

Initial REMS approval: 05/2016
Last modified/revised: 11/2017

BLA 761029 ZINBRYTA® (daclizumab)
Alpha subunit, Interleukin-2 receptor antagonist
Biogen Inc.
225 Binney Street, Cambridge, MA 02142
Phone: 781-464-2000

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(s)

To mitigate the risks of severe and fatal hepatic injury and serious immune-mediated disorders associated with ZINBRYTA by:

- Ensuring that prescribers are educated on the following:
 - the potential risks of severe and fatal hepatic injury and serious immune-mediated disorders associated with the use of ZINBRYTA
 - the need to counsel patients about these risks and the need for appropriate baseline and monthly monitoring
- Ensuring that prescribers are educated on and adhere to:
 - required baseline and monthly monitoring and evaluation of patients who receive ZINBRYTA
- Ensuring that patients are informed about:
 - the potential risks of severe and fatal hepatic injury and serious immune-mediated disorders associated with the use of ZINBRYTA
 - appropriate baseline and monthly monitoring
- Enrollment of all patients in a registry to further support long-term safety and safe use of ZINBRYTA

II. ELEMENTS

A. Communication Plan

Biogen must implement the following communication plan to healthcare providers likely to prescribe ZINBRYTA:

1. REMS Letters

Biogen must send a *ZINBRYTA REMS Program Letter for Healthcare Providers* within 60 calendar days of the approval of the REMS. Biogen must send a second and third mailing of the *ZINBRYTA REMS Program Letter for Healthcare Providers* at 12 and 24 months from the date of

the REMS approval. The REMS Letter must address the risks of severe and fatal hepatic injury and serious immune-mediated disorders as well as support implementation of the REMS Program. The REMS Letter must be distributed by mail. A copy of the Prescribing Information must accompany each *REMS Program Letter for Healthcare Providers*. Biogen must make the *ZINBRYTA REMS Program Letter for Healthcare Providers* available via a link from the ZINBRYTA REMS Program Website (www.zinbrytarems.com) and through Biogen field based sales and medical representatives upon request for one year after the initial approval of the REMS.

REMS letters must be mailed in hard copy letter format. If a mailed letter is returned as undeliverable, Biogen must send an email, within 20 business days after the letter is returned for those healthcare providers for whom an email address is available.

The intended audience for the *ZINBRYTA REMS Program Letter for Healthcare Providers* must be prescribers who have written at least one prescription within the previous 2 years for a prescription drug indicated for the treatment of multiple sclerosis.

The following materials are part of the REMS and are appended:

- [*ZINBRYTA REMS Program Letter for Healthcare Providers*](#)

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe ZINBRYTA must be specially certified.
 - a. To become specially certified to prescribe ZINBRYTA, healthcare providers must:
 - i. Review the Prescribing Information for ZINBRYTA
 - ii. Review the *ZINBRYTA REMS Program Overview* and *ZINBRYTA REMS Program Prescriber Training* and successfully complete the *ZINBRYTA REMS Program Prescriber Knowledge Assessment*
 - iii. Enroll in the ZINBRYTA REMS Program by signing and completing the *ZINBRYTA REMS Program Prescriber Enrollment Form* and submitting it to the ZINBRYTA REMS Program
 - b. As a condition of certification, prescribers must:
 - i. Enroll each patient in the ZINBRYTA REMS Program by performing the following:
 - 1) Counsel the patient about the risks of severe and fatal hepatic injury, serious immune-mediated disorders associated with ZINBRYTA, and the need for baseline and monthly monitoring, and provide the *ZINBRYTA REMS Program Patient Guide* and *ZINBRYTA REMS Program Patient Wallet Card*
 - 2) Complete the *ZINBRYTA REMS Program Patient Enrollment Form* for each patient and provide a completed copy to the patient. Submit

the completed form to the ZINBRYTA REMS Program and store a copy in the patient's records

- ii. Report any adverse events suggestive of hepatic injury and immune-mediated disorders to the ZINBRYTA REMS Program
 - iii. Perform the baseline monitoring as described in the Prescribing Information and attest that this monitoring will be completed and evaluated prior to the patient's first dose of ZINBRYTA on the *ZINBRYTA REMS Program Patient Enrollment Form*
 - iv. Perform monthly monitoring as described in the Prescribing Information
 - v. Submit a *ZINBRYTA REMS Program Patient Status Form* via online, fax, or mail to the REMS Program indicating completion and evaluation of each patient's monthly monitoring every 90 calendar days during treatment and every 90 calendar days for 6 months after discontinuation of the drug
 - vi. Inform Biogen if an enrolled patient is no longer under your care or has discontinued therapy
- c. Biogen must:
- i. Ensure that healthcare providers who prescribe ZINBRYTA are specially certified, in accordance with the requirements described above
 - ii. Provide all the following mechanisms for healthcare providers to complete the certification process for the ZINBRYTA REMS Program: online, fax, and mail
 - iii. Ensure that healthcare providers are notified when they have been certified by the ZINBRYTA REMS Program
 - iv. Maintain a validated, secure database of healthcare providers who are certified to prescribe ZINBRYTA in the ZINBRYTA REMS Program
 - v. Ensure that healthcare providers meet the REMS requirements and de-certify healthcare providers who do not maintain compliance with REMS requirements
 - vi. Ensure that certified prescribers are provided access to the database of certified pharmacies and their enrolled patients
 - vii. Provide all the materials listed below and the Prescribing Information to healthcare providers who (1) attempt to prescribe ZINBRYTA and are not yet certified, or (2) inquire about how to become certified

The following materials are part of the REMS and are appended:

- [*ZINBRYTA REMS Program Overview*](#)
- [*ZINBRYTA REMS Program Prescriber Training*](#)
- [*ZINBRYTA REMS Program Prescriber Enrollment Form*](#)
- [*ZINBRYTA REMS Program Prescriber Knowledge Assessment*](#)
- [*ZINBRYTA REMS Program Patient Enrollment Form*](#)
- [*ZINBRYTA REMS Program Patient Status Form*](#)

- [ZINBRYTA REMS Program Patient Guide](#)
- [ZINBRYTA REMS Program Patient Wallet Card](#)

2. Pharmacies that dispense ZINBRYTA must be specially certified.

a. To become specially certified to dispense ZINBRYTA, pharmacies must:

