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MED CITY PHARMA
Axantia Group

Olyma® (Fingolimod 0.5 mg)

Physicians Checklist

Summary of Recommendations Important Safety Information

Call for Reporting:

The treating healthcare physicians are advised to report the adverse events in accordance with the national spontaneous reporting system.

Med City Pharma, Pharmacovigilance:

Phone: 00996920003288
Mobile: 00966533314875
Eax: 00966126358138
Email: pharmacovigilance-KSA@Axantia.com

National Pharmacovigilance Center

(NPC) (SFDA):
+ 966 11- 203 8222
ext 2317-2356-2340
SFDA call Center: 19999
E-m ail: npc.drug@sfda.gov.sa

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.
Olyma EU RMP V18 April 2024

Objectives

This Physician Checklist is essential to ensure the safe and effective use of Olyma and for the appropriate management of important safety risks

Please be advised to carefully read before prescribing, dispensing, and administering the product

Considerations in (fingolimod) Patient Selection

Olyma is suitable for adult and pediatric patients (≥10 years old) for the treatment of highly active relapsing remitting MS (RRMS)*. While many patients may be suitable for treatment, the following section highlights patients in whom Gilenya is contraindicated or not recommended.

Considerations for treatment initiation

Gilenya causes transient heart rate reduction and may cause atrioventricular (AV) conduction delays following initiation of treatment. All patients should be monitored for a minimum of 6 hours on treatment initiation. Below is a brief overview of monitoring requirements. Refer to page 4 for more information.

Contraindications

• hypersensitivity to fingolimod hydrochloride or to any of the excipients in the formulation of Olyma® (fingolimod) or component of the container
• increased risk for opportunistic infections, including those who are immunocompromised due to treatment (e.g. antineoplastic,immunosuppressive or immunomodulating therapies, total lymphoid irradiation or bone marrow transplantation) or disease (e.g.immunodeficiency syndrome)
• severe active infections, including active chronic bacterial, fungal orviral infections (e.g. hepatitis, turberculosis)
• known active malignancies (except patients with basal cell carcinoma (BCC))
• severe hepatic impairment (Child-Pugh class C)
• in the previous 6 months, myocardial infarction (MI), unstable angina pectoris, stroke/transient ischaemic attack (TIA), decompensated heart failure (requiring inpatient treatment), or New York Heart Association (NYHA) class III/IV heart failure
• Patients with severe cardiac arrhythmias requiring anti-arrhythmic treatment with Class Ia or Class III anti-arrhythmic drugs
• Patients with second-degree Mobitz type II AV block or third-degree AV block, or sick-sinus syndrome (if they do not wear a pacemaker),
patients with a baseline QTc interval of ≥ 500 msec
• Pregnant women and women of childbearing potential not using

Not recommended **Consider only after performing risk/benefit analysis and consulting a cardiologist**	
Sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QT-interval prolongation†, history of cardiac arrest, uncontrolled hypertension or severe sleep apnea	At least overnight extended monitoring is recommended. Consult cardiologist regarding appropriate first-dose monitoring.
Taking beta-blockers, heart-rate–lowering calcium channel blockers‡, or other substances that are known to lower the heart rate§.	Consult cardiologist regarding possibility of switching to non-heart-rate-lowering drugs If change in medication is not possible, extend monitoring to at least overnight

such as verapamil or diltiazem || Includes digoxin, cholinesterase inhibitors, or pilocarpine

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PHYSICIAN'S CHECKLIST: Recommended steps to managing patients on **Olyma**

The checklist and schematic that follow are intended to assist in the management of patients on Fingolimod. Key steps and considerations while starting, continuing, or discontinuing treatment are provided.

