevation of creatinin, reduction in urine volume, hematuria and proteinuria	
Hepatic	Elevation of AST (GOT) and ALT (GPT), etc.	Elevation of Al-P and LDH, etc.	
Psychoneurologic	Dizziness and light-headedness	Headache, sleepiness and sensation of numbness	Convulsions, tremor, depression, insomnia and disturbed consciousness
Cardiovascular		Palpitations and increase in blood pressure	

	5% > ≥0.1%	<0.1%	Incidence unknown
Others	Edema	Malaise, hot flushes, pollakiuria, fever, chest pain and hypothermia	Hyperglycemia, epistaxis and diaphoresis

## Note

- 1) In the event of such symptoms, treatment should be discontinued.
- 2) It has been reported that indometacin, the active metabolite of INFREE caused such symptoms.
- 3) It has been reported that corneal opacity and retinal disorders occurred with the use of indometacin, the active metabolite of INFREE in patients with rheumatoid arthritis or other diseases during long-term therapy. If any prodromal syndromes (such as blurred vision) occur, treatment should be immediately discontinued.

**5. Use in the Elderly**

Adverse reactions may occur frequently in the elderly. The patients should be closely observed and administration should be performed with care, such as initiating at lowest dosage.

**6. Use during Pregnancy, Delivery or Lactation**

- (1) INFREE should not be used in pregnant women or women suspected of being pregnant.

1) It has been reported that persistent fetal circulation (PFC), contraction of arteries in the fetus, patent ductus arteriosus, renal failure in the fetus, enterobrosis in the fetus and oligoamnios occurred when indometacin, the active metabolite of INFREE, was administered during the late stage of pregnancy. In addition, when indometacin was administered during the late stage of pregnancy, increases in the incidence rates of necrotizing colitis, perforation of the digestive tract, and intracranial hemorrhage were reported in premature neonates.

2) It has been reported that indometacin, the active metabolite of INFREE, exhibited a teratogenic action in an animal study (in mice) and that INFREE induced a reduction in the rate of implantation and an increase in the frequency of dead and resorbed fetuses in rats.

3) In an experiment with rats administered INFREE at the late stage of pregnancy, contraction of arteries in fetuses was reported.

- (2) Nursing mothers should discontinue breast feeding during treatment.

[It has been reported that INFREE is excreted in breast milk of rats.]

**7. Pediatric Use**

The safety in children has not been established (no clinical experience).

**8. Precautions concerning Use**

- (1) Caution in administration

1) In patients with biliary stasis or reduced biliary secretion, the absorption of INFREE is considered to be

decreased. Therefore, INFREE should not be administered to these patients.

- 2) The absorption rate of INFREE decreases as the dose is increased. Clinical benefits should be evaluated, when the total daily dose exceeds 400 mg.
- (2) Caution in oral administration  
Since the absorption of INFREE may decrease when it is administered during fasting, it should be administered after meals or with milk.
- (3) Caution in handing over drug  
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.]

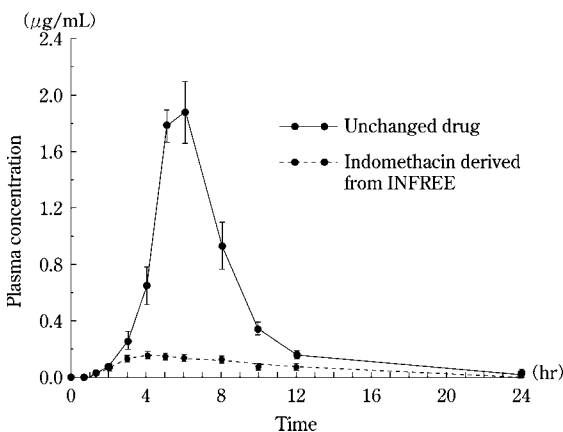
## 9. Other Precautions

- (1) It has been reported that peptic ulcer and perforation of the digestive tract occurred when indometacin, the active metabolite of INFREE was coadministered with lentinan in an animal study (in mice.)
- (2) Reversible infertility has been reported in women receiving non-steroidal anti-inflammatory analgesics for long periods.