- i. Designate an authorized representative to complete the enrollment process by submitting the completed *ZINBRYTA REMS Program Pharmacy Enrollment Form* on behalf of the pharmacy
- ii. Ensure that the authorized representative oversees implementation and compliance with the ZINBRYTA REMS Program requirements by the following:
 - 1) Review the *ZINBRYTA REMS Program Overview*
 - 2) Ensure all relevant staff involved in the dispensing of ZINBRYTA are trained on the ZINBRYTA REMS Program requirements as described in the *ZINBRYTA REMS Program Overview* and maintain a record of training
 - 3) Put processes and procedures in place to ensure the following requirements are completed prior to dispensing ZINBRYTA:
 - a) Verify the prescriber is certified and the patient is enrolled and authorized by accessing the ZINBRYTA REMS Program Website, or calling the ZINBRYTA REMS Program; and
 - b) Dispense no more than a one month supply of ZINBRYTA to a patient

b. As a condition of certification, pharmacies must:

- i. Dispense ZINBRYTA to patients only after obtaining authorization by calling the ZINBRYTA REMS Program or accessing the ZINBRYTA REMS Program Website. The authorization confirms the following:
 - 1) The prescriber is certified and the patient is enrolled in the ZINBRYTA REMS Program
 - 2) The *ZINBRYTA REMS Program Patient Status Form* is received by Biogen within the designated time frame
- ii. Dispense no more than a one month supply of ZINBRYTA
- iii. Recertify in the ZINBRYTA REMS Program if the pharmacy designates a new authorized representative
- iv. Report any adverse events suggestive of hepatic injury and immune-mediated disorders to the ZINBRYTA REMS Program
- v. Maintain appropriate documentation that all processes and procedures are in place and are being followed for the ZINBRYTA REMS Program and provide upon request to Biogen, FDA, or a third party acting on behalf of Biogen or FDA

- vi. Comply with audits by Biogen, FDA, or a third party acting on behalf of Biogen or FDA to ensure that all processes and procedures are in place and are being followed for the ZINBRYTA REMS Program
- c. Biogen must:
- i. Ensure that pharmacies that dispense ZINBRYTA are specially certified, in accordance with the requirements described above
 - ii. Provide all the following mechanisms for pharmacies to complete certification for the ZINBRYTA REMS Program: fax and mail
 - iii. Ensure that pharmacies are notified when they have been certified by the ZINBRYTA REMS Program
 - iv. Ensure that certified pharmacies are provided access to the database of certified prescribers and enrolled and authorized patients
 - v. Verify every year that the authorized representative's name and contact information correspond to those of the current designated authorized representative for the certified pharmacy. If different, the pharmacy must be required to recertify with a new authorized representative
 - vi. Maintain a database of enrolled patients and their current authorization status. Authorization to dispense requires that Biogen receives a *ZINBRYTA REMS Program Patient Status Form* within 115 calendar days (See Section 4bii.) for each patient. If not received, the patient will not be authorized for further dispensing until a *ZINBRYTA REMS Program Patient Status Form* is received.

The following materials are part of the REMS and are appended:

- [ZINBRYTA REMS Program Pharmacy Enrollment Form](#)
- [ZINBRYTA REMS Program Overview](#)
- [ZINBRYTA REMS Program Website](http://www.zinbrytarems.com) (www.zinbrytarems.com)

3. ZINBRYTA must be dispensed to patients with evidence or other documentation of safe-use conditions.
 - a. To become enrolled in the ZINBRYTA REMS Program, a patient/caregiver must sign a *ZINBRYTA REMS Program Patient Enrollment Form* indicating that he/she has:
 - i. Received and has read the *ZINBRYTA REMS Program Patient Guide*
 - ii. Received counselling from the prescriber regarding
 - a. the risks of severe and fatal hepatic injury and serious immune-mediated disorders;
 - b. required baseline and monthly monitoring
 - iii. Received the *ZINBRYTA REMS Program Patient Wallet Card*

- b. To authorize a patient to receive ZINBRYTA under the ZINBRYTA REMS Program, a certified prescriber must complete and submit via online, fax, or mail to the REMS Program a *ZINBRYTA REMS Program Patient Status Form* every 90 calendar days during treatment and every 90 calendar days for 6 months after discontinuation of the drug

c. Biogen must:

- i. Provide all the following mechanisms for the certified prescriber to be able to submit the completed *ZINBRYTA REMS Program Patient Enrollment Form* and *ZINBRYTA REMS Program Patient Status Form* to the ZINBRYTA REMS Program: online, fax, and mail
- ii. Ensure that the certified pharmacies verify the required authorization for each patient prior to dispensing

The following materials are part of the REMS and are appended:

- [*ZINBRYTA REMS Program Patient Enrollment Form*](#)
- [*ZINBRYTA REMS Program Patient Guide*](#)
- [*ZINBRYTA REMS Program Patient Wallet Card*](#)
- [*ZINBRYTA REMS Program Patient Status Form*](#)

4. Each patient using ZINBRYTA is subject to certain monitoring.

a. The prescriber must:

- i. Perform the baseline and monthly monitoring for each patient as described in the Prescribing Information, and
- ii. Submit via online, fax, or mail a *ZINBRYTA REMS Program Patient Status Form* to the REMS Program indicating completion of each patient's monthly monitoring every 90 calendar days during treatment and every 90 calendar days for 6 months after discontinuation of the drug

b. Biogen must:

- i. Ensure that the *ZINBRYTA REMS Program Patient Status Form* is received every 90 calendar days after the first dispensation of the drug and every 90 calendar days for 6 months after discontinuation
- ii. Ensure that if the *ZINBRYTA REMS Program Patient Status Form* is not received for each patient within 95 calendar days, Biogen will attempt to contact the prescriber to receive the form. If the form has not been received within 115 calendar days then the patient will not be authorized for further dispensing until the form is received. If a form has not been received at 145 calendar days Biogen must begin de-enrollment procedures for the patient
- iii. Ensure that the *ZINBRYTA REMS Program Patient Status Form* is available to certified prescribers for patient monitoring

The following materials are part of the REMS and are appended:

- [*ZINBRYTA REMS Program Patient Status Form*](#)

