SUMMARY OF RECOMMENDATIONS*

**Table:**

<table>
<thead>
<tr>
<th>Treatment initiation (first dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monitor blood pressure and pulse frequently.</strong></td>
</tr>
<tr>
<td><strong>Observe all patients for signs and symptoms of bradycardia for the period of at least 6 hours after the first dose of GILENYA.</strong></td>
</tr>
<tr>
<td><strong>All patients should be on ECG prior to and after the first observation period.</strong></td>
</tr>
<tr>
<td><strong>Continue observation beyond 24 hours until stabilized if:</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Monitor heart rate and heart rate recovery.</strong></td>
</tr>
<tr>
<td><strong>Perform ophthalmologic examination 3–4 months after starting GILENYA, and at any time if patient reports visual disturbances.</strong></td>
</tr>
<tr>
<td><strong>Avoid live attenuated vaccines</strong></td>
</tr>
<tr>
<td><strong>Instruct patients to report symptoms of infection for up to 2 months after first dose.</strong></td>
</tr>
<tr>
<td><strong>Continue to be alert to patient reports of cardiac symptoms.</strong> Clinical data show effects of GILENYA on heart rate are maximal after first dose. Milder effects on heart rate may persist for, on average, 2–4 weeks after initiation of treatment when heart rate generally returns to baseline.</td>
</tr>
</tbody>
</table>

**During treatment:**

| **Monitor blood pressure and heart rate frequently.** |
| **Instruct patients to report symptoms of infection.** |
| **Avoid live attenuated vaccines.** |
| **Perform ophthalmologic examination 3–4 months after starting GILENYA, and at any time if patient reports visual disturbances.** |
| **Perform regular follow-up ophthalmologic evaluations to continue monitoring glaucoma incidence or a history of glaucoma.** |
| **Monitor liver function tests (AST, ALT, bilirubin) and at increments if >2-fold baseline.** |
| **Other serum evaluations: review complete blood count and blood chemistry profile at baseline.** |
| **Obtain spirometric evaluation of respiratory function and diffusion lung capacity for carbon monoxide (DLCO) if clinically indicated.** |
| **Avoid live attenuated vaccines in patients who develop progressive signs suggestive of hypogammaglobulinemia.** |
| **Continue to be alert to patient reports of cardiac symptoms.** Clinical data show effects of GILENYA on heart rate are maximal after first dose. Milder effects on heart rate may persist for, on average, 2–4 weeks after initiation of treatment when heart rate generally returns to baseline. |

**After treatment discontinuation:**

| **Instruct patients to report symptoms of infection for up to 2 months.** |
| **Obtain spirometric evaluation of respiratory function and diffusion lung capacity at intervals if >2-fold baseline.** |
| **Obtain ophthalmologic examination 3–4 months after stopping GILENYA, and at any time if patient reports visual disturbances.** |
| **Instruct patients to report symptoms of infection for up to 2 months after stopping GILENYA.** |

Novartis, a research-based global pharmaceutical company, is committed to improving the health and well-being of all who suffer from serious illness. To learn more about Novartis, please visit Novartis.com.

*Please see the accompanying complete updated full Prescribing Information (updated May 2012) for more information.

**GILENYA®**

**GILENYA®** is a registered trademark of Novartis Pharmaceuticals Corporation. The full prescribing information (updated May 2012) is available at www.gilenyapregnancyregistry.com.

**GILENYA®** is a registered trademark of Novartis Pharmaceuticals Corporation. The full prescribing information (updated May 2012) is available at www.gilenyapregnancyregistry.com.
Patients receiving concurrent therapies that slow heart rate or AV conduction should be evaluated with the possibility of switching all these drugs to prior to initiation of GILENYA. In patients who cannot tolerate overnight observation in a medical facility with continuous ECG monitoring is recommended.

Reinstitution of therapy following discontinuation and appropriate monitoring:

If GILENYA therapy is discontinued for more than 14 days after the first month of treatment, the effects on heart rate and AV conduction may occur on reintroduction of GILENYA treatment and the same precautions (first dose monitoring) as for initial dosing should apply. Within the first 2 weeks of treatment, first dose procedures should be repeated after the first dose of GILENYA is given.

Contraindications

- Patients with a history of Mobitz Type II 2nd or higher AV block at 6 hours post-dose or patients with a heart rate < 45 bpm or new onset 2nd degree or higher AV block at 6 hours post-dose or patients with symptoms of symptomatic bradycardia may be at increased risk of developing symptomatic bradycardia or bradyarrhythmia.

