

## A New Herbal Extract Medicine for Osteoarthritis

# SHINBARO Tablet

**[Description]**

Osteoarthritis (OA; also known as degenerative arthritis) is a mechanical abnormality or disorder caused by abrasion and degeneration of cartilage tissues covering joints due to the aging process. The most common symptoms are joint pain and stiffness. In severe case, it results in the inconvenience of general activity. Shinbaro is a new herbal extracted medicine developed by Green Cross Corporation by using six (6) herbal drugs well known for the treatment of osteoarthritis in the oriental medicine. The efficacy, stability, and safety of the product are scientifically approved by clinical studies and other related researches.

**[Characteristics]**

- 1) Anti-inflammatory action: Shinbaro suppresses various inflammatory mediators, such as iNOS, COX-2, and TNF- $\alpha$ , and shows a strong anti-inflammatory action.
- 2) Analgesic action: Shinbaro shows analgesic action by suppressing the activation of pain inducing factors and improving the pain detection level.
- 3) Joint protection: Shinbaro inhibits the activity of MMP-2 and MMP-9 and prevents the degeneration of joint tissues.
- 4) Osteoblast proliferation: Shinbaro increases the activity of ALP and promotes osteoblast proliferation (promotion of synthesis of joint tissues).

**[Composition]** 1 tablet contains,

Acanthopanax senticosi radix et rhizoma, Achyranthis radix, Saposhnikovia radix, Eucommiae cortex, Cibotii rhizoma, and Glycine semen nigra dried extract (20 → 1) ..... 300.0 mg

**[Appearance]** Brown colored and film coated oblong tablet**[Indications]** For anti-inflammatory, analgesic, and osteoarthritis**[Directions]** Take 2 tablets twice daily for adults**[Precautions]****1. Warnings**

- 1) Patients, who regularly drink alcoholic beverages, must consult with a doctor or pharmacist, when taking Shinbaro or other antipyretic-analgesics.
- 2) Cardiovascular and Gastrointestinal Risk: during the administration of Shinbaro, cardiovascular and gastrointestinal signs and symptoms should be carefully monitored. Precise diagnosis and treatment should be conducted, if severe adverse reactions are suspected.

**2. Contraindications**

- Patients with
- 1) Peptic ulcer
  - 2) Severe cardiovascular problem
  - 3) Severe hepatic impairment
  - 4) Severe renal impairment
  - 5) A hypersensitivity to the components of the drug
  - 6) Asthma, rash, allergic reactions or medical history to other NSAIDs (nonsteroidal anti-inflammatory drugs) including COX-2 inhibitors

**3. Special Precautions**

- Patients with a medical history of
- 1) Peptic ulcer
  - 2) Cardiovascular or similar case
  - 3) Hepatic impairment similar case
  - 4) Renal impairment or similar case
  - 5) Hypersensitivity
  - 6) Asthma

**4. Undesirable Effects**

- 1) According to the result of phase III clinical study performed on the patients with osteoarthritis in Korea, the following site specific adverse drug reactions were occurred  
[Often: 1% ~ 10%, Occasional: 0.1% ~ 1%, Rare: below 0.1%]

| Expression Area           | Frequency  | Adverse Reaction                                                              |
|---------------------------|------------|-------------------------------------------------------------------------------|
| Gastrointestinal<br>(18%) | Occasional | Vomiting (1%), constipation (2%), indigestion (1%)                            |
|                           | Often      | Indigestion (7%), gastritis (3%), nausea (4%)                                 |
| Body<br>(5%)              | Occasional | Edema (1%), abdominal inflation (1%), hot flush (1%)                          |
|                           | Often      | Pain (2%)                                                                     |
| Neurological<br>(8%)      | Occasional | Skin tingling (1%), intracranial hypertension (1%), sensory disturbances (1%) |
|                           | Often      | Dizziness (2%), headache (3%)                                                 |
| Others(3%)                | Occasional | Sleepiness (1%), thirst (1%), weight gain (1%)                                |

- 2) Adverse events found from domestic Post Market Surveillance

- In accordance to the results of PMS conducted domestically for 4 years on 714 patients, the incidence rate of adverse events had shown 5.32% (38 patients/714 patients, 48 cases), and the incidence rate of adverse drug reactions which cannot be ruled out from the causality with this drug is 1.96% (14 patients/714 patients, 17 cases), each indigestion and diarrhea is 0.28% (2 patients/714 patients, 2 cases), each heartburn, gastritis, constipation, upper abdominal pain, xerostomia, glossitis, paresthesia, headache, dizziness, facial edema, edema, palpebritis, pharyngoxerosis is 0.14% (1 patient/714 patients, 1 case). The incidence rate of Severe Adverse Event had shown 0.14% (1 patient/714 patient, 1 case), lumbar spinal stenosis was reported. Severe Adverse drug reactions which cannot be ruled out from the causality with this drug were not found.