5. Each patient using ZINBRYTA is enrolled in a registry.
 - a. Biogen must maintain a ZINBRYTA REMS Program Registry. The primary objectives of the registry are to ensure that only enrolled and authorized patients receive ZINBRYTA and to provide information on the incidence of severe and fatal hepatic injury and serious immune-mediated events
 - b. Biogen must ensure that certified prescribers enroll all patients in the ZINBRYTA REMS Program Registry using the *ZINBRYTA REMS Program Patient Enrollment Form*
 - c. Biogen must provide all the following mechanisms for prescribers to complete patient enrollment: online, fax, and mail
 - d. Biogen must ensure that once a report for an adverse event that is required to be reported to the REMS is received, Biogen follows up with the healthcare provider to procure all necessary information to complete the report, and captures all required data for the registry

The following materials are part of the REMS and are appended:

- *ZINBRYTA REMS Program Patient Enrollment Form*

C. Implementation System

1. Biogen must ensure that ZINBRYTA is only distributed to certified pharmacies by:
 - a. Ensuring that wholesalers/distributors who distribute ZINBRYTA comply with the program requirements for wholesalers/distributors. The wholesalers/distributor must:
 - i. Put processes and procedures in place to verify, prior to distributing ZINBRYTA, that the pharmacies are certified
 - ii. Train all relevant staff on the ZINBRYTA REMS Program requirements
 - iii. Comply with audits by Biogen, FDA, or a third party acting on behalf of Biogen or FDA to ensure that all procedures are in place and are being followed for the ZINBRYTA REMS Program. In addition, wholesalers/distributors must maintain appropriate documentation and make it available for audits
 - iv. Provide distribution data to the ZINBRYTA REMS Program to verify compliance with the REMS
 - b. Ensuring that wholesalers/distributors maintain distribution records of all shipments of ZINBRYTA and provide the data to the ZINBRYTA REMS Program
2. Biogen must monitor distribution data to ensure all the processes and procedures are in place and functioning to support the requirements of the ZINBRYTA REMS Program
3. Biogen must audit the wholesalers/distributors within 180 calendar days after the wholesaler/distributor receives the first shipment of ZINBRYTA to ensure that all processes and procedures are in place and functioning to support the requirements of the ZINBRYTA REMS Program. Corrective action must be instituted by Biogen if noncompliance is identified.

4. Biogen must maintain a validated, secure database of pharmacies that are certified to dispense ZINBRYTA in the ZINBRYTA REMS Program
5. Biogen must maintain records of ZINBRYTA distribution and dispensing, certified prescribers, certified pharmacies, wholesalers/distributors, and enrolled patients, to meet REMS requirements
6. Biogen must maintain a ZINBRYTA REMS Program Call Center (800-456-2255) and ZINBRYTA REMS Program Website (www.zinbrytarems.com). The REMS Program Website must include the capability to complete prescriber certification/enrollment online, enroll and manage patients online, and the option to print the Prescribing Information, Medication Guide, and ZINBRYTA REMS materials. The ZINBRYTA product website must include a prominent REMS-specific link to the ZINBRYTA REMS Program Website.
7. Biogen must ensure that the ZINBRYTA REMS Program Website is fully operational; and the REMS materials listed in or appended to the ZINBRYTA REMS document are available through the ZINBRYTA REMS Program Website and by calling the ZINBRYTA REMS Program Call Center.
8. Biogen must monitor on an ongoing basis the certified pharmacies to ensure the requirements of the ZINBRYTA REMS Program are being met. Biogen must institute corrective action if noncompliance is identified and decertify pharmacies that do not maintain compliance with the REMS requirements.
9. Biogen must maintain an ongoing annual audit plan that involves wholesaler/distributors and certified pharmacies.
10. Biogen must audit 25% of the certified pharmacies within 90 calendar days after the pharmacy receives its first order of ZINBRYTA to ensure that all processes and procedures are in place and functioning to support the requirements of the ZINBRYTA REMS Program. The certified pharmacies must be included in Biogen's ongoing annual audit plan. Biogen must institute corrective action if noncompliance is identified.
11. Biogen must send monthly reminders to patients while receiving ZINBRYTA treatment and up to 6 months after discontinuing, reminding them of the requirement for ongoing monitoring
12. Biogen must take reasonable steps to improve implementation of, and compliance with, the requirements in the ZINBRYTA REMS Program based on monitoring and evaluation of the ZINBRYTA REMS Program

III. Timetable for Submission of Assessments

Biogen must submit REMS assessments to the FDA at 6 months, 1 year, and annually thereafter from the date of the initial approval of the REMS (May 27, 2016). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Biogen must submit each assessment so that it will be received by the FDA on or before the due date.

May 2018**ZINBRYTA REMS Program Letter for Healthcare Providers****Subject: Risk of severe and fatal liver injury, including autoimmune hepatitis and liver failure, and other immune-mediated disorders with ZINBRYTA (daclizumab)**

Dear Healthcare Provider:

The purpose of this letter is to inform you about serious risks associated with ZINBRYTA (daclizumab) injection and the need for monitoring for these risks. ZINBRYTA is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of ZINBRYTA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of ZINBRYTA outweigh the serious risks. ZINBRYTA is available only through the ZINBRYTA REMS Program, a restricted distribution program. Only prescribers, pharmacies, and patients enrolled in the Program are able to prescribe, dispense, and receive ZINBRYTA.

Serious Risks of ZINBRYTA**Hepatic Injury Including Autoimmune Hepatitis**

ZINBRYTA can cause severe liver injury, including autoimmune hepatitis and liver failure. Fatal cases have occurred. Liver injury, including autoimmune hepatitis and acute liver failure, can occur at any time during treatment with ZINBRYTA, with cases reported up to 5 months after the last dose of ZINBRYTA.

ZINBRYTA is contraindicated in patients with pre-existing hepatic disease or hepatic impairment.

Other Immune-Mediated Disorders

In addition to autoimmune hepatitis, a variety of immune-mediated disorders including skin reactions, lymphadenopathy, and immune-mediated colitis, and other serious conditions can occur in patients treated with ZINBRYTA. Overall, serious immune-mediated disorders were observed in 5% of patients treated with ZINBRYTA.

If a patient develops a serious immune-mediated disorder, consider stopping ZINBRYTA and refer the patient to a specialist to ensure comprehensive diagnostic evaluation and appropriate treatment.

Some patients required systemic corticosteroids or other immunosuppressant treatment for autoimmune hepatitis or other immune-mediated disorders and continued this treatment after the last dose of ZINBRYTA.

ZINBRYTA Healthcare Provider Training

It is important that healthcare providers understand the serious risks associated with ZINBRYTA. As part of the REMS, healthcare providers must be trained and specially certified to prescribe ZINBRYTA.