GILENYA causes a dose–dependent, reversible sequestration of lymphocytes in lymphoid tissues resulting in a reduction of peripheral blood lymphocyte count to 20-30% of baseline values.

Infections

GILENYA causes a dose–dependent, reversible sequestration of lymphocytes in lymphoid tissues resulting in a reduction of peripheral blood lymphocyte count to 20-30% of baseline values.

- Before initiating treatment with GILENYA, recent CBC (i.e. within 6 months) should be available.

- There are no adequate and well-controlled studies of GILENYA in pregnant women.

- Women who are pregnant or breast-feeding should not be given this drug in order to avoid harm to the fetus or nursing infant.

- There are no adequate and well-controlled studies of GILENYA in patients with diabetes mellitus or a history of uveitis undergoing an ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmologic evaluations while receiving GILENYA therapy.

- Women taking medications that increase the risk of bleeding or promote coagulation should be evaluated as for initial dosing should apply. Within the first 2 weeks of treatment, first dose procedures should be repeated after the first dose of GILENYA.

- Patients receiving concurrent therapies that slow heart rate or AV conduction should be evaluated with the possibility of switching all these drugs to prior to initiation of GILENYA. In patients who cannot tolerate overnight observation in a medical facility with continuous ECG monitoring is recommended.

- During the first 2 weeks of treatment, first dose procedures should be repeated after the first dose of GILENYA.

- Patients with a history of Mobitz Type II 2nd or higher AV block at 6 hours post-dose or patients with a heart rate < 45 bpm or new onset 2nd degree or higher AV block at 6 hours post-dose or patients with symptoms of symptomatic bradycardia may be at increased risk of developing symptomatic bradycardia or bradyarrhythmia.

- There are no adequate and well-controlled studies of GILENYA in pregnant women.

- Women who are pregnant or breast-feeding should not be given this drug in order to avoid harm to the fetus or nursing infant.

- There are no adequate and well-controlled studies of GILENYA in patients with diabetes mellitus or a history of uveitis undergoing an ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmologic evaluations while receiving GILENYA therapy.
Recommendations for first dose monitoring

For the reasons outlined above, it has been recommended that all patients be observed for a period of at least 6 hours after the first dose of GILENYA. After the first dose of GILENYA, the heart rate decreases to about 50-60 bpm with continuous ECG monitoring. Patients with a heart rate < 45 bpm or new onset 2nd degree or higher AV block at 6 hours post-dose or patients with initiation of appropriate treatment and observation until the symptoms have resolved; if pharmacological intervention is initiated, and first-dose monitoring procedures should be repeated after the second dose of GILENYA.

Patients who report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.

Patients who have a history of uveitis or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus or a history of uveitis undergo an ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmologic evaluation while receiving GILENYA therapy.

Reinitiation of therapy following discontinuation and appropriate monitoring:

- If GILENYA therapy is discontinued for more than 14 days after the first month of treatment, the effects on heart rate and associated conduction abnormalities will persist for up to 3 months after discontinuation. In patients who cannot or will not discontinue their concomitant medications, an adequate ophthalmologic evaluation should be performed at baseline and 3-4 months after treatment initiation. Following initiation of appropriate treatment and observation until the symptoms have resolved; if pharmacological intervention is initiated, and first-dose monitoring procedures should be repeated after the second dose of GILENYA.

- Spirometric evaluation of respiratory function and evaluation of diffusion lung capacity for carbon monoxide (DLCO) should be performed during therapy with GILENYA if clinically indicated.

Respiratory Effects

Elevations of liver function tests may occur in patients receiving GILENYA. The majority of elevations occurred within 6-9 months.

- Frequent (i.e. within last 6 months) transaminase and bilirubin levels should be available before initiation of GILENYA therapy.

- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be discontinued if significant liver injury is confirmed. If patients have pre-existing liver disease may be at increased risk of developing elevated liver function tests while taking GILENYA.

Fetal Risk

Based on animal studies, GILENYA may cause fetal harm.

- There are no adequate and well-controlled studies in pregnant women.

- Women of childbearing potential should be counseled on the potential risk to the fetus and advised to use effective contraception during and for at least 1 month following discontinuation of GILENYA.

- Women who become pregnant while therapy is continued should be counseled on potential risk to the fetus.