- Incidences of unexpected adverse events were 4.06% (29 patients/714 patients, 36 cases), heartburn 0.56% (4 patients/714 patients, 4 cases), each diarrhea, nasopharyngitis, facial edema is 0.28% (2 patients/714 patients, 2 cases), each canker sore, abdominal pain, upper abdominal pain, gastric ulcer, gastrointestinal disturbance, xerostomia, glossitis, herpes zoster, athlete's foot, onychomycosis, folliculitis, musculoskeletal pain, lumbar spinal stenosis, herniated intervertebral disc, radiating pain, Alzheimer's dementia, paralysis, rash, hypertrichosis, Raynaud syndrome, venous insufficiency, blepharitis, gout, desmitis, insomnia, pharyngoxerosis is 0.14% (1 patient/714 patients, 1 case). Incidences of unexpected adverse drug reactions which cannot be ruled out from the causality with this drug were 1.12% (8 patients/714 patients, 9 cases). Incidence of unexpected severe adverse events was 0.14% (1 patient/714 patients, 1 case), lumbar spinal stenosis was reported. There was no incidence of unexpected severe adverse drug reaction. Incidences of unexpected adverse drug reactions were 1.12% (8 patients/714 patients, 9 cases), diarrhea is 0.28% (2 patients/714 patients, 2 cases), each heartburn, upper abdominal pain, glossitis, facial edema, blepharitis, pharyngoxerosis is 0.14% (1 patient/714 patients, 1 case).

- 3) Result of Reassessment Adverse Event Analysis

From the results of integrated assessments for this product and all the authorized pharmaceutical products using the same Drug Substance (DS) through the domestic Post Marketing Surveillance (PMS) on adverse event (1989-2015.6) and spontaneous reporting on side-effect in Korea, the additionally defined and statistically significant adverse events which are more reported when compared to the previously reported adverse events from all other drug products are follows. However, this result does not mean that causality has been established between the components of this drug and the following adverse events.

Skin and appendages disorders: erythematous eruption

Musculoskeletal system disorders: fracture, musculoskeletal pain

Gastrointestinal system disorders: abdominal pain, gastroesophageal reflux, gastric ulcer, benign neoplasm of gastrointestinal

Metabolic and nutritional disease: gout

General cardiovascular disease: hypertension

Respiratory system disease: pharyngitis

Urinary system disease: facial edema, cystitis

Systemic disease: back pain, peripheral edema

Other terms: discopathy

**5. General Precautions**

- 1) Prior to the administration of Shinbaro, the potential risks and benefits of Shinbaro and alternative therapies should be considered.
- 2) Gastrointestinal signs and symptoms should be carefully monitored during the administration of Shinbaro. If severe gastrointestinal symptoms are suspected, precise diagnosis and treatment should be immediately conducted.
- 3) If cardiovascular symptoms occur during the administration of Shinbaro, precise diagnosis and treatment should be immediately conducted.
- 4) According to the result of clinical trials, edema was observed in some patients taking Shinbaro. Therefore, special cares and cautions are required for the patients with fluid retention or heart failure.
- 5) Clinical trials on the patients with advanced kidney failure or impairment have not been conducted. Thus, the administration of Shinbaro is not recommended to the patients with advanced kidney failure or impairment.
- 6) Deterioration of liver function should be carefully monitored during the administration of Shinbaro to the patients with hepatic impairment or patients have abnormal test results on the hepatic function test.  
If patients show clinical symptoms or general symptoms(eg. Eosinophilia, rash) related to liver disorders, the administration of Shinbaro should be discontinued.
- 7) Discontinuing administration of Shinbaro when patients have clinical symptoms or other symptoms, such as eosinophilia and rash, associated with renal or hepatic impairment, or patients have abnormal results in renal or hepatic function test.
- 8) Positive cases of anaphylactic reactions were not reported during clinical trials. However, anaphylactic reactions may occur to patients, who have not exposed to the drug. If anaphylactic reactions appear, immediate treatment should be conducted.
- 9) Shinbaro cannot be used to replace corticoid products and to treat corticoid deficiency.
- 10) Shinbaro may cause delay of the diagnosis of infectious complication under painful and non-infectious conditions due to the pharmacological characteristics of the products, which make other symptoms and signs of inflammation not appear.
- 11) Patients show symptoms, such as headache, dizziness, or other central nervous system disorder should not drive a car or operate other dangerous machines after taking this drug. Also, patients should keep away from dangerous environments, which need special attentions and cautions.

**6. Drug Interactions**

Studies on drug interactions of Shinbaro with certain drugs have not been carried out.

**7. Pregnancy**

Avoid the administration of Shinbaro to pregnant women, since clinical trials on pregnant women have not been performed.

**8. Lactation**

The safety or stability of Shinbaro in lactating women is not established, and it is unknown whether the drug is excreted in human breast milk or not. However, there are many cases reported in other medicines and concerns in terms of causing adverse reactions to infants and children. Considering the importance of taking the drug to lactating or nursing mothers, discontinuing breast feeding or taking drugs are highly recommended.

**9. Pediatric Use**

The safety or stability of the drug in children is not established.

**10. Geriatric Use**

Special care and caution are required when administering the drug to the elderly.

**11. Overdose**

Even though typical symptoms caused by overdose are unknown, precise diagnosis and treatment are required in case of taking a drug overdose.

**12. Precautions for Storage and Handling**

- 1) Keep it out of the reach of children
- 2) Changing the container may affect quality of the product.

**[Storage Condition]**

Store at room temperature (1~30°C) in tight container

**[How Supplied]**

30, 120, 240 tablets/ pack

\* Keep and handle the medicine in dry condition and close the lid immediately after use

MANUFACTURED BY

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