effect, may occur, if gastrointestinal symptoms such as bloody stool occur, discontinue administration and take appropriate measures.

Interstitial Pneumonia

Pay attention to symptoms such as fever, cough, and dyspnea. If any abnormalities are found, promptly perform a chest X-ray, etc., and check laboratory test values such as KL-6 and CRP, discontinue administration, and take appropriate measures such as administering corticosteroids, taking into consideration differential diagnosis from Pneumocystis pneumonia (e.g., measurement of β-D-glucan).

Overdose and Treatment

Signs and Symptoms

In clinical trials, the incidence of abnormal laboratory test results was higher in the 75 mg/day group than in the 50 mg/day group.

In clinical trials in Japan and overseas, one case of pancytopenia occurred at doses of 100 mg or more per day, and the overseas case was fatal.

Effects on Ability to Drive and Use Machines

Iguramod does not interfere with the ability to drive and use machines.

Dosage Forms and Packaging Available

HOW SUPPLIED

Iguramod (iguratimod) 25mg tablets are available in blister pack of 10's,20's and 30's.

Incompatibilities

Not applicable.

Shelf life

2 years

Special precautions for storage

- Store below 30°C in a dry place, protect from light.
- To be dispensed on the prescription of a registered medical practitioner only.
- Keep out of the reach of children

Nature and contents of container

Alu-Alu Blister

DATE OF REVISION OF THE TEXT

N/A

ہدایات:

- خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
- دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
- صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
- بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.
E-127-129, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

Art No: 901

IGURAMOD

(Iguratimod)

25 mg Tablets

ایگوراموڈ

(ایگوراٹیموڈ)

۲۵ ملی گرام گولیاں

Composition

Each film coated tablet contains:

Iguratimod.....25mg

Product Description

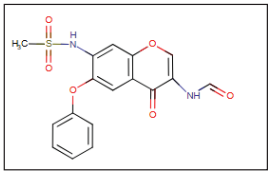
Chemical Name:

N-(7-(Methylsulfonamido)-4-oxo-6-phenoxy-4H-chromen-3-yl) formamide

Molecular Weight

374.4 g/mol

Structural Formula



Pharmacodynamics and Pharmacokinetics

Pharmacotherapeutic group: Antirheumatic drugs.

Mechanism of action

Iguratimod exerts its antirheumatic effects mainly by suppressing the production of immunoglobulins (IgG, IgM) by B cells and the production of inflammatory cytokines (TNFα, IL-1β, IL-6, IL-8, MCP-1) by monocytes/macrophages and synovial cells. These effects are accompanied by a decrease in the mRNA expression of immunoglobulins and inflammatory cytokines, suggesting that they act via the suppression of activation of the transcription factor Nuclear Factor κB (NFκB).

Pharmacokinetic properties

Absorption

A single dose of 25 mg was orally administered after a meal to elderly and non-elderly healthy adult males, and the plasma concentration over time was examined up to 72 hours after administration. The plasma concentration reached its peak approximately 4 hours after administration, and the elderly subjects showed a slightly higher concentration over time compared to non-elderly subjects.

When this drug was administered orally (25 mg twice daily for 14 days) to healthy adult males, both elderly and non-elderly, the plasma concentration of the unchanged drug reached steady stat e from the 4th day of administration, while metabolites M1 (3-amino form of the unchanged drug) and M2 (3-acetylamino form of the unchanged drug) reached steady state from the 10th day. These plasma concentrations remained slightly higher in elderly subjects than in non-elderly subjects. Pharmacokinetic parameters obtained by investigating plasma concentrations up to 168 hours after the final dose.

Distribution

The human serum protein binding rate in in vitro tests was 93.0-93.2% (measurement method: centrifugal ultrafiltration, drug concentration: 0.3-30 μg/mL)

Metabolism

When this drug was administered orally repeatedly to healthy adult males (25 mg twice

daily for 14 days), M1, M2, M3 (6-hydroxylated phenoxy group of M2), M4 (6-hydroxylated phenoxy group of the unchanged compound), and M5 (6-hydroxylated phenoxy group of M1) were detected in the plasma, of which M1 and M2 were active metabolites5.

Excretion

When this drug was administered orally (25 mg twice daily for 14 days) to elderly and non-elderly healthy adult males, the 24-hour urinary excretion rate at steady state was approximately 20%, with M3 and M4 being the main components excreted, and the unchanged drug and active metabolites M1 and M2 accounted for less than 1%)

Recommended Dose

Posology

The usual adult dosage for oral administration of iguratimod is 25 mg once daily after breakfast for at least four weeks, after which the dosage is increased to 25 mg twice daily (after breakfast and dinner).

Precautions regarding use and dosage

When starting at 50 mg per day, the incidence of increased AST and ALT was higher than when starting at 25 mg per day. Therefore, administer 25 mg per day for the first 4 weeks of treatment.