- GILENYA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
GILENYA® (Eliglustat) is a sphingomyelinase inhibitor indicated for treatment of patients with relapsing forms of multiple sclerosis (MS). GILENYA has been shown to be effective in reducing clinical exacerbations and delaying the accumulation of physical disability in those patients.

Newborns are providing the following information concerning potential risks to consider when prescribing GILENYA.

IMPORTANT SAFETY INFORMATION

Bradyarrhythmia and Atrioventricular (AV) Block

Recommendations for first dose monitoring

- Patients receiving consecutive treatments that slow heart rate or AV conduction should be evaluated with the possibility of switching all these drugs prior to initiation of GILENYA. In patients who cannot tolerate overnight observation in a medical facility with continuous ECG monitoring is recommended.
- Refinements of therapy following discontinuation and appropriate monitoring:
  - If GILENYA therapy is discontinued for more than 14 days after the first month of treatment, the effects on heart rate and AV conduction may remain, and first-dose monitoring procedures should be repeated after the second dose of GILENYA.
- If patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Patients with a heart rate < 45 bpm or new onset 2nd degree or higher AV block at 6 hours post-dose or patients with a prolonged QTc interval at baseline or during the observation period, or at additional risk for QT prolongation or taking drugs with known risk of torsades de pointes should be observed overnight in a medical facility with continuous ECG monitoring.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients develop a serious infection, and reassess the benefits and risks prior to recommencing therapy.
- Patients without a history of chickenpox or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- If patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Patients with a history of seizures or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients develop a serious infection, and reassess the benefits and risks prior to recommencing therapy.
- Patients without a history of chickenpox or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- If patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Patients with a history of seizures or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients develop a serious infection, and reassess the benefits and risks prior to recommencing therapy.
- Patients without a history of chickenpox or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- If patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Patients with a history of seizures or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients develop a serious infection, and reassess the benefits and risks prior to recommencing therapy.
- Patients without a history of chickenpox or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- If patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Patients with a history of seizures or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients develop a serious infection, and reassess the benefits and risks prior to recommencing therapy.
- Patients without a history of chickenpox or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- If patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Patients with a history of seizures or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients develop a serious infection, and reassess the benefits and risks prior to recommencing therapy.
- Patients without a history of chickenpox or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- If patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
- Patients with a history of seizures or diabetes are at increased risk of macular edema. It is recommended that MS patients with diabetes mellitus and a history of previous angina on ophthalmologic examination prior to initiating GILENYA therapy and have regular follow-up ophthalmic evaluation while receiving GILENYA therapy.
- Liver enzymes should be monitored in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. GILENYA should be interrupted if patients report visual disturbances at any time while taking GILENYA, additional ophthalmic evaluation should be undertaken.
**SUMMARY OF RECOMMENDATIONS**

**Contraindications prior to initiating treatment**

- **GIENLYA treatment in combination with**
  - Anti-TNF agents
  - Immunosuppressants or biologics of hematopoietic origin
  - Antimalarials
  - Immunosuppressants or biologics of hematopoietic origin

**Incipient Condition**

- New onset of 2nd degree or higher AV block

**With a baseline QTc interval**

- Patients with prolonged QTc interval at baseline or during the observation period, or taking drugs with known risk of torsades de pointes or at additional risk for QT prolongation

**With a history or presence of Mobitz Type II 2nd or 3rd degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker**

- Antimotility or DKIs, placebo, or no disease

- Continuous treatment with Class Ia or III anti-arrhythmic drugs

**During observation period**

- Patients who get VZV vaccination should not begin GIENLYA treatment for one month

**After treatment discontinuation**

- Zoster vaccine is given 1 month after discontinuation

**Monitoring Analysis**

- Post-dose heart rate is observed at end of the observation period

**For Management**

- Overnight observation in a medical facility with continuous ECG monitoring should be initiated in:
  - Patients at a higher risk for symptomatic bradycardia or bradyarrhythmia due to coexisting medical conditions
  - With a baseline QTc interval ≥ 500 msec

**Patients at a higher risk for symptomatic bradycardia or bradyarrhythmia due to coexisting medical conditions (refer to full PI)**

- With recent (i.e. within 6 months) occurrence of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization on Class I or IV heart failure

- With a history or presence of Mobitz Type II or 3rd degree AV block or sinus node dysfunction, unless patient has a functioning pacemaker

- With anti-TNF, placebo, or no disease

- Continuous treatment with Class Ia or III anti-arrhythmic drugs

**The first dose of GILENYA should be administered in a setting in which monitoring is available to appropriately manage symptomatic bradycardia or bradyarrhythmia**

