Fingolide®

Generic name
Fingolimod

Category
Sphingosine 1-Phosphate (S1P) Receptor Modulator. Multiple sclerosis therapy agent, Immunomodulatory agent

Indication
Treatment of patients with relapsing forms of multiple sclerosis (MS).

Mechanism of action
Fingolimod is metabolized by sphingosine kinase to the active metabolite, fingolimod-phosphate. Fingolimod-phosphate is a sphingosine 1-phosphate receptor modulator; and blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The exact mechanism of action of Fingolimod in multiple sclerosis is unknown, but may involve reduction of lymphocyte migration into the central nervous system.

Pharmacokinetics
Apparent absolute oral bioavailability is 93%. Food does not alter AUC or C_{max} .T_{max} is 12-16 hours. Protein binding is >%99.7.
Clearance is approximately 6.3 L/h and half-life is 6 to 9 days. Approximately 81% of a dose is excreted in the urine as inactive metabolites and less than 2.5% of a dose is excreted as fingolimod and fingolimod-phosphate in the feces.

Dosage and Administration
The recommended dose of Fingolimod is 0.5 mg orally once daily. Take Fingolimod with or without food.

- Safety and efficacy in children younger than 18 years of age have not been established.

Contraindications
None well documented.

Precautions

AV block: AV conduction delays have occurred after initiation of treatment. These reactions are usually transient and asymptomatic, resolving in the first 24 hours on treatment, but have occasionally required treatment.

Blood pressure effects: Elevations in blood pressure may occur after approximately 2 months of treatment and may persist with continued treatment.

Bradycardia: A decrease in heart rate may occur, especially after the first dose.

Hepatic effects: Elevations of liver enzymes may occur.

Infection: May increase the risk of infections, some serious, because of a reduction in peripheral lymphocyte count to 20% to 30% of baseline values. Consider therapy interruption in patients who develop a serious infection during therapy.

Macular edema: May occur typically in the first 3-4 months of treatment. The risk may be increased in patients with diabetes mellitus or a history of uveitis.

Pregnancy and lactation

Pregnancy Category: C

It is not known whether this drug is excreted in human milk. breast feeding is not recommended.

Drug Interactions

- ✓ **Class Ia or Class III antiarrhythmic drugs:** Class Ia (e.g., quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic drugs have been associated with cases of torsades de pointes in patients with bradycardia. Since initiation of Fingolimod treatment results in decreased heart rate, patients on Class Ia or Class III antiarrhythmic drugs should be closely monitored.
- ✓ **Ketoconazole:** The blood levels of Fingolimod and fingolimod-phosphate are increased by 1.7-fold when coadministered with ketoconazole. The risk of adverse reactions may be increased. Closely monitor the clinical response.
- ✓ **Vaccines:** Vaccination may be less effective during and for up to 2 months after discontinuing fingolimod. Live attenuated vaccine administration should be avoided during this period.
- ✓ **Antineoplastic, immunosuppressive or immunomodulating therapies:** they are expected to increase the risk of immunosuppression. Use caution when

switching patients from long-acting therapies with immune effects (e.g., natalizumab or mitoxantrone).

- ✓ **Heart rate-lowering drugs (e.g., beta blockers or diltiazem):** The heart rate–lowering effects may be increased. Carefully monitor patients during initiation of therapy.
- ✓ Varicella zoster virus (VZV): Consider varicella zoster virus vaccination prior to initiation of treatment in VZV-antibody negative patients; postpone fingolimod treatment for 1 month after varicella zoster vaccination.
- ✓ BCG: Immunosuppressants may diminish the therapeutic effect of BCG. Avoid combination
- ✓ Vaccines (Inactivated): Fingolimod may diminish the therapeutic effect of Vaccines (Inactivated). Monitor therapy
- ✓ Vaccines (Live): Fingolimod may enhance the adverse/toxic effect of Vaccines (Live). Vaccinial infections may develop. Fingolimod may diminish the therapeutic effect of Vaccines (Live). Avoid use of live organism vaccines with fingolimod; live-attenuated vaccines should not be given for at least 3 months after fingolimod. Avoid combination

Laboratory test interaction: Because Fingolimod reduces blood lymphocyte counts via redistribution in secondary lymphoid organs, peripheral blood lymphocyte counts cannot be utilized to evaluate the lymphocyte subset status of a patient treated with Fingolimod. A recent CBC should be available before initiating treatment with Fingolimod.

Side effects

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Central Nervous system: Headache
Gastrointestinal: Diarrhea
Neuromuscular & skeletal: Back pain
Hepatic: Liver enzyme elevations
Miscellaneous: Flu-like syndrome
1% to 10%
Cardiovascular: Hypertension, bradycardia
Central Nervous System: Depression, dizziness
Respiratory: Cough, bronchitis, dyspnea
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Macular edema

Storage

Fingolimod capsules should be stored below 30ºC (86ºF).
Protect from moisture and light.
Keep out of the reach of children.

Packaging

Fingolimod is available as 0.5 mg capsules in box of 30 capsules.

References

1. Uptodate 2012
2. http://www.drugs.com
3. Micromedex 2010