LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Gaxenim
(fingolimod hydrochloride)

SE/H/2020/01/DC

This module reflects the scientific discussion for the approval of Gaxenim. The procedure was finalised on 2020-12-02. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Gaxenim, 0,5 mg, Capsule, hard.

The active substance is fingolimod hydrochloride. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The application for Gaxenim, 0,5 mg, capsule, hard, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Bausch Health Ireland Limited, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and CZ, DE, DK, ES, FI, HU, IT, NO, PL and SK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Gilenya, 0,5 mg, capsule, hard, authorised in EU since 2011, with Novartis Europharm Limited as marketing authorisation holder.

The reference product used in the bioequivalence study is Gilenya, 0,5 mg, capsule, hard from DE with Novartis Europharm Limited as marketing authorisation holder.

Potential similarity with orphan medicinal products
According to the application form and a check of the Community Register of orphan medicinal products there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of active substance are well known. As active substance is a widely used, well-known active substance, no further studies are required and the applicant provides none. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since product name is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

There are no objections to approval of Gaxenim from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted one bioequivalence study comparing Gaxenim with the reference product Gilenya.

Pharmacokinetic properties of the active substance
Fingolimod has an oral bioavailability of 93%. The pharmacokinetics of fingolimod is not affected by food, and therefore there are no restrictions with respect to food in the SmPC of the originator. Fingolimod concentrations increase in an apparently dose proportional manner after multiple once-daily doses of 0.5 mg and 1.25 mg. The terminal half-life (t1/2) of fingolimod is 6-9 days.

Methods
This was a single-dose, two-treatment, single-period, parallel study conducted in 36 healthy volunteers, comparing fingolimod, 0.5 mg, capsule with Gilenya, 0.5 mg, capsule under fasting conditions. Blood samples for concentration analysis were collected pre-dose and up to 72 hours post-dose. Blood concentrations of fingolimod were determined with an LC-MS/MS method. Analysis of variance (ANOVA) was performed on the log-transformed data for $AUC_{0\text{-}72h}$ and C_{max}. The study was conducted between 22nd and 26th of March 2019.

Results
The results from the pharmacokinetic and statistical analysis are presented in

Table 1 below.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range) for fingolimod, n=36.

Treatment	AUC_{0-72h} pg*h/ml	C_{max} pg/ml	t_{max} h
Test	**23114 ± 4512**	**404 ± 77**	**24.00 (14.00 - 30.00)**
Reference	**24996 ± 3766**	**442 ± 68**	**20.50 (9.00 - 36.00)**
***Ratio (90% CI)**	**91.78 (83.31-101.11)**	**90.84 (82.65-99.84)**	**-**

AUC_{0-t}	area under the blood concentration-time curve from time zero to t hours
C_{max}	maximum blood concentration
t_{max}	time for maximum blood concentration

**calculated based on ln-transformed data*

For AUC_{0-72h} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Discussion and overall conclusion

The bioequivalence study and its statistical evaluation were in accordance with accepted standards for bioequivalence testing, as stated in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr). The bioanalytical methods were adequately validated.

Based on the submitted bioequivalence study, Gaxenim is considered bioequivalent with Gilenya.

Pharmacodynamics/Clinical efficacy/Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Gaxenim.

Safety specification

The MAH has submitted an updated version 1.0-20201019 RMP dated 2020-10-19 and proposed the following summary safety concerns:

Important identified risks	• Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose • Hypertension • Liver transaminase elevation • Posterior Reversible Encephalopathy Syndrome (PRES) • Macular edema • Infections, including opportunistic infections (PML, VZV, herpes viral infections other than VZV, fungal infection) • Reproductive toxicity • Bronchoconstriction