ZINBRYTA REMS Program training materials for healthcare providers may be obtained at www.zinbrytarems.com or by calling 1-800-456-2255.

Reporting Adverse Events

Healthcare providers and patients are encouraged to report adverse events in patients taking ZINBRYTA to Biogen at 1-800-456-2255. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

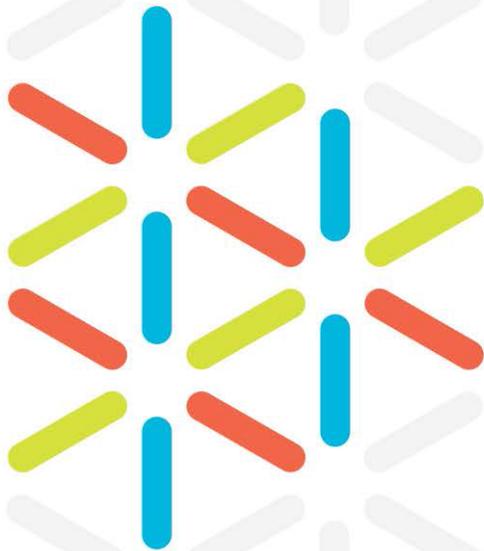
Healthcare providers should report any adverse events suggestive of hepatic injury and immune-mediated disorders with the use of ZINBRYTA to Biogen at 1-800-456-2255.

All REMS information/materials may be accessed at www.zinbrytarems.com or by calling 1-800-456-2255.

Please see the enclosed Prescribing Information for ZINBRYTA.

Sincerely,

Alfred Sandrock
EVP, Chief Medical Officer
Biogen



ZINBRYTA REMS (Risk Evaluation and Mitigation Strategy) Program Overview

This overview describes the requirements of the ZINBRYTA REMS Program and the responsibilities of prescribers, pharmacies and patients.

If you have any questions regarding the ZINBRYTA REMS Program, please visit www.zinbrytarems.com or call: 1-800-456-2255.

Please see Prescribing Information, including BOXED WARNING, for additional Important Safety Information.

Reference ID: 4175674

 **Zinbryta**[®]
(daclizumab)
150 mg Subcutaneous Injection



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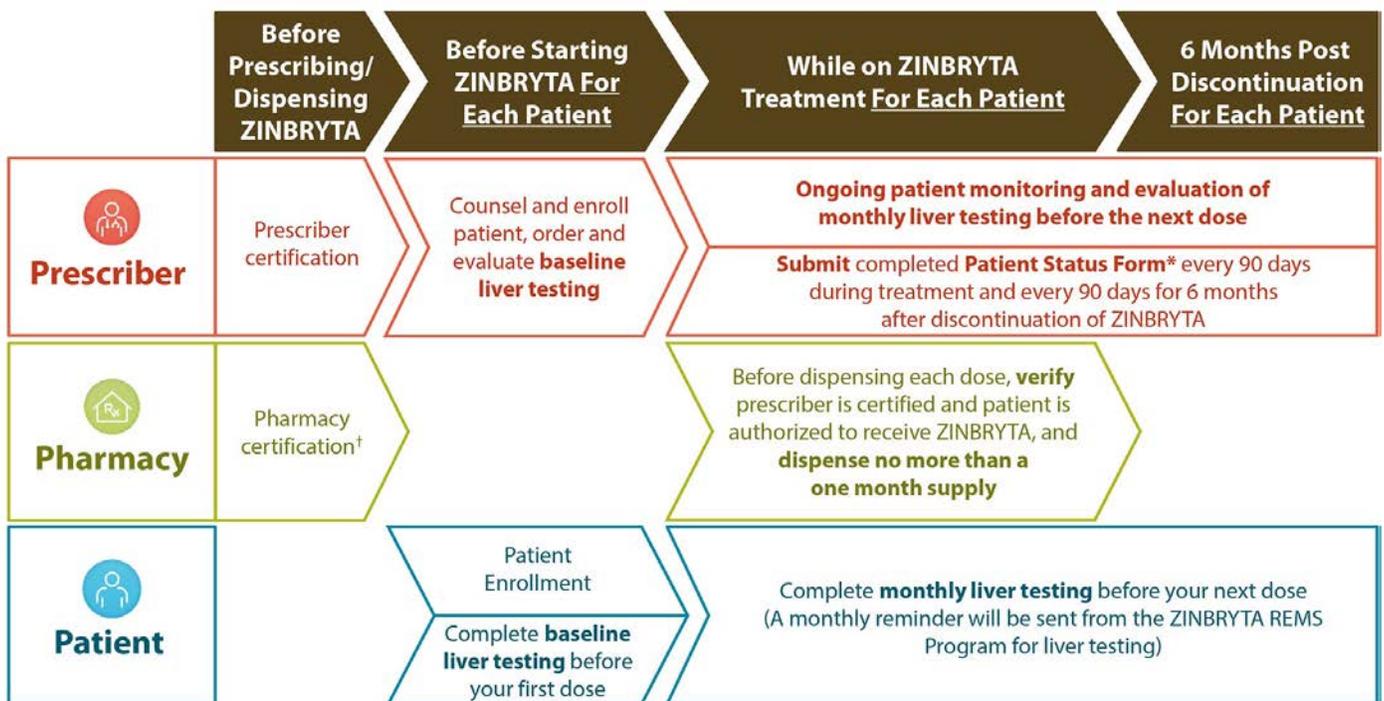
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What is the ZINBRYTA REMS Program?

- A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug continue to outweigh its risks.
- Due to the risks of severe and fatal liver injury, including autoimmune hepatitis and liver failure, and other immune-mediated disorders such as skin reactions, lymphadenopathy, immune-mediated colitis, and other serious conditions, ZINBRYTA is available only through a restricted program called the ZINBRYTA REMS Program.

How Does the ZINBRYTA REMS Program Work?



* Every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA, the ZINBRYTA REMS Program will send an individualized Patient Status Form to the certified prescriber for completion.

[†] Recertify if there is a change in authorized representative.



What are the Requirements of the ZINBRYTA REMS Program?

- In order to receive ZINBRYTA, prescribers, patients, and pharmacies must comply with the requirements of the ZINBRYTA REMS Program.

