Prescribing Information

FOSTEUM™ Capsules
genistein aglycone (27 MG)
citrated zinc bisglycinate (20 MG)
cholecalciferol (200 IU)
FOSTEUM is a specially formulated prescription medical food product for the clinical dietary management of the metabolic processes of osteopenia and osteoporosis. ***FOSTEUM must be administered under physician supervision.***

DESCRIPTION

FOSTEUM™ consists of a specially formulated proprietary blend of high purity genistein aglycone from soy, citrated zinc bisglycinate and cholecalciferol (vitamin D_3). Genistein aglycone reduces osteoclast activity and stimulates osteoblast activity. Citrated zinc bisglycinate works synergistically with genistein aglycone, while both citrated zinc bisglycinate and vitamin D_3 also work independently to promote mineralization activity in bone. Vitamin D_3 also facilitates calcium absorption from the intestine.

Genistein aglycone

Each FOSTEUM capsule contains 27 mg of genistein aglycone, isolated and purified from soy, for a total daily intake of 54 mg. In clinical trials, this level of intake has been shown to increase bone mineral density (BMD). The genistein aglycone in FOSTEUM is produced from organic, non-genetically modified (non-GMO) soybeans.

Citrated zinc bisglycinate

Each FOSTEUM capsule contains 20 mg citrated zinc bisglycinate, a glycine amino acid chelate of zinc formed in the presence of citric acid that provides approximately 4 mg of elemental zinc per capsule. Zinc is an essential mineral co-factor required by enzymes involved in bone metabolism and has important physiological functions in other tissues throughout the body. Elemental zinc has also been shown to have synergistic effects with genistein aglycone on bone formation.

Cholecalciferol

Each FOSTEUM capsule contains cholecalciferol equivalent to 200 IU vitamin D_3.Vitamin D is necessary for proper absorption of calcium from the intestine and the use of absorbed calcium in the mineralization of bone. Cholecalciferol is the natural precursor of calcitriol (1.25-dihydroxy-cholecalciferol), the physiologically active form of vitamin D in bone.

Other Ingredients

FOSTEUM contains the following other ingredients as excipients: dicalcium malate, magnesium oxide, micro-crystalline cellulose, magnesium stearate and silicon dioxide in a capsule made from plant sources. FD&C Blue #2 is used for the imprint on the capsule. FOSTEUM does not contain fructose, glucose, sucrose, lactose, gluten, maltodextrin, tree nuts, peanuts, flavors or products of animal or seafood origin. Fosteum is suitable for vegans.

CLINICAL EXPERIENCE

Hepatic and Renal Effects

In clinical studies, the effects of genistein aglycone in FOSTEUM on blood chemical, hepatic and renal functional measures were compared in post-menopausal subjects receiving genistein aglycone plus calcium carbonate (calcium) and vitamin D_3 with post-menopausal, age-matched subjects receiving only calcium and vitamin D_3. No changes were noted over a three year period in either group and all measures remained within normal limits. Since the precursor form of vitamin D_3 is transformed to the active form in the liver and then kidney, it is expected that patients with severe liver or kidney impairment may not transform the vitamin adequately.

Effects on Reproductive Tissues

Effects of the genistein aglycone in FOSTEUM on breast density, vaginal cytology and endometrial thickness were tested in double-blind, placebo-controlled clinical trials. One trial with 30 post-menopausal subjects in each arm found that genistein aglycone did not affect endometrial thickness over a one year period compared to placebo. In other controlled trials, daily administration of 54 mg of genistein aglycone over one, two and three year periods produced no increases in endometrial thickness or breast density in post-menopausal women. Furthermore, a subset of 115 post-menopausal women showed no change in vaginal cytology following one year of daily genistein aglycone therapy. These data suggest that the genistein aglycone in FOSTEUM does not produce adverse estrogenic effects in reproductive tissues.

Cardiovascular Safety

In a study of 60 post-menopausal subjects comparing those receiving the genistein aglycone in FOSTEUM to a matched group receiving placebo, homocysteine and C-reactive protein (CRP) were assessed at baseline and again at 6 months. No statistically significant differences were seen between groups. Soluble intercellular adhesion molecule-1 (iCAM), vascular cell adhesion molecule-1 (vCAM), fibrinogen and F2-isoprostane levels were assessed at baseline and again at 12 and 24 months in 389 post-menopausal subjects randomized to receive either genistein aglycone, calcium and vitamin D_3 or calcium and vitamin D_3 only (placebo). At both 12 and 24 months, the levels of all four cardiovascular markers were reduced in the genistein aglycone group compared to both baseline and placebo. No significant changes in lipid profile were observed in either group over the course of the study. These data indicate that genistein aglycone does not adversely affect markers of cardiovascular risk. An additional study of 53 post-menopausal women measured changes in flow-mediated vasodilation and plasma nitric oxide status. The genistein aglycone in FOSTEUM significantly increased plasma nitrite/nitrate levels and reduced levels of endothelin-1 compared to placebo. After 12 months of use, forearm blood flow increased significantly during reactive hyperemia in the genistein aglycone group compared to placebo. Flow-mediated dilation in the proximal and distal brachial arteries both increased significantly after genistein aglycone administration. The purified genistein aglycone in FOSTEUM improved endothelial function in a cohort of post-menopausal women.