	• Skin cancer (Basal cell carcinoma, Kaposi's sarcoma, Malignant melanoma, Merkel cell carcinoma, Squamous cell carcinoma) • Convulsions
Important potential risks	•Acute disseminated encephalomyelitis-like (ADEM-like) events • Lymphoma • Other malignant neoplasms • Thrombo-embolic events • QT interval prolongation
Missing information	• Long-term use in paediatric patients, including impact on growth and development (including cognitive development) • Elderly patients (≥65 years) • Lactating women • Patients with diabetes mellitus •Patients with cardiovascular conditions including myocardial infarction, angina pectoris, Raynaud's phenomenon, cardiac failure or severe cardiac disease, increased QTc interval, uncontrolled hypertension, patients at risk for bradyarrhythmia and who may not tolerate bradycardia, patients with second degree Mobitz type 2 or higher AV block, sick-sinus syndrome, sino-atrial heart block, history of cardiac arrest, cerebrovascular disease and severe sleep apnea •Long-term risk of cardiovascular morbidity/mortality •Long-term risk of malignant neoplasms •Unexplained death • Switch from other disease modifying therapy

The summary of safety concerns is in line with the reference product Gilenya (RMP, version 16.1, dated 2019-08-06).

Pharmacovigilance Plan

Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

However, specific adverse reaction follow-up questionnaires for the events below were proposed in line with the reference product (Annex 4).

Risk minimisation measures

The Applicant provided a table describing the routine risk minimisation measures by safety concern.

Additional risk minimisation measures in form of educational material for physicians (checklist) and patients (patient reminder card) were proposed in line with the reference product. The following risks need to be addressed by the educational material:

- Bradyarrhythmia (including conduction defects and bradycardia complicated by hypotension) occurring post-first dose
- Liver transaminase elevation
- Macular edema
- Infections, including opportunistic infections (PML, VZV, herpes viral infections other than VZV, fungal infection)
- Reproductive toxicity
- Skin cancer (Basal cell carcinoma, Kaposi's sarcoma, Malignant melanoma, Merkel cell carcinoma, Squamous cell carcinoma)

- Convulsions
- Long-term use in paediatric patients, including impact on growth and development (including cognitive development)

Summary of the RMP
The submitted Risk Management Plan, version 1.0-20201019 signed 2020-10-19 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English. The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Gaxenim, is found adequate. There are no objections to approval of Gaxenim, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. The product information is acceptable. The application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

- **Additional risk minimisation measures (including educational material)**
  The educational material should contain the following key elements:

Prior to launch of Gaxenim in each Member State the Marketing Authorisation Holder (MAH) must agree about the content and format of the educational programme, including communication media, distribution modalities, and any other aspects of the programme, with the National Competent Authority (NCA).

The MAH shall ensure that in each Member State (MS) where Gaxenim is marketed, all physicians who intend to prescribe Gaxenim are provided with an updated Physician Information Pack, including:

1. Summary of Product Characteristics (SmPC);
2. Physician's checklist for adult and pediatric patients, to consider prior to prescribing Gaxenim, including information about the Pregnancy Exposure Registry;
3. The Patient / Parent / Caregiver's guide, to be provided to all patients, their parents (or legal representatives), and caregivers.
4. The pregnancy-specific patient reminder card, to be provided to all patients, their parents (or legal representatives), and caregivers, as applicable.

Physician's checklist
The physician's checklist shall contain the following key messages:

 Monitoring requirements at treatment initiation:

Before first dose
- Perform baseline ECG prior to the first dose of Gaxenim;
- Perform blood pressure measurement prior to the first dose of Gaxenim;
- Perform a liver function test prior to (within 6 months) treatment initiation;
- Arrange ophthalmological assessment before starting Gaxenim treatment in patients with diabetes mellitus or with a history of uveitis.
- A negative pregnancy test result must be confirmed prior to starting treatment.

Until 6 hours after first dose
- Monitor the patient for 6 hours after the first dose of Gaxenim has been administered for signs and symptoms of bradycardia, including hourly pulse and blood pressure checks. Continuous (real time) ECG monitoring is recommended;
- Perform an ECG at the end of the 6-hour monitoring period.

>6 to 8 hours after first dose
- If, at the 6-hour time point, the heart rate is at the lowest value following the first dose, extend heart rate monitoring for at least 2 more hours and until the heart rate increases again.

 Recommendation for re-initiating Gaxenim therapy after treatment interruption: The same first dose monitoring as for treatment initiation is recommended 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 at least 1 month of treatment.