## PHARMACOKINETICS

### 1. Blood concentration (absorption)

INFREE was administered orally to 5 healthy adult male volunteers at a single dose of two 100 mg hard capsules after a meal. The time to reach peak plasma concentration ( $t_{max}$ ) and the peak plasma concentration ( $C_{max}$ ) of the unchanged drug was about 5 to 6 hr and  $2.01\mu\text{g/mL}$ , respectively. It disappeared from the plasma in 24 hrs after administration.<sup>1)</sup>



Changes in plasma concentration of unchanged indometacin farnesil and indometacin derived from INFREE

(Dosage: 200 mg, Mean±S.E.M., n=5)

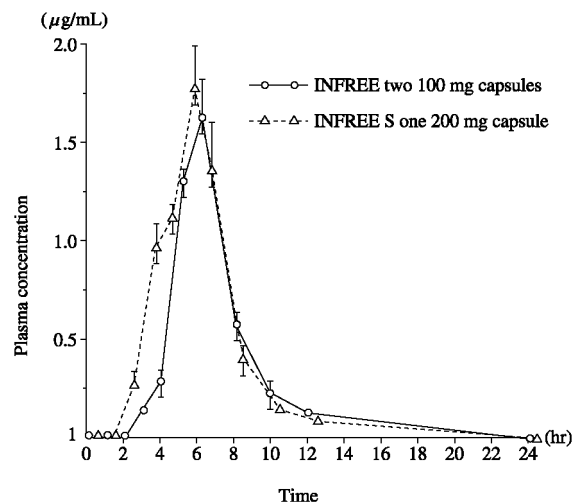
### Pharmacokinetic parameters of unchanged indometacin farnesil after single oral administration of INFREE

$t_{max}$ (hr)	$C_{max}$ (µg/mL)	$AUC_0^{48}$ (µg·hr/mL)	$t_{1/2}$ (hr)
$5.6\pm 0.2$	$2.01\pm 0.16$	$9.14\pm 1.07$	1.50

(Dosage: 200 mg, Mean±S.E.M., n=5)

A study in 5 healthy adult male volunteers given repeated oral administration of the drug (INFREE two 100 mg hard capsules b.i.d., 11 times) indicated that the plasma concentration of the unchanged drug does not accumulate in the body.  $C_{max}$  was  $0.30\pm 0.04\mu\text{g/mL}$ .<sup>1)</sup>

When two 100 mg hard capsules or one 200 mg soft capsule of INFREE were administered orally to 24 healthy adult male volunteers in a single dose after a meal in a cross-over design trial, the differences in the mean values until 24 hr of the area under the plasma concentration-time curve and  $C_{max}$  of the unchanged drug were within approx.  $\pm 20\%$ .



Changes in plasma indometacin farnesil concentration after oral administration of INFREE two 100 mg Capsules and INFREE S one 200 mg Capsule

(Dosage: 200 mg, Mean±S.E.M., n=24)

### 2. Effect of meal

The absorption of unchanged drug was markedly decreased when a 150 mg hard capsule of indometacin farnesil was administered to 8 healthy adult male volunteers after 12 hr of fasting in a cross-over design trial, but INFREE was well absorbed following an ordinary meal (containing about 10 g of fat).<sup>2)</sup>

### 3. Metabolism and excretion

When INFREE was administered orally to 5 healthy adult male volunteers at a single dose of two 100 mg hard capsules, no unchanged drug was detected in their urine; desbenzoylindometacin (5.5% of the dose), indometacin (2.9% of the dose), and desmethylindometacin (1.9% of the dose) were detected.<sup>1)</sup>

## CLINICAL STUDIES

### Clinical efficacy

The clinical efficacy of INFREE was determined in 1,751 patients with the diseases indicated below in clinical trials, including double-blind clinical trials. The following improvement ratings were achieved.<sup>3-8)</sup>

Improvement rating Disease	Moderately to remarkably improved(%)	Fairly to remarkably improved(%)
Rheumatoid arthritis	175/692 (25.3)	405/692 (58.5)
Osteoarthritis	235/339 (69.3)	296/339 (87.3)
Low back pain	323/508 (63.6)	430/508 (84.6)
Scapulohumeral peri-arthritis	58/109 (53.2)	90/109 (82.6)
Neck-shoulder-arm syndrome	49/103 (47.6)	75/103 (72.8)