- All patients should be on beta-blockers (BCG) prior to the first day of GILENYA and for the end of the observation period

- Patients in whom the lowest post-dose heart rate is observed at end of the observation period

- Patients with prolonged QTc interval at baseline or during the observation period, or taking drugs with known risk of torsades de pointes or at additional risk for QT prolongation

- Patients who have recently (within last 6 months) occurrence of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization on Class I or IV heart failure

- Patients with recent (i.e. within 6 months) occurrence of myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization on Class I or IV heart failure

- Patients with a history or presence of Mobitz Type II 2nd or 3rd degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker

**Please see the accompanying complete updated full Prescribing Information updated May 2012 for more information.**

**Receiving Anti-Retrosynaptic Drugs**

- Healthcare providers should report all suspected adverse events associated with the use of GIENLYA. Please contact Novartis Drug Safety and Epidemiology at 1-888-NOW-NOVA (669-6682) or FDA at 1-800-FDA-1088 or www.fda.gov/drugs

**Novartis Pharmaceuticals Corporation (Novartis), in collaboration with the Food and Drug Administration, developed a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of GIENLYA outweigh the risks. This Guide is Important Safety Information as prescribed to use as part of the REMS and is considered part of the full prescribing information updated May 2012. The purpose of this guide is to highlight key safety issues and provide a summary of recommendations healthcare professionals should consider before prescribing GIENLYA. Please review the full prescribing information (updated May 2012) for detailed safety information.**
SUMMARY OF RECOMMENDATIONS*

**TABLE**

<table>
<thead>
<tr>
<th>Treatment initiation (First Dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring blood pressure and pulse hourly.</td>
</tr>
<tr>
<td>Continue to be alert to patient reports of cardiac symptoms. Clinical data show effects of GILENYA on heart rate are maximal after first dose. Milder effects on heart rate may persist for, on average, 2–4 weeks after initiation of treatment when heart rate is 50 bpm or less.</td>
</tr>
<tr>
<td>Continue blood pressure monitoring and pulse hourly.</td>
</tr>
<tr>
<td>Over-night observation in a medical facility with continuous ECG monitoring should be initiated in:</td>
</tr>
<tr>
<td>Patients with a history or presence of Mobitz Type II 2nd or 3rd degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker.</td>
</tr>
<tr>
<td>All patients should have baseline electrocardiograms (ECG) prior to the first dose of GILENYA and at the end of the observation period.</td>
</tr>
<tr>
<td>Patients at a higher risk for symptomatic bradycardia or bradyarrhythmia due to coexisting medical conditions (refer to full PI).</td>
</tr>
<tr>
<td>Over-night observation is a medical facility with continuous ECG monitoring should be initiated in:</td>
</tr>
<tr>
<td>Patients with prolonged QTc interval or at additional risk for QT prolongation.</td>
</tr>
<tr>
<td>Prescribers with an eligible patient, or patients themselves, can contact the Pregnancy Exposure Registry by calling 1-877-598-7237, sending an email to <a href="mailto:gpr@outcome.com">gpr@outcome.com</a> or visiting <a href="http://www.gilenyapregnancyregistry.com">www.gilenyapregnancyregistry.com</a>.</td>
</tr>
<tr>
<td>Since there are no adequate and well-controlled studies of GILENYA in pregnant women, no controlled studies of GILENYA in pregnant women have been established to collect information about the effects in GILENYA during pregnancy. Physicians are encouraged to register pregnant women who become pregnant while exposed to GILENYA in or within 2 months after stopping therapy.</td>
</tr>
<tr>
<td>GILENYA treatment is contraindicated in patients:</td>
</tr>
<tr>
<td>a) with recent (within the last 30 days) evidence of uncontrolled hypertension, valvular heart disease, stroke, transient ischemic attack, or decompressed heart failure requiring hospitalization on Class III/IV heart failure drugs, b) with a history or presence of Mobitz Type II or 3rd degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker, c) with baseline ECG interval ≥ 500 msec.</td>
</tr>
</tbody>
</table>

**Outcome at 1-877-598-7237, sending an email to gpr@outcome.com or visiting www.gilenyapregnancyregistry.com.**

Novartis Pharmaceutical Corporation (Novartis), in collaboration with the Food and Drug Administration, developed a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of GILENYA outweigh the risks. The Guide to Important Safety Information is provided to you as part of the REMS and is revised based on the full prescribing information updated May 2012.