 Recommendation for overnight monitoring after the first dose (or if the first dose monitoring applies during treatment re-initiation):
- Extend heart rate monitoring for at least overnight in a medical facility and until resolution of findings in patients requiring pharmacological intervention during monitoring at treatment initiation/re-initiation. Repeat the first dose monitoring after the second dose of Gaxenim;
- Extend heart rate monitoring for at least overnight in a medical facility and until resolution of findings in patients:
    - With third degree AV block occurring at any time;
    - Where at the 6-hour time point:
        a. Heart rate <45 bpm, <55 bpm in paediatric patients aged 12 years old and above, or <60 bpm in pediatric patients 10 to below 12 years of age;
        b. New onset second degree or higher AV block;
        c. QTc interval ≥ 500 msec.

 Gaxenim is contraindicated in patients with:
- Known immunodeficiency syndrome;
- Patients with increased risk for opportunistic infections, including immunocompromised patients (including those currently receiving immunosuppressive therapies or those immunocompromised by prior therapies);
- Severe active infections, active chronic infections (hepatitis, tuberculosis);
- Known active malignancies; o Severe liver 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;
- Severe cardiac arrhythmias requiring anti-arrhythmic treatment with class Ia or class III anti-arrhythmic medicinal products;
- Second-degree Mobitz type II atrioventricular (AV) block or third-degree AV block, or sick-sinus syndrome, if they do not wear a pacemaker;
- Patients with a baseline QTc interval ≥500 msec;
- Pregnant women and women of childbearing potential not using effective contraception;
- Hypersensitivity to the active substance or to any of the excipients.

 Gaxenim is not recommended in patients with:
- Sino-atrial heart block;
- QTc prolongation >470 msec (adult females), QTc >460 msec (pediatric females) or >450 msec (adult and pediatric males);
- History of cardiac arrest;
- Severe sleep apnea;
- History of symptomatic bradycardia;
- History of recurrent syncope;
- Uncontrolled hypertension.

  If Gaxenim treatment is considered in these patients anticipated benefits must outweigh potential risks and a cardiologist must be consulted to determine appropriate monitoring, at least overnight extended monitoring is recommended.

 Gaxenim is not recommended in patients concomitantly taking medicines known to decrease the heart rate. If Gaxenim treatment is considered in these patients anticipated benefits must outweigh potential risks and a cardiologist must be consulted to switch to non heart-ratelowering therapy or, if not possible, to determine appropriate monitoring. At least overnight extended monitoring is recommended.

 Gaxenim reduces peripheral blood lymphocyte counts. Peripheral lymphocyte count (CBC) should be checked in all patients prior to initiation (within 6 months or after discontinuation of prior therapy) and monitored during treatment with Gaxenim. Treatment should be interrupted if lymphocyte count is confirmed as <0.2x109/L. The approved dosing of 0.5 mg once daily (or 0.25 mg once daily in pediatric patients 10 years of age and above with a body weight of ≤40 kg) when restarting Gaxenim should be administered. Other dosing regimens have not been approved.

 Gaxenim has an immunosuppressive effect that predisposes patients to an infection risk, including opportunistic infections that can be fatal, and increases the risk of developing lymphomas (including mycosis fungoides) and other malignancies, particularly those of the skin. Surveillance should include vigilance for both skin malignancies and mycosis fungoides. Physicians should carefully monitor patients, especially those with concurrent conditions or known factors, such as previous immunosuppressive therapy. If this risk is suspected, discontinuation of treatment should be considered by the physician on a case-by-case basis.

- Treatment initiation in patients with severe active infection should be delayed until the infection is resolved. Suspension of treatment during serious infections should be considered. Anti-neoplastic, immunomodulatory or immunosuppressive therapies should not be co-administered 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.

- Vigilance for basal cell carcinoma and other cutaneous neoplasms including malignant melanoma, squamous cell carcinoma, Kaposi's sarcoma and Merkel cell carcinoma is recommended, with skin examination prior to treatment initiation and then every 6 to 12 months taking into consideration clinical judgement. Patients should be referred to a dermatologist if suspicious lesions are detected. Caution patients against exposure to sunlight without protection. These patients should not receive concomitant phototherapy with UV-B-radiation or PUVA-photochemotherapy.

 Patients should be instructed to report signs and symptoms of infections immediately to their prescriber during and for up to two months after treatment with Gaxenim.