## PHARMACOLOGY

### 1. Anti-inflammatory action

Indometacin farnesil exhibited a definite anti-inflammatory action after oral administration in experimental rat models, including acute or chronic experimental by induced inflammations, such as carrageenin podedema, kaolin podedema, carrageenin bullosis, adjuvant arthritis, and type II collagen arthritis.<sup>9, 10)</sup>

### 2. Analgesic action

Indometacin farnesil exhibited a definite analgesic action after oral administration to adjuvant arthritis rats with inflammatory pain induced by extension stimuli and to dogs with pain induced by intra-arthral injection of carrageenin.<sup>11, 12)</sup>

### 3. Mechanism of action

It is presumed that the anti-inflammatory and analgesic actions exhibited by indometacin farnesil occur by a mechanism in which indometacin is first released in its active moiety from indometacin farnesil; this indometacin inhibits prostaglandin biosynthesis by inhibiting cyclooxygenase. When indometacin farnesil is administered orally, it is absorbed as unchanged drug, and is only mildly injurious to the gastrointestinal tract. A major fraction of the drug administered to dogs or humans is detected as unchanged drug in the blood; Unchanged drug is metabolized to indometacin, the active moiety, in the liver and kidney, and released into the blood. It has been demonstrated by *in vivo* and *in vitro* studies that the unchanged drug is metabolized releasing active indometacin in inflammatory tissue (in rat) or inflammatory target cells (in human or rat synovial membrane cell).<sup>1, 10, 12- 17)</sup>

## PHYSICOCHEMISTRY

**Nonproprietary name:** Indometacin Farnesil (JAN, INN)

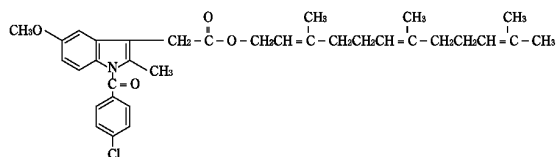
**Chemical name:**

7:3 (2E: 2Z) geometric mixture of (6E)-3,7,11-trimethyl-2,6,10-dodecatrienyyl 1-(p-chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetate

**Molecular formula:** C<sub>34</sub>H<sub>40</sub>ClNO<sub>4</sub>

**Molecular weight:** 562.15

**Structural formula:**



## Description:

Indometacin farnesil occurs as a yellow, clear, oily liquid. It has a slight characteristic odor. It is very soluble in acetonitrile, in acetone, in chloroform and in diethyl ether, freely soluble in ethanol (99.5), sparingly soluble in methanol, and practically insoluble in water.

## PRECAUTIONS FOR HANDLING

1. PTP packages of INFREE Capsules 100mg should be protected from moisture after opening aluminum bag. (INFREE Capsules 100mg may change in color by light. Colored film is used for Press-through package.)
2. Bottle packages of INFREE Capsules 100mg should be protected from light and moisture after opening cap.
3. PTP packages of INFREE S Capsules 200mg should be protected from high temperature and moisture after opening aluminum bag. Bottle packages should be protected from high temperature and moisture after opening cap. (Softening, and adherence to the inside of press through package may occur in capsule shells.)

## PACKAGING

### INFREE Capsules 100 mg:

Boxes of 100, 140 (14Caps. × 10), 700 (14Caps. × 50), 1,000 and 1,400 (14Caps. × 100) in press-through packages (PTP), and bottles of 500

### INFREE S capsules 200 mg:

Boxes of 100, 140 (14Caps. × 10), 700 (14Caps. × 50), 1,000 and 1,400 (14Caps. × 100) in press-through packages (PTP), and bottles of 500

## REFERENCES

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## REQUEST FOR LITERATURE SHOULD BE MADE TO:

Safety Management Department

Fax: 03-3811-2710

Eisai Co., Ltd.

**REQUEST FOR DRUG INFORMATION SHOULD BE  
MADE TO:**

Customer Information Service  
Free Dial: 0120-419-497  
Eisai Co., Ltd.

**Manufactured and marketed by:**

Eisai Co., Ltd.  
6-10, Koishikawa 4-chome, Bunkyo-ku, Tokyo, 112-8088

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**BRAND NAMES IN OTHER COUNTRIES**

Dialon (Indonesia)