Prescribers



To prescribe ZINBRYTA:

- Become certified** by completing a one-time certification process
- As you start patients on ZINBRYTA, **counsel and enroll** them into the ZINBRYTA REMS Program, complete the prescription, and order and evaluate baseline liver testing
- Perform** ongoing patient monitoring, evaluate **monthly liver testing** prior to each patient's next dose, and complete the ZINBRYTA REMS Program Patient Status Forms for each patient every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA

Pharmacies



To dispense ZINBRYTA*:

- Designate an authorized representative, become certified, and recertify** if there is a change in the authorized representative
- Train** staff and **comply** with REMS requirements
- Before dispensing each dose, **verify** prescriber is certified and patient is authorized to receive ZINBRYTA, and **dispense no more than a one month supply**

Patients



To receive ZINBRYTA:

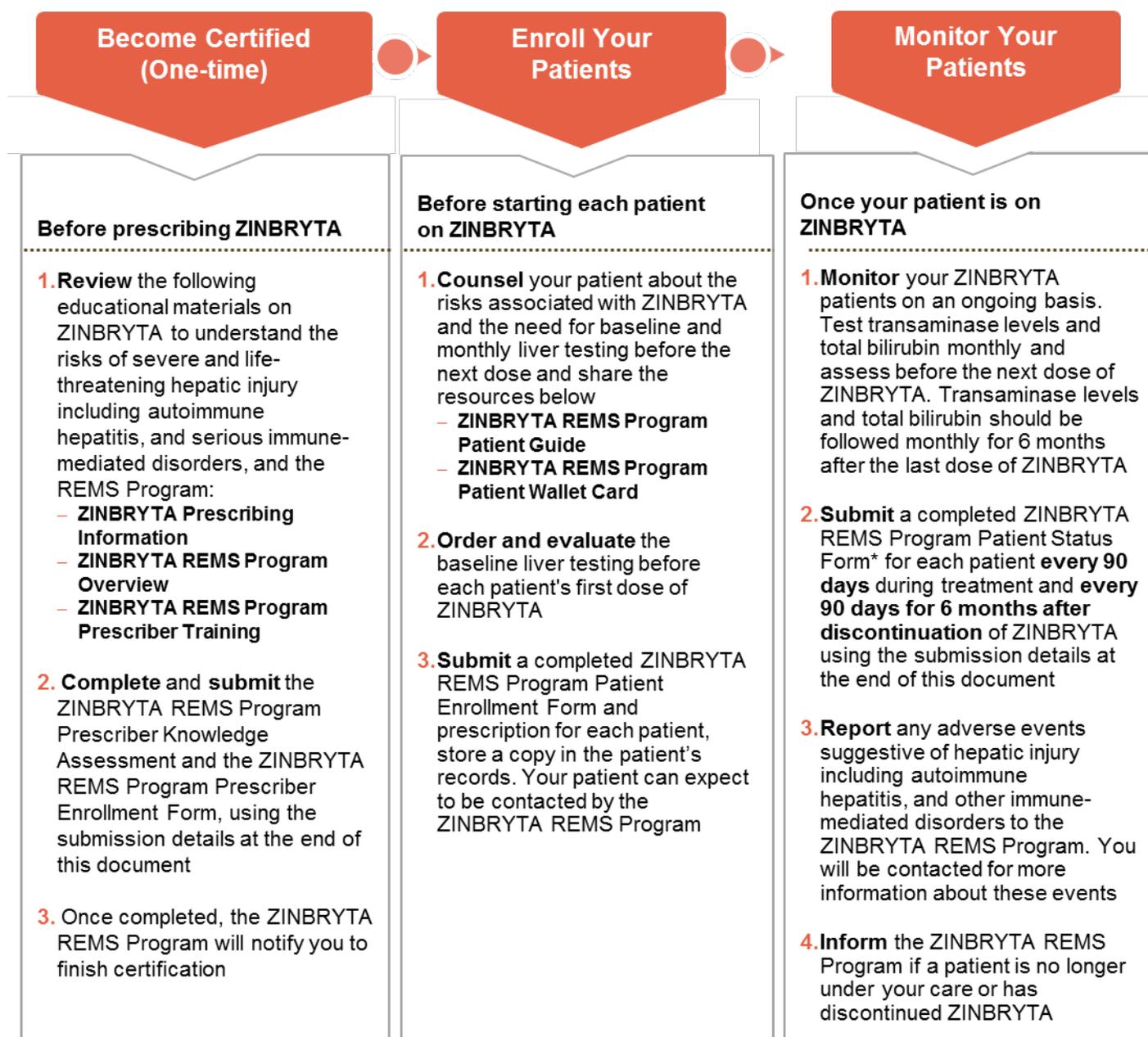
- Understand the risks** associated with ZINBRYTA
- Enroll** in the ZINBRYTA REMS Program by completing the ZINBRYTA REMS Program Patient Enrollment Form with your doctor
- Complete** baseline liver testing before your first dose and monthly liver testing before your next dose of ZINBRYTA. A monthly reminder will be sent from the ZINBRYTA REMS Program for liver testing

* ZINBRYTA is not available to all pharmacies. If you have any questions about the ZINBRYTA REMS Program or how to obtain ZINBRYTA, call 1-800-456-2255.

Prescribers and pharmacies must report any adverse events suggestive of hepatic injury and immune-mediated disorders to the ZINBRYTA REMS Program.



Prescriber Requirements



* Every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA, the ZINBRYTA REMS Program will send an individualized Patient Status Form to the certified prescriber for completion.

The completed forms should be submitted to the ZINBRYTA REMS Program online, using the ZINBRYTA Program Portal at www.zinbrytarems.com, via fax to 1-855-474-3067, or by mail to 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709.