Do not administer more than 50 mg per day.

The effects of this drug usually appear within 16 weeks after the start of administration. Therefore, it is advisable to continue administration for up to 16 weeks to confirm the effect.

The efficacy and safety of coadministration with methotrexate at doses exceeding 8 mg/week or with antirheumatic drugs other than methotrexate have not been established, so particular caution should be exercised in these cases.

Special Patient Populations

Hepatic Impairment

Liver function tests should be performed before administration of this drug. In addition, during administration, clinical symptoms should be closely observed and liver function tests should be performed periodically, such as once every two weeks for the first two months after starting administration, and once a month thereafter.

Renal Impairment

Blood, renal function, etc. tests should be performed before administration of this drug. In addition, during administration, clinical symptoms should be closely observed and blood, renal function, etc. tests should be performed periodically, such as once every two weeks for the first two months after starting administration and once a month thereafter.

Method of administration

Oral

Contraindications

Do not administer to the following patients

- Pregnant women or women who may be pregnant
- Patients with severe hepatic impairment
- Patients with peptic ulcers [Peptic ulcers may occur as a side effect, and may worsen the condition.]
- Patients with a history of hypersensitivity to any of the ingredients of this drug.
- Patients receiving warfarin

Warnings and Precautions

Patients with a history of peptic ulcer

There is a risk of causing recurrence of peptic ulcer.

Underweight patients

Patients should be closely monitored, and appropriate measures should be taken, such as discontinuing administration, if any abnormalities are found. In clinical trials of this drug alone, the incidence of side effects was high in patients with low body weight (less than 40 kg). However, there has been no experience of use of this drug in combination with methotrexate in low body weight patients, and safety has not been examined.

Patients with anemia, leukopenia, thrombocytopenia, or bone marrow dysfunction

There is a risk of further worsening blood disorders.

Patients with renal impairment

There is a risk of increased incidence of side effects.

Patients with severe hepatic impairment

Do not administer this medicine. Since liver dysfunction may occur as a side effect, it may worsen liver dysfunction.

Children

No clinical trials have been conducted on children or other subjects.

Elderly

The drug should be administered while observing the patient's condition. Generally, physiological functions are often impaired, and it is assumed that side effects are more likely to occur. In a clinical pharmacology study of healthy adult males, the plasma concentration was slightly higher in elderly patients than in non-elderly patients. In clinical trials of this drug administered alone, no differences were observed in efficacy or incidence of side effects, but in a study of its use in combination with methotrexate, the incidence of side effects was higher in elderly patients than in non-elderly patients.

Interactions with other medicaments

Warfarin (coumadin, etc.)

When Iguramod drug is used in combination with warfarin, the effects of warfarin have been enhanced, and cases of severe bleeding have been reported.

If a patient requires warfarin treatment, prioritize warfarin treatment and do not administer this drug.

Nonsteroidal anti-inflammatory drugs (Naproxen, Pranoprofen, Mofezolac et al.)

An increase in the incidence of gastrointestinal disorders has been observed. If peptic ulcer occurs, discontinue administration of this drug and take appropriate measures.

Cimetidine

There is a risk of increased plasma concentration of this drug, resulting in an increase in side effects. If any abnormalities are observed, appropriate measures should be taken, such as reducing the dosage or suspending administration of this drug.

Phenobarbital

There is a risk of decreasing the plasma concentration of this drug.

Pregnancy and lactation

Pregnancy

Do not administer to pregnant women or women who may be pregnant. In a study on rat embryo-fetal development, teratogenicity (cardiac and large vascularabnormalities) and an increase in early fetal mortality were observed, and in a study on the effects on fetal ductus arteriosus in late-pregnant rats, ductus arteriosus constriction was observed in the fetus1.

Breastfeeding

Consider whether to continue or discontinue breast-feeding, taking into account the therapeutic benefits and the benefits of breast-feeding. In animal studies (rats), excretion of the drug into breast milk has been observed.

Undesirable effects

The following adverse reactions may occur, so observe closely, and if any abnormalities are found, discontinue administration or take appropriate measures.

Hepatic dysfunction (0.5%), jaundice (0.1%)

Hepatic dysfunction and jaundice accompanied by increased AST and ALT may occur. Regarding liver function, since the incidence of increased AST and ALT was high in clinical trials, if abnormalities are observed, consider whether to continue administration. In particular, if the level increases to 100 IU or more, discontinue administration.

Pancytopenia (0.1%), agranulocytosis (incidence unknown), leukopenia (0.1%)

If any abnormality is observed, consider whether to continue administration and take appropriate measures. If blood disorders such as red blood cell decrease, white blood cell decrease, or thrombocytopenia are observed, discontinue or suspend administration of this drug as necessary and take appropriate measures.

Peptic Ulcers

Since peptic ulcers, which are thought to be due to the cyclooxygenase inhibitory