For further information, please consult the complete Summary of Product Characteristics for Olican® (fingolimod).

Healthcare professionals should report any suspected adverse reactions associated with the use of Olican® (fingolimod) to the following contacts:
Saudi Food and Drug Authority, National Pharmacovigilance Center
Unified Contact Center: 19999
Email: npc.drug@sfda.gov.sa
Or by online
https://ade.sfda.gov.sa
Pharmacovigilance department, Pharmascience Inc :Local QPPV
Tel: +9082 779 55 966
Email: aalimousa@balsam-cr.com
Deputy Local QPPV
Tel: +2128 426 55 966
Email: sbinhuwaimel@balsam-cr.com

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.

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Olican® (fingolimod) Physician's Checklist

Important Safety Information – Summary of Recommendations

Objectives

This Physician Checklist is essential to ensure the safe and effective use of Olican®(fingolimod) and for the appropriate management of important safety risks.

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

Considerations in Olican® (fingolimod) Patient Selection

Olican® (fingolimod) is indicated as single disease modifying therapy in highly active relapsing remitting multiple sclerosis (MS) for the following groups of adult patients. While many patients are suitable for treatment, the following section highlights patients in whom Olican® (fingolimod) is contraindicated or not recommended.

Fingolimod 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.

Olican® (fingolimod) is generally recommended in MS patients who have had an inadequate response to, or are unable to tolerate, one or more therapies for multiple sclerosis.

Contraindications

Olican® (fingolimod) is contraindicated in patients with:

- hypersensitivity to fingolimod hydrochloride or to any of the excipients in the formulation of Olican® (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 or viral 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 effective contraception

Should not be used

Consider fingolimod only after performing risk/benefit analysis and consulting a cardiologist

Consult cardiologist regarding appropriate first-dose monitoring	
Sino-atrial heart block, history of symptomatic bradycardia or recurrent syncope, significant QTc prolongation > 470 msec (females) or > 450 msec (males), or risk factors for QT prolongation, history of cardiac arrest, uncontrolled hypertension or severe sleep apnoea	At least overnight extended monitoring is recommended
Consult cardiologist regarding possibility of switching to non-heart-rate-lowering drugs	
Taking beta-blockers, heart-rate-lowering calcium channel blockers[§], or other substances that are known to lower the heart rate[||]	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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Patient's name: ..... Date of birth: .....

	Prior to initiating treatment
☐	Ensure patients are not concomitantly taking Class Ia or Class III antiarrhythmic medicines.
☐	Conduct baseline electrocardiogram (ECG) and blood pressure measurement.
☐	Treatment with Olican® (fingolimod) should not be used in the following patients, unless anticipated benefits outweigh the potential risks. • Those with sino-atrial block, history of symptomatic bradycardia, significant QT-interval prolongation, or in patients with relevant risk factors for QT prolongation (e.g., hypokalemia, hypomagnesemia or congenital QT prolongation), history of cardiac arrest, uncontrolled hypertension or severe untreated sleep apnoea • ☐ 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 (such as verapamil or diltiazem), or other substances which may decrease heart rate (e.g., digoxin, cholinesterase inhibitors, 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

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☐	Avoid co-administration of anti-neoplastic, immunosuppressive or immunomodulatory 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) peripheral lymphocyte count (complete blood count (CBC)). Treatment should not be initiated when lymphocyte counts are consistently below normal range.
☐	Fingolimod is teratogenic. Inform women of child-bearing potential, including adolescent females, their parents/caregivers that it is contraindicated in women of childbearing potential not using effective contraception and in pregnant women.
☐	Confirm a negative pregnancy test result in women of childbearing potential, including adolescent females, prior to starting treatment, and it must be repeated at suitable intervals during treatment.
☐	Counsel women of child-bearing potential including adolescent females, their parents (or legal representatives), and caregivers about the serious risks of Fingolimod to the fetus, facilated by the Patient Reminder Card. Counsel also on the need for effective contraception in women of childbearing age up to at least 2 months after completion or discontinuation of treatment, due to teratogenic risk to fetus.
☐	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.

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☐	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 if suspicious lesions, potentially indicative of basal cell carcinoma, or other cutaneous neoplasms (squamous cell carcinoma, Kaposi's sarcoma and Merkel cell carcinoma), are detected
☐	Provide patients with a Patient Reminder Card

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 are resolved.
☐	Extend monitoring if: • Heart rate at 6 hours is < 45 bpm or is lowest post-dose value • Heart rate 6 at hours shows new onset second degree or higher AV block • If ECG at 6 hours shows QTc ≥ 500 msec. (overnight monitoring required) • If patient required pharmacological intervention during the monitoring period (overnight monitoring required)
☐	Counsel patients that their ability to drive and use machines may be affected during and potentially after this period.

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	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 have occurred 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, at month 3 and at least yearly thereafter. Treatment should be interrupted if lymphocyte count is confirmed as $<0.2x10^9$/L. The approved dosing of 0.5 mg once daily when restarting Olican® (fingolimod) should be administered. Other dosing regimens have not been approved.

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☐	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 with serum 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.
☐	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 representatives/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.

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☐	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 1 month of treatment
☐	Counsel patients to report signs and symptoms of infection for up to 2 months after discontinuation
☐	Counsel patients that effective contraception is needed for 2 months after discontinuation
☐	Advise women who stop treatment with Fingolimod 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

Treatment initiation algorithm

All patients will need to be monitored for at least 6 hours during treatment initiation, as described in the algorithm below. In addition, for patients in whom fingolimod is not recommended, advice should be sought from a cardiologist regarding appropriate monitoring; at least overnight monitoring is recommended for this group.

Monitor for a minimum of 6 hours

☐ Perform ECG and BP measurement

☐ Monitor for a minimum of 6 hours for signs and symptoms of bradycardia, with hourly pulse and BP checks. If patient is symptomatic, continue monitoring until resolution

- Continuous (real-time) ECG is recommended throughout the 6-hour period

☐ Perform ECG at 6 hours

☐ Did the patient require pharmacologic intervention at any time during the monitoring period?

Yes → Monitor overnight. First-dose monitoring should be repeated after the second dose of Olican® (fingolimod)

No

☐ Did third-degree AV block occur at any time during the monitoring period?

Yes → Extend monitoring at least overnight, until the findings have resolved

No

At the end of the monitoring period, have any of the following criteria been met?

☐ HR < 45 bpm

☐ ECG shows new-onset second-degree or higher AV block or QTc interval ≥ 500 msec

Yes → Extend monitoring at least overnight, until the findings have resolved

No

☐ At the end of the monitoring period, is the HR the lowest since the first dose was administered?

Yes → Extend monitoring by at least 2 hours and until heart rate increases

No

☐ First-dose monitoring is complete

Yes → The above first-dose monitoring procedure should also be followed at reinitiation of treatment if Olican® (fingolimod) therapy is discontinued for

- One day or longer within the first 2 weeks of treatment
- More than 7 days during weeks 3 and 4 of treatment
- More than 2 weeks after the first month of treatment.

BP= blood pressure;
ECG=electrocardiogram;
HR= heart rate;
QTc= heart-rate-corrected QT interval