Pharmacy Requirements

Become Certified

Before dispensing ZINBRYTA

1. **Designate** an authorized representative for the pharmacy. He or she will need to review the ZINBRYTA REMS Program Overview and will oversee implementation and ensure compliance with the ZINBRYTA REMS Program requirements
2. **Have the authorized representative complete and submit** the ZINBRYTA REMS Pharmacy Enrollment Form using the submission details at the end of this document
 - Once this step is completed, the ZINBRYTA REMS Program will contact you to complete certification
3. **Have the authorized representative ensure** that all relevant staff involved in the dispensing of ZINBRYTA are trained on the ZINBRYTA REMS Program requirements and that a record of training is maintained by the pharmacy

Ensure Compliance With REMS Requirements

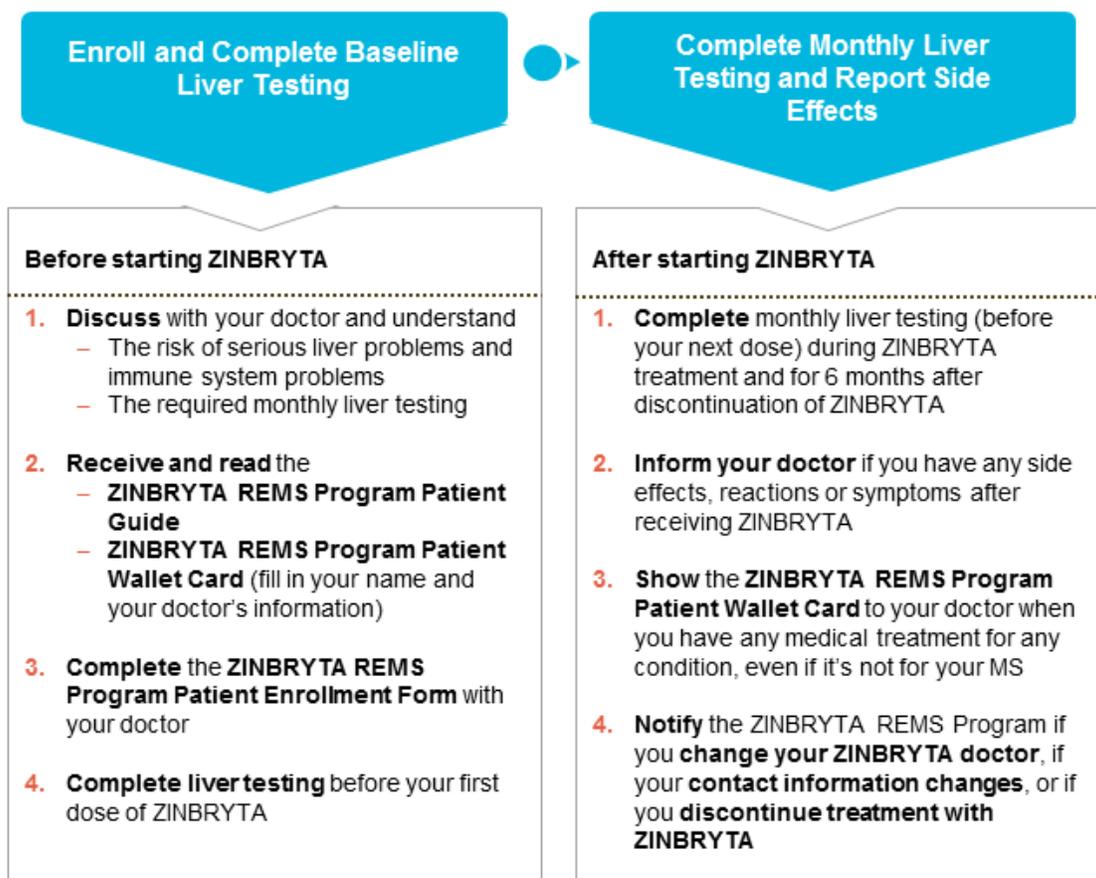
When dispensing ZINBRYTA

1. Before dispensing each dose, **verify** that the prescriber is certified and the patient is authorized to receive ZINBRYTA by calling the ZINBRYTA REMS Program. **Do not dispense more than a one month supply per patient**
2. **Report** any adverse events suggestive of hepatic injury including autoimmune hepatitis, and other immune-mediated disorders to the ZINBRYTA REMS Program. You may be contacted for more information about these events
3. **Maintain** appropriate documentation that all processes and procedures are in place and are being followed so that it can be provided upon request to Biogen, the FDA, or a third party acting on behalf of Biogen or the FDA
4. **Recertify** in the ZINBRYTA REMS Program if a new authorized representative is designated by completing and submitting the ZINBRYTA REMS Pharmacy Enrollment Form

ZINBRYTA is not available to all pharmacies. If you have questions about the ZINBRYTA REMS Program or how to obtain ZINBRYTA, call 1-800-456-2255.