Prior to initiating treatment

- ☐ Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines. Conduct baseline electrocardiogram (ECG) and blood pressure (BP) measurement.
- ☐ Treatment with Gilenya is not recommended in the following patients, unless anticipated benefits outweigh the potential risks:
  - Those with sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QT-interval prolongation*, history of cardiac arrest, uncontrolled hypertension, or severe sleep apnea.
    - ☐ Seek advice from a cardiologist regarding the most appropriate monitoring at treatment initiation; at least overnight extended monitoring is recommended.
  - Those receiving concurrent therapy with beta- blockers, heart-rate-lowering calcium channel blockers (e.g. verapamil or diltiazem), or other substances which may decrease heart rate (e.g. ivabradine, digoxin, anticholinesteratic agents, or pilocarpine).
    - ☐ Seek advice from a cardiologist regarding a switch to non-heart-rate-lowering medicinal products prior to initiation of treatment.
    - ☐ If heart-rate-lowering medication cannot be stopped, seek advice from a cardiologist regarding the most appropriate monitoring at treatment initiation; at least overnight extended monitoring is recommended.
- ☐ For pediatric patients, assess Tanner staging, measure height and weight, and consider a complete vaccination schedule, as per standard of care.
- ☐ Avoid co-administration of anti-neoplastic, immunomodulatory or immunosuppressive therapies due to the risk of additive immune system effects. For the same reason, a decision to use prolonged concomitant treatment with corticosteroids should be taken after careful consideration. Obtain recent (within 6 months) transaminase, and bilirubin levels.
- ☐ Obtain recent (within 6 months or after discontinuation of prior therapy) full blood count. Inform WOCBP that fingolimod is contraidicated in pregnant women and WOCBP not using effective contraception.
- ☐ Gilenya is teratogenic. Confirm a negative pregnancy test result in WOCBP prior to starting treatment and repeat at suitable intervals during treatment. Inform
- ☐ WOCBP about the serious risks of Gilenya to the fetus
- ☐ Provide all patients, parents (or legal representatives) and caregivers with the Pregnancy-Specific Patient Reminder Card.
- ☐ Counsel WOCBP (including female adolescents and their parents/caregivers) to avoid pregnancy and use effective contraception both during treatment and for 2 months after treatment discontinuation. Counseling should be facilitated by the Pregnancy-Specific Patient Reminder Card.
- ☐ Delay initiation of treatment in patients with severe active infection until resolved.
- ☐ Human papilloma virus (HPV) infection, including papilloma, dysplasia, warts and HPV-related cancer, has been reported in the post-marketing setting. Cancer screening (including a Pap test), and vaccination for HPV-related cancer is recommended for patients as per standard of care.
- ☐ Check varicella zoster virus (VZV) antibody status in patients without a healthcare professional confirmed history of chickenpox or documentation of a full course of varicella vaccination. If negative, a full course of vaccination with varicella vaccine is recommended and treatment initiation should be delayed for 1 month to allow full effect of vaccination to occur.
- ☐ Conduct an ophthalmologic evaluation in patients with history of uveitis or diabetes mellitus.
- ☐ Conduct a dermatologic examination. The patient should be referred to a dermatologist in case suspicious lesions, potentially indicative of basal cell carcinoma, or other cutaneous neoplasms (including malignant melanoma, squamous cell carcinoma, Kaposi's sarcoma and Merkel cell carcinoma), are detected.
- ☐ Provide patients, parents and caregivers with the Patients, Parent's and Caregiver's Guide.

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First-dose monitoring up to 6 hours post-dose and beyond, as necessary
• Perform ECG and blood pressure measurement prior and 6 hours after the first dose • Monitor for signs and symptoms of bradyarrhythmia with hourly pulse and blood pressure measurements at least up to 6 hours post-dose.If symptoms of bradyarrhythmia or AV block occur, initiate continuous ECG monitoring as required until the symptoms areresolved. • Extend monitoring if: 1- Heart rate at 6 hours is < 45 bpm or is lowest post-dose value 2- Heart rate 6 at hours shows new onset second degree or higher AV block 3- If ECG at 6 hours shows QTc ≥ 500 msec. (overnight monitoring required) 4- If patient required pharmacological intervention during the monitoring period (overnight monitoring required) • Counsel patients that their ability to drive and use machines maybe affected during and potentially after this period.