- Prompt diagnostic evaluation should be performed in patient with symptoms and signs consistent with cryptococcal meningitis; appropriate treatment, if diagnosed, should be initiated. Reports of cryptococcal meningitis (sometimes fatal) have been received after approximately 2-3 years of treatment, although an exact relationship with the duration of treatment is unknown.

- Physicians should be vigilant for clinical symptoms or MRI findings suggestive of PML. If PML is suspected, treatment with Gaxenim should be suspended until PML has been excluded. Cases of PML have occurred after approximately 2-3 years of monotherapy treatment although an exact relationship with the duration of treatment is unknown.

- Specific recommendations regarding vaccination for patients initiating Gaxenim treatment. 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.

- Human papilloma virus (HPV) infection, including papilloma, dysplasia, warts and HPVrelated cancer, has been reported in the post-marketing setting. Cancer screening, including Pap test, and vaccination for HPV-related cancer is recommended for patients, as per standard of care.

 A full ophthalmological assessment should be considered:
- 3-4 months after starting Gaxenim therapy for the early detection of visual impairment due to drug-induced macular oedema;
- During treatment with Gaxenim in patients with diabetes mellitus or with a history of uveitis.

 Gaxenim is teratogenic. It is contraindicated in women of childbearing potential (including female adolescents) not using effective contraception and in pregnant women.

- A negative pregnancy test result must be confirmed prior to starting treatment, and it must be repeated at suitable intervals.

- Women of child-bearing potential, including adolescent females, their parents (or legal representatives), and caregivers, should be counselled before treatment initiation and regularly

thereafter about the serious risks of Gaxenim to the foetus, facilitated by the pregnancy-specific patient reminder card.

- Women of childbearing potential must use effective contraception during treatment and for two months following treatment discontinuation.

- While on treatment, women must not become pregnant. If a woman becomes pregnant while on treatment, Gaxenim must be discontinued. When stopping Gaxenim therapy due to pregnancy or for planning a pregnancy, the possible return of disease activity should be considered. Medical advice should be given regarding the risk of harmful effects to the foetus associated with Gaxenim treatment and ultrasonography examinations should be performed.

- Gaxenim must be stopped 2 months before planning a pregnancy.

 Liver function should be monitored at months 1, 3, 6, 9 and 12 during Gaxenim therapy and periodically thereafter; the approved dosing of 0.5 mg daily (or 0.25 mg once daily in pediatric patients 10 years of age and above with a body weight of ≤40 kg) should be administered. Other dosing regimens have not been approved.

 In the post-marketing setting, severe exacerbation of disease has been observed rarely in some patients stopping Gaxenim. The possibility of recurrence of exceptionally high disease activity should be considered.

 Cases of seizure, including status epilepticus, have been reported. Physicians should be vigilant for seizures and especially in those patients with underlying conditions or with a pre-existing history or family history of epilepsy.

 Physicians should reassess on an annual basis the benefit of Gaxenim treatment versus risk in each patient, especially pediatric patients.

 Physicians should provide patients/parents/caregivers with the patient/parents/caregiver guide and with the pregnancy-specific patient reminder card.

The safety profile in pediatric patients is similar to adults and therefore the warnings and precautions in adults also apply for pediatric patients.

Specifically with pediatric patients, physicians should also:
- Assess Tanner staging and measure height and weight as per standard of care;
- Perform cardiovascular monitoring;
- Take precautions when the first dose is administered / patients are switched from 0.25 to 0.5 mg daily, due to the potential for bradyarrhythmia;
- Monitor the patient for sign and symptoms of depression and anxiety;
- Emphasize treatment compliance and misuse to patients, especially about treatment interruption and the importance of repeating cardiovascular monitoring;
- Emphasize Gaxenim immunosuppressive effects;
- Consider a complete vaccination schedule before starting Gaxenim;
- Provide guidance on seizure monitoring.

Patient / Parent / Caregiver guide
The patient/parents/caregiver guide shall contain the following key messages:
 What Gaxenim is and how it works;
 What multiple sclerosis is;
 Patients should read the package leaflet thoroughly before starting treatment and should keep it in case they need to refer to it again during treatment;
 Importance of reporting adverse reactions;

 Patients should have a baseline ECG and blood pressure measurement prior to receiving the first dose of Gaxenim;
 Heart rate should be monitored for 6 or more hours after the first dose of Gaxenim, including hourly pulse and blood pressure checks. Patients may be monitored with continuous ECG during the first 6 hours. An ECG at 6 hours should also be performed and, in some circumstances, monitoring may involve an overnight stay;
 Patients should call their doctor in case of treatment interruption as the first dose monitoring may need to be repeated, depending on duration of interruption and time since starting of Gaxenim treatment;
 Patients should report immediately symptoms indicating low heart rate (such as dizziness, vertigo, nausea or palpitations) after the first dose of Gaxenim;
 Gaxenim is not recommended in patients with cardiac disease or those taking medicines concomitantly known to decrease heart rate, and they should tell any doctor they see that they are being treated with Gaxenim;
 Signs and symptoms of infection, which should be immediately reported to the prescriber physician during and up to two months after Gaxenim treatment;
 The need to undergo cancer screening, including Pap test, and vaccination for HPV-related cancer, as per standard of care, will be assessed by the prescriber physician;
 Any symptoms of visual impairment should be reported immediately to the prescriber during and for up to two months after the end of treatment with Gaxenim;
 Gaxenim is teratogenic. Women of child-bearing potential, including adolescent females, should:
- Be informed before treatment initiation and regularly thereafter by their physician about Gaxenim's serious risks to the foetus, and about the contraindication in pregnant women and in women of childbearing potential not using effective contraception, facilitated by the pregnancy-specific patient reminder card;
- Have a negative pregnancy test before starting Gaxenim;
- Be using effective contraception during and for at least two months following discontinuation of Gaxenim treatment;
- Report immediately to the prescribing physician any (intended or unintended) pregnancy during and up to two months following discontinuation of Gaxenim treatment;

 A liver function test should be performed prior to treatment initiation; liver function monitoring should be performed at months 1, 3, 6, 9 and 12 during Gaxenim therapy, and periodically thereafter;
 Skin cancers have been reported in multiple sclerosis patients treated with Gaxenim. Patients should inform their doctor immediately if any skin nodules (e.g., shiny, pearly nodules), patches or open sores that do not heal within weeks are noted. Symptoms of skin cancer may include abnormal growth or changes of skin tissue (e.g., unusual moles) with a change in color, shape or size over time; Seizure may occur. The doctor should be informed about a pre-existing history or family history of epilepsy;
 Stopping Gaxenim therapy may result in return of disease activity. The prescribing physician should decide whether and how the patient should be monitored after stopping Gaxenim.

Specifically for Paediatric patients:

The following should be considered:
 Physicians should assess Tanner staging and measure height and weight as per standard of care;
 Precautions should be taken during the first dose of Gaxenim and when patients are switched from 0.25 to 0.5 mg daily;
 Depression and anxiety are known to occur with increased frequency in the multiple sclerosis population and have been reported also in paediatric patients treated with Gaxenim;
 Cardiac monitoring guidance;
 Patients should ensure medication compliance and avoid misuse, especially treatment interruption, and repeat cardiac monitoring;
 Signs and symptoms of infection;
 Seizure monitoring guidance.

Pregnancy-specific patient reminder card

The pregnancy-specific patient reminder card shall contain the following key messages:

 Gaxenim is contraindicated during pregnancy and in women of childbearing potential not using effective contraception.
 Doctors will provide counselling before treatment initiation and regularly thereafter regarding the teratogenic risk of Gaxenim and required actions to minimise this risk.
 Patients must use effective contraception while taking Gaxenim.
 A pregnancy test must be carried out and negative results verified by the doctor before starting treatment. It must be repeated at suitable intervals.
 Patients will be informed by their doctor of the need for effective contraception while on treatment and for 2 months after discontinuation.
 Doctors will provide counselling in the event of pregnancy and evaluation of the outcome of any pregnancy.
 While on treatment, women must not become pregnant. If a woman becomes pregnant or wants to become pregnant, Gaxenim must be discontinued.
 Patients should inform their doctor straight away if there is worsening of multiple sclerosis after stopping treatment with Gaxenim.

VII. APPROVAL

The decentralised procedure for Gaxenim, 0,5 mg, Capsule, hard was positively finalised on 2020-12-02.

LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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