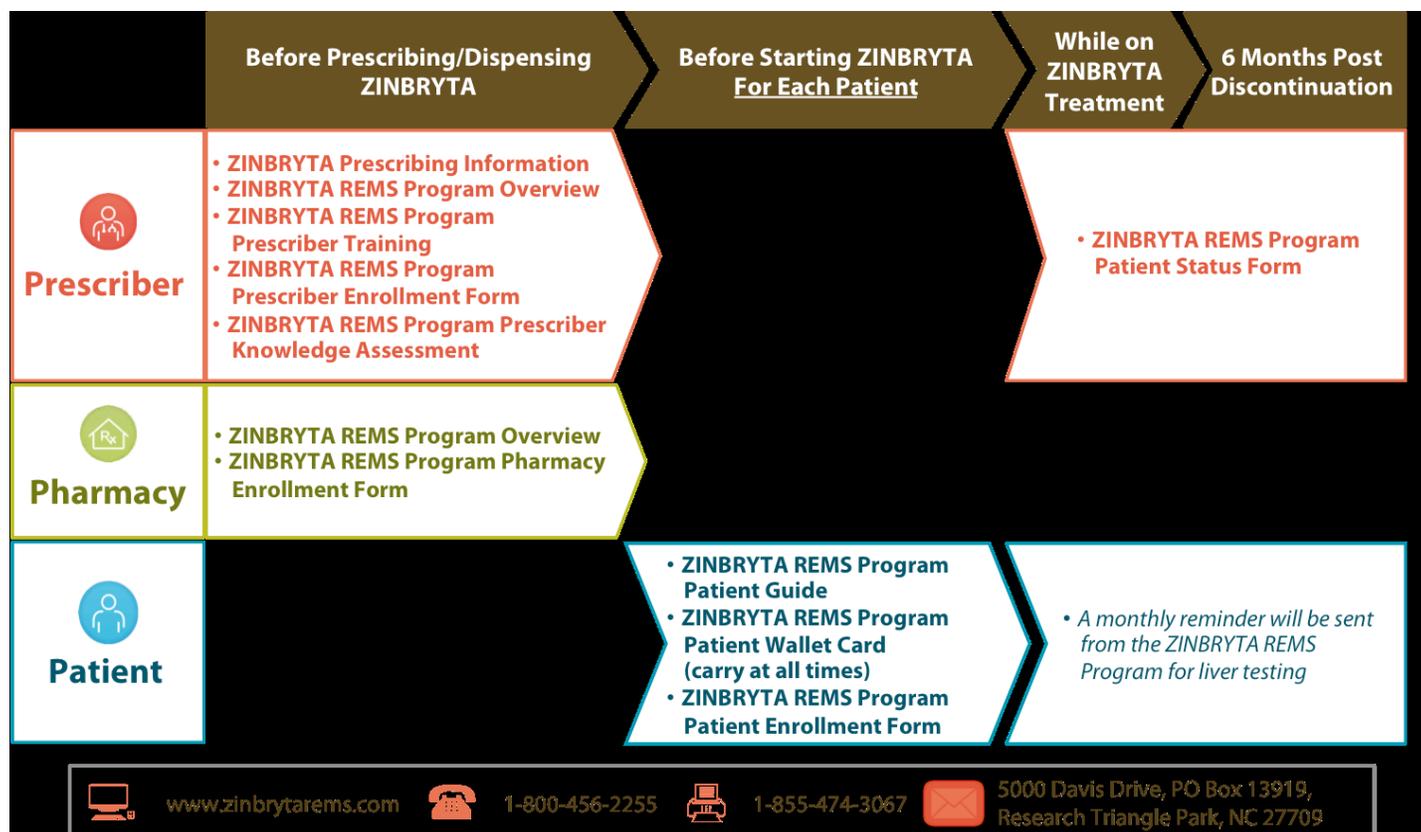


Patient Requirements





ZINBRYTA REMS Program Resources



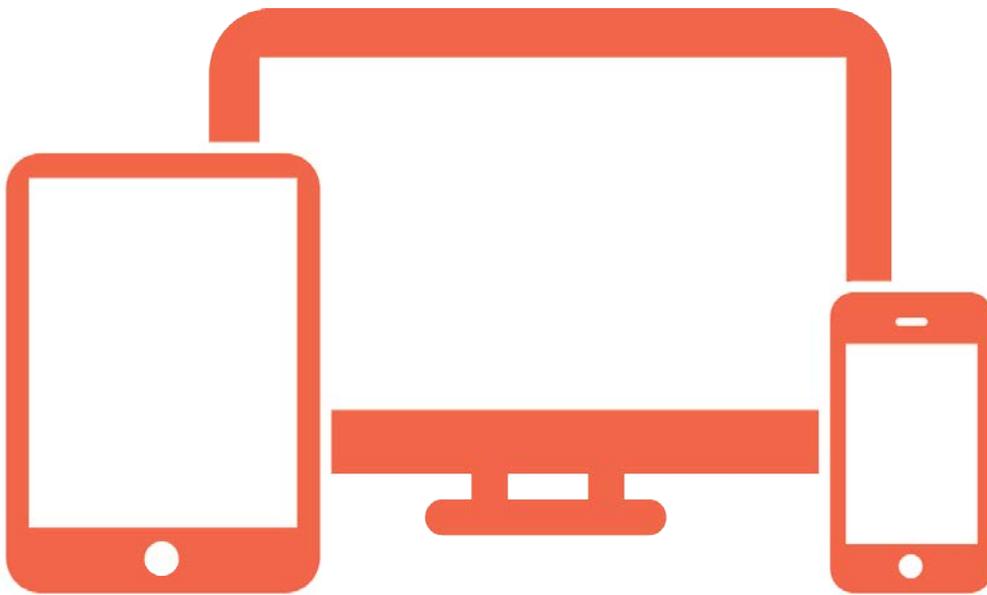
ZINBRYTA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of ZINBRYTA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

Please see Prescribing Information, including BOXED WARNING, for additional Important Safety Information.



ZINBRYTA Program Portal Overview

- ZINBRYTA Program Portal is a web-based tool designed to:
 - Provide real-time access to ZINBRYTA patient data
 - Maintain compliance with the ZINBRYTA REMS Program
 - Streamline communication to/from prescribers
- ZINBRYTA Program Portal is now available for prescribers to instantly enroll, train, certify, and manage their patients online
- ZINBRYTA Program Portal is accessed with secure user name and password





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 **Zinbryta**[®]
(daclizumab)
150 mg Subcutaneous Injection

If you have any questions regarding the ZINBRYTA REMS Program, please visit www.zinbrytarems.com or call: **1-800-456-2255**.

Online: www.zinbrytarems.com

Fax: **1-855-474-3067**

Mail: **5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709**



abbvie

 **Zinbryta[®]**
(daclizumab)
150 mg Subcutaneous Injection



ZINBRYTA REMS (Risk Evaluation and Mitigation Strategy) Program Prescriber Training

This training includes information about:

- Risks of severe and fatal hepatic injury and serious immune-mediated disorders associated with ZINBRYTA
- Requirements for monthly monitoring and evaluation of your patient
- The ZINBRYTA REMS Program requirements



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The review of this document is necessary to successfully pass the ZINBRYTA REMS Program Prescriber Knowledge Assessment in order to prescribe ZINBRYTA





What Is ZINBRYTA?

- ZINBRYTA is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of ZINBRYTA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.
- Please see Prescribing Information, including BOXED WARNING, for additional Important Safety Information.



Risks Associated With ZINBRYTA: *Hepatic Injury*

- **ZINBRYTA can cause severe liver injury, including autoimmune hepatitis and liver failure. Fatal cases have occurred.**
 - Elevations of serum transaminases and severe hepatic injury have occurred in patients treated with ZINBRYTA. Liver injury, including autoimmune hepatitis and acute liver failure, can occur at any time during treatment with ZINBRYTA, with cases reported up to 5 months after the last dose of ZINBRYTA.
 - In controlled studies, an increased incidence of elevations of alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >5 times the upper limit of normal (ULN) was reported in ZINBRYTA-treated patients compared with placebo-treated patients (4% vs 1%) and compared with AVONEX-treated patients (6% vs 3%).
 - Across all clinical studies (controlled and open-label), serious drug-related hepatic injury occurred in 1.7% of ZINBRYTA-treated patients.
 - In a clinical trial, a case of fatal autoimmune hepatitis with acute liver failure occurred in a patient reinitiating treatment with ZINBRYTA after a planned 6-month treatment interruption period.
 - A case of acute liver failure occurred in a patient receiving ZINBRYTA in the postmarketing setting after 4 doses of ZINBRYTA, resulting in transplant and death. The patient was also receiving concomitant treatment with another drug known to be associated with hepatic injury.
 - In the active-controlled study, the incidence of drug discontinuation due to hepatic disorders was 5% in ZINBRYTA-treated patients and 4% in AVONEX-treated patients.