Menopausal Symptoms

In two published studies with a combined enrollment of more than 300 postmenopausal women, the genistein aglycone in FOSTEUM progressively reduced the number of symptomatic vasomotor episodes by an average of more than 50% at the 12 month follow-up. In these studies, vasomotor symptoms were unchanged in the placebo groups.

Blood Glucose and Insulin Resistance

The genistein aglycone in FOSTEUM was also found to significantly reduce fasting glucose and insulin levels, as well as insulin resistance, in 198 post-menopausal women over a 2 year period and in a subset of 91 patients over a 3 year period when compared to placebo.

INDICATIONS AND USAGE

Indications

FOSTEUM is indicated for the clinical dietary management of the metabolic processes of osteopenia and osteoporosis.

Usage

FOSTEUM should be taken with sufficient calcium and vitamin D_3 as directed by a physician. In clinical trials of the genistein aglycone in FOSTEUM, patients also received 1,000 mg of calcium carbonate and 800 IU vitamin D_3 per day in two divided doses. See Dosage and Administration for additional information.

Interactions with Food

FOSTEUM can be taken with or without other foods. FOSTEUM may be taken with any beverage desired. PRECAUTIONS AND CONTRAINDICATIONS

General

Causes of osteopenia or osteoporosis other than menopause or aging should be considered.

Hypersensitivity

FOSTEUM is contraindicated for anyone having a hypersensitivity to any ingredient in the product. See "Other ingredients" for a full list of ingredients.

Patients with Cancer

Since no studies have been done in these populations, as a precaution, FOSTEUM is contraindicated for patients with a history of cancer of the breast or reproductive organs and should be used with caution by women who have a history of breast or reproductive cancer in first degree female relatives.

Vitamin D Deficiency

FOSTEUM is not intended to treat vitamin D deficiency.

Pregnancy

FOSTEUM is contraindicated in pregnant and lactating women. Women capable of becoming pregnant should use appropriate contraception when taking FOSTEUM. The genistein aglycone in FOSTEUM has not been tested in women capable of becoming pregnant.

ADVERSE EVENTS

Study discontinuation in clinical trial subjects was due to gastrointestinal symptoms, including abdominal and epigastric pain, dyspepsia, vomiting and constipation. The incidence of adverse events was statistically higher in the genistein aglycone group. The major adverse events are shown in the table below without attribution of causality.

Adverse Events	Year 1		Year 2	
	Genistein aglycone + Ca/D (n=178)	Ca/D (n=172)	Genistein aglycone + Ca/D (n=150)	Ca/D (n=172)
Abdominal Pain	4 (2.2%)	2 (1.1%)	2 (1.3%)	1 (0.6%)
Dyspepsia	2 (1.1%)	1 (0.6%)	7 (4.7%)	2 (1.3%)
Constipation	5 (2.8%)	2 (1.7%)	8 (5.3%)	3 (1.9%)

Some of these adverse event occurrences may be attributable to the intake of 1,000 mg per day of calcium carbonate by subjects in both groups. Taking FOSTEUM with food may reduce or eliminate some gastrointestinal symptoms.

OVER USAGE

Genistein aglycone

There are no known cases of over usage of the genistein aglycone in FOSTEUM. Animal studies have shown that consuming the equivalent of 75 FOSTEUM capsules at one time did not produce adverse events. However, as in most over usage situations, symptoms following an over usage of FOSTEUM could vary according to the patient. If an over usage were to occur, patients should be managed by systematic and supportive care as soon as possible following product consumption.

Zinc (Elemental)

Symptoms of acute zinc toxicity occur after ingestion of 2 g or more of elemental zinc, the equivalent of 500 FOSTEUM capsules at one time. Chronic zinc toxicity is increasingly common as the use of large doses of zinc in supplements becomes more routine. Those on long-term supplementation or high doses of zinc-containing cold medication, such as zinc lozenges, should be monitored for zinc and copper status.

Cholecalciferol

There is limited information regarding acute vitamin D_3 toxicity in humans. In patients suffering from diseases, such as leukemia, lymphoma or sarcoidosis, that are associated with unregulated overproduction of calcitriol, supplemental vitamin D_3 may worsen hypercalcemia and/or hypercalciuria. Regular monitoring of urine and serum calcium may be indicated in this population.

DOSAGE AND ADMINISTRATION

FOSTEUM should be taken twice a day, approximately 12 hours apart, and may be taken with or without food.
FOSTEUM has no food. There are no postural limitations. Patients taking FOSTEUM should ensure adequate calcium and vitamin D intake, as directed by a physician.

HOW SUPPLIED

FOSTEUM is an off-white capsule with "FOSTEUM" and "52003" printed in blue on the cap and body, respectively.
They are supplied as follows:

- 59630-415-60 unit-of-use bottles of 60 capsules with desiccant (30-day supply)
- 59630-415-40 carton of 10 2-day sample envelopes (40 capsules total)

Storage

Store at room temperature 59° - 86°F (15° - 30°C). Protect from light and moisture. Store capsules in original bottle until usage. Keep out of reach of children.

Manufactured for:
Primus Pharmaceuticals, Inc.
Scottsdale, AZ 85251
www.primusrx.com

Manufactured for:
Sciele Pharma, Inc.
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Manufactured by:
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Manufactured by:
PAL Laboratories
Miami, FL 33172

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Fosteum ...When Calcium+D is not enough

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