DURING TREATMENT
Conduct a full ophthalmologic evaluation in all patients at 3 to 4 months after starting treatment and in any patient complaining of visual disturbances • Conduct periodic ophthalmologic evaluations in patients with history of uveitis or diabetes mellitus • Counsel patients to report any visual disturbance during treatment • Evaluate the fundus, including the macula, and discontinue treatment if macular oedema is confirmed
Counsel patients to report signs and symptoms of infection • Prompt antimicrobial treatment should be initiated if indicated • Perform prompt diagnostic evaluation in patients with symptoms and signs consistent with cryptococcal meningitis,and initiate appropriate treatment if diagnosed (cryptococcal meningitis, sometimes fatal, has occurred after 3-2 years of treatment, although an exact relationship with the duration of treatment is unknown) • Be vigilant for clinical symptoms or MRI findings that may be suggestive of progressive multifocal leukoencephalopathy (PML). If PML is suspected, treatment with fingolimod should be suspended until PML has been excluded (cases of PML haveoccurred 3-2 years of treatment, although an exact relationship with the duration of treatment is unknown) • If a patient develops a serious infection, treatment should be suspended • Discontinue treatment in disseminated herpetic infections.
Full blood count (CBC) should be monitored during treatment, atmonth 3 and at least yearly thereafter. Treatment should be interrupted if lymphocyte count is confirmed as <0.2x109/L. The approved dosing of 0.5 mg once daily when restarting Olican® (fingolimod) should be administered. Other dosing regimens have not been approved.
Check liver transaminases and bilirubin levels prior to initiating treatment if no recent (i.e. within the last 6 months) results is available, and at months 1, 3, 6, 9, and 12 and at regular intervals thereafter on therapy, until 2 months after fingolimod discontinuation, or at any time there are signs or symptoms of hepatic dysfunction • Institute more frequent monitoring, including ALP, if liver transaminases rise above 3 times the reference range • Interrupt treatment if liver injury is confirmed (ALT above 5 times the reference range or ALT above 3 times the reference range withserum total bilirubin above 2 times the reference range)
during treatment and for up to 2 months after discontinuation • Vaccinations may be less effective • Live attenuated vaccines may carry a risk of infection and should be avoided
while on treatment, women must not become pregnant. Counsel patient to advise physician immediately if she becomes pregnant.Discontinue treatment if a woman becomes pregnant while on treatment with Fingolimod. Fingolimod must be stopped 2 months before planning a pregnancy.When stopping Fingolimod therapy due to pregnancy or for planning a pregnancy, the possible return of disease activity should be considered. Counsel the patient regarding the risk of harmful effects to the foetus associated with Fingolimod treatment and ultrasonography examinations should be performed.

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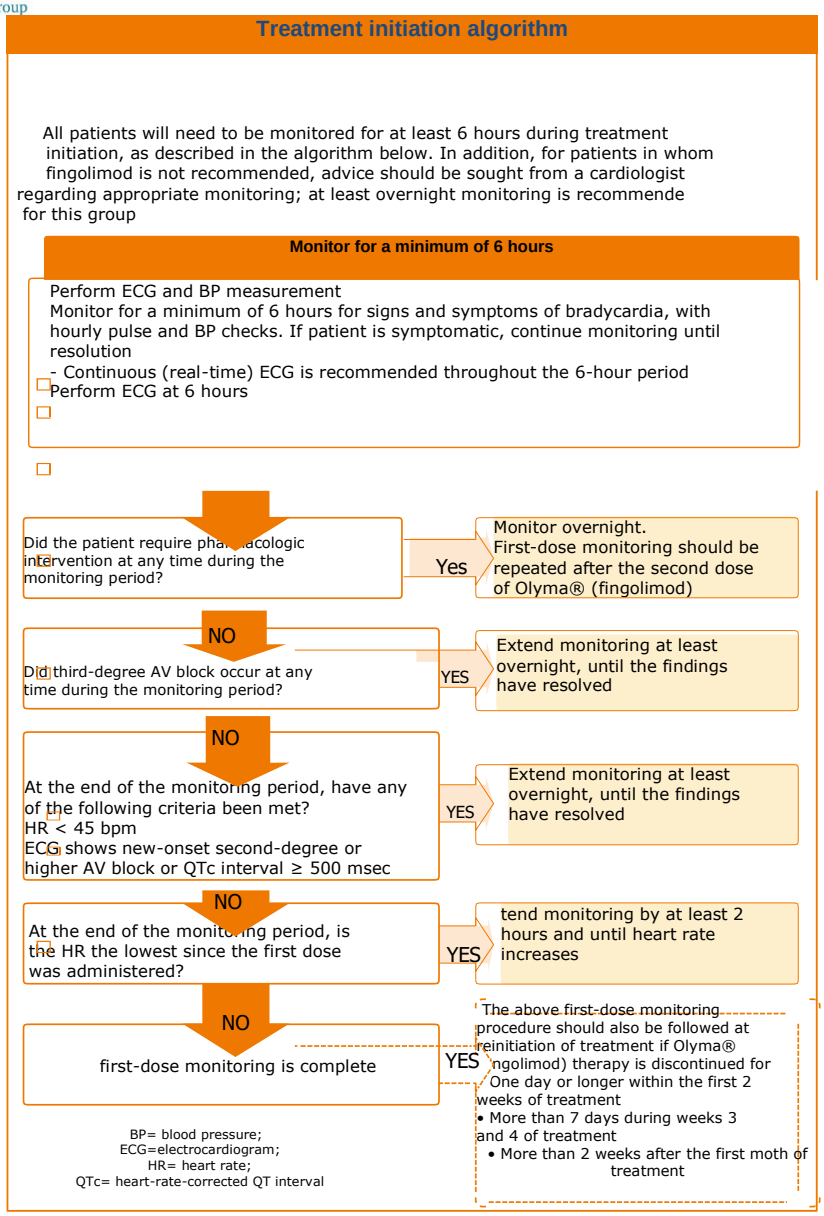
Advise women of childbearing potential (including adolescents and their parents/legal representatives/caregiver) that effective contraception must be used during treatment and for at least 2 months after treatment discontinuation. Pregnancy tests must be repeated at suitable intervals ensure women of childbearing potential (including adolescents and their parents/legal epresentatives/caregivers) receive regular counselling facilitated by the Patient Reminder Card
To help determine the effects of fingolimod exposure in pregnant women with MS, physicians are encouraged to report any pregnancy outcomes by contacting the National Pharmacovigilance Centre (NPC)at the Unified Contact Center: 19999, or Email: npc.drug@sfda.gov.sa or online: https://ade.sfda.gov.sa.
Vigilance for basal cell carcinoma and other cutaneous neoplasms is recommended, with skin examination prior to treatment initiation and then yearly taking into consideration clinical judgment and referral to a dermatologist if suspicious lesions, potentially indicative of basal cell carcinoma or other cutaneous neoplasms, are detected. Caution patients against exposure to sunlight without protection. These patients should not receive concomitant phototherapy with UV-B-radiation or PUVA-photochemotherapy.
Fingolimod has an immunosuppressive effect and can increase the risk of developing lymphomas (including mycosis fungoides), and other malignancies (particularly those of the skin), and serious opportunistic infections. Surveillance should include vigilance for both skin malignancies and mycosis fungoides. Closely monitor patients during treatment, especially those with concurrent conditions, or known factors, such as previous immunosuppressive therapy; and discontinue treatment if a risk is suspected. Fingolimod should be discontinued if lymphoma is suspected. Treatment discontinuation should be considered in those with a suspected risk on an individual basis.

After treatment discontinuation

- ☐ Repeat first-dose monitoring as for treatment initiation when treatment is interrupted for
  - One day or more during the first 2 weeks of treatment
  - More than 7 days during weeks 3 and 4 of treatment
  - More than 2 weeks after one month of treatment
- ☐ Counsel patients to report signs and symptoms of infection immediately to their prescriber for up to 2 months after discontinuation.
- ☐ Instruct patients to be vigilant for signs of encephalitis, meningitis or meningoencephalitis infection and PML.
- ☐ Inform WOCBP (including female adolescents and their parents/caregivers) that effective contraception is needed for 2 months after discontinuation because of the serious risks of Gilenya to the fetus.
- ☐ Advise women who stop treatment with Gilenya because they are planning a pregnancy that their disease activity may return
- ☐ Vigilance for the possibility of severe exacerbation of disease following discontinuation of treatment is recommended.
  - **In cases of severe exacerbation appropriate treatment should be initiated as required.**



for Further information please read the SPC (Summary of product characteristics

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