The purpose of this guide is to highlight safety issues and provide a summary of recommendations healthcare professionals should consider before prescribing GILENYA. Please review the full prescribing information updated May 2012 for detailed safety information for GILENYA.

*Please see the accompanying complete updated full Prescribing Information for more information.

**GILENYA® (fingolimod) for the treatment of relapsing forms of multiple sclerosis (MS) including relapsing-remitting MS (RRMS) or primary progressive MS (PPMS). GILENYA® is indicated as monotherapy for the treatment of adult patients with relapsing forms of multiple sclerosis (MS), to reduce the frequency of clinical exacerbations, delay the accumulation of physical disability and improve physical function.*

**Please see the accompanying complete updated full Prescribing Information for more information.**

**SUMMARY OF RECOMMENDATIONS**

<table>
<thead>
<tr>
<th>Table</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment initiation (First Dose)</td>
<td>Monitoring blood pressure and pulse hourly.</td>
</tr>
<tr>
<td></td>
<td>Continue to be alert to patient reports of cardiac symptoms. Clinical data show effects of GILENYA on heart rate are maximal after first dose. Milder effects on heart rate may persist for, on average, 2–4 weeks after initiation of treatment when heart rate is 50 bpm or less.</td>
</tr>
<tr>
<td></td>
<td>Continue blood pressure monitoring and pulse hourly.</td>
</tr>
<tr>
<td></td>
<td>Over-night observation in a medical facility with continuous ECG monitoring should be initiated in:</td>
</tr>
<tr>
<td></td>
<td>Patients with a history or presence of Mobitz Type II 2nd or 3rd degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker.</td>
</tr>
<tr>
<td></td>
<td>All patients should have baseline electrocardiograms (ECG) prior to the first dose of GILENYA and at the end of the observation period.</td>
</tr>
<tr>
<td></td>
<td>Patients at a higher risk for symptomatic bradycardia or bradyarrhythmia due to coexisting medical conditions (refer to full PI).</td>
</tr>
<tr>
<td></td>
<td>Over-night observation is a medical facility with continuous ECG monitoring should be initiated in:</td>
</tr>
<tr>
<td></td>
<td>Patients with prolonged QTc interval or at additional risk for QT prolongation.</td>
</tr>
<tr>
<td></td>
<td>Prescribers with an eligible patient, or patients themselves, can contact the Pregnancy Exposure Registry by calling 1-877-598-7237, sending an email to <a href="mailto:gpr@outcome.com">gpr@outcome.com</a> or visiting <a href="http://www.gilenyapregnancyregistry.com">www.gilenyapregnancyregistry.com</a>.</td>
</tr>
<tr>
<td></td>
<td>Since there are no adequate and well-controlled studies of GILENYA in pregnant women, no controlled studies of GILENYA in pregnant women have been established to collect information about the effects in GILENYA during pregnancy. Physicians are encouraged to register pregnant women who become pregnant while exposed to GILENYA in or within 2 months after stopping therapy.</td>
</tr>
<tr>
<td></td>
<td>GILENYA treatment is contraindicated in patients:</td>
</tr>
<tr>
<td></td>
<td>a) with recent (within the last 30 days) evidence of uncontrolled hypertension, valvular heart disease, stroke, transient ischemic attack, or decompressed heart failure requiring hospitalization on Class III/IV heart failure drugs, b) with a history or presence of Mobitz Type II or 3rd degree AV block or sick sinus syndrome, unless patient has a functioning pacemaker, c) with baseline ECG interval ≥ 500 msec.</td>
</tr>
</tbody>
</table>

**Outcome at 1-877-598-7237, sending an email to gpr@outcome.com or visiting www.gilenyapregnancyregistry.com.**

Novartis Pharmaceutical Corporation (Novartis), in collaboration with the Food and Drug Administration, developed a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of GILENYA outweigh the risks. The Guide to Important Safety Information is provided to you as part of the REMS and is revised based on the full prescribing information updated May 2012.

The purpose of this guide is to highlight safety issues and provide a summary of recommendations healthcare professionals should consider before prescribing GILENYA. Please review the full prescribing information updated May 2012 for detailed safety information for GILENYA.

*Please see the accompanying complete updated full Prescribing Information for more information.*

**Guide to Important Safety Information**

**Using GILENYA® In Patients with Relapsing Forms of Multiple Sclerosis**

June 2013