Risks Associated With ZINBRYTA: *Immune-Mediated Disorders*

- **Immune-mediated disorders including skin reactions, lymphadenopathy, and immune-mediated colitis can occur in patients treated with ZINBRYTA. Overall, serious immune-mediated disorders were observed in 5% of patients treated with ZINBRYTA.**
 - Treatment with ZINBRYTA can increase the risk of immune-mediated disorders, including autoimmune disorders such as autoimmune hepatitis.
 - Immune-mediated disorders including skin reactions, lymphadenopathy, autoimmune hemolytic anemia, and immune-mediated colitis occurred in patients treated with ZINBRYTA.
 - Additionally, a wide variety of other immune-mediated disorders, some serious, have occurred with the use of ZINBRYTA. These include single organ or systemic multi-organ inflammatory reactions.
 - Overall in clinical trials, immune-mediated disorders occurred in 28% of patients on ZINBRYTA, the most common of which were skin reactions and lymphadenopathy.
 - In the active controlled study, immune-mediated disorders were observed in 32% of ZINBRYTA-treated patients compared with 12% for AVONEX-treated patients.
 - Serious immune-mediated disorders were observed in 4% of patients treated with ZINBRYTA compared with less than 1% for AVONEX-treated patients.
- **Some patients required systemic corticosteroids or other immunosuppressant treatment for autoimmune hepatitis or other immune-mediated disorders and continued this treatment after the last dose of ZINBRYTA.**



Risks Associated With ZINBRYTA: *Immune-Mediated Disorders*

1. Skin Reactions

- In clinical trials, skin reactions occurred in 18% of ZINBRYTA-treated patients compared to 13% of patients on placebo, and in 37% of ZINBRYTA-treated patients compared to 19% of AVONEX-treated patients.
- Skin reactions occurred at any time during treatment with ZINBRYTA.
- The most common skin reactions were dermatitis and eczema.
- Serious skin reactions occurred in 2% of subjects treated with ZINBRYTA and 0.1% of patients on AVONEX. One death resulted from infectious complications following a serious cutaneous reaction. In patients with a history of skin conditions, including eczema or psoriasis, use of ZINBRYTA may exacerbate those conditions.
- In addition to serious cases of dermatitis, eczema, psoriasis and drug eruptions, cases of erythema multiforme, erythema nodosum, exfoliative rash, and oral ulcers occurred in ZINBRYTA clinical trials.
- Treatment of skin reactions included treatment with topical or systemic corticosteroids, or immunosuppressant drugs, including tacrolimus.
- In clinical trials, discontinuation because of skin reactions was 4% in ZINBRYTA-treated patients. Rashes took a mean of 3 months to resolve, some were unresolved at the time of the last evaluation.



Risks Associated With ZINBRYTA: *Immune-Mediated Disorders*

2. Lymphadenopathy

- In clinical trials, ZINBRYTA increased the incidence of lymphadenopathy, with onset occurring throughout the treatment period. In a controlled trial, 6% of ZINBRYTA-treated patients compared to 1% of AVONEX-treated patients developed lymphadenopathy or lymphadenitis.
- Serious events related to lymphadenopathy or lymphadenitis included infections, benign salivary neoplasm, skin reactions, thrombocytopenia, and interstitial lung changes.

3. Autoimmune Hemolytic Anemia

- Across all clinical studies (controlled and open-label), autoimmune hemolytic anemia occurred in <1% of patients treated with ZINBRYTA.
- Autoimmune hemolytic anemia resolved with discontinuation of ZINBRYTA, corticosteroid or other immunosuppressant treatment, and blood transfusions in most cases.
- If a patient develops signs or symptoms of autoimmune hemolytic anemia (eg, pallor, fatigue, dark urine, jaundice, shortness of breath), consider discontinuing ZINBRYTA and referring to an appropriate specialist for further evaluation and treatment.



Risks Associated With ZINBRYTA: *Immune-Mediated Disorders*

4. Immune-Mediated Colitis

- An increased incidence of serious colitis (less than 1%) was reported in patients treated with ZINBRYTA compared with placebo and AVONEX in clinical trials.
- Cases have included reports of colitis, ulcerative colitis, Crohn's disease, microscopic colitis, inflammatory bowel disease, proctitis, and proctocolitis.
- Consider discontinuing ZINBRYTA and referring patients who develop symptoms of colitis (eg, abdominal pain, fever, prolonged diarrhea, bloody stools) to a specialist.

5. Other Immune-Mediated Disorders

- A wide variety of other immune-mediated disorders, some serious, have occurred with the use of ZINBRYTA. These include single organ or systemic multi-organ inflammatory reactions.
- Some required treatment with systemic corticosteroids or other immunosuppressants. Some required several months for resolution after the last dose of ZINBRYTA, and some had not resolved even several months after discontinuation of ZINBRYTA, at the time of last reported follow-up.



Additional Risks and Safety Information

- The information presented in this training program does not include a complete list of all safety information for ZINBRYTA.
- To review the complete safety information on ZINBRYTA, please refer to the Prescribing Information, including BOXED WARNING, for ZINBRYTA at www.zinbrytarems.com.



Clinical Considerations and Assessment



Assessment Prior to Initiating ZINBRYTA

Baseline Tests Required

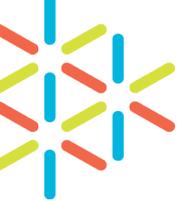
- Early identification of elevated liver enzymes may decrease the risk of a serious outcome. Prior to starting ZINBRYTA, obtain and evaluate serum transaminases (ALT and AST) and total bilirubin levels.

Contraindications

ZINBRYTA is contraindicated for patients with:

- Pre-existing hepatic disease or hepatic impairment, including ALT or AST at least 2 times the ULN, because ZINBRYTA could exacerbate existing liver dysfunction.
- A history of autoimmune hepatitis or other autoimmune condition involving the liver.
- A history of hypersensitivity to daclizumab or any other components of the formulation. Use in such patients may result in anaphylaxis or life-threatening multi-organ hypersensitivity.

ULN=upper limit of normal.



Upon Initiation of ZINBRYTA: *Monitoring for Hepatic Injury*

Ongoing Tests Required

- Testing of serum transaminase (ALT and AST) levels and total bilirubin should be done monthly and assessed before the next dose of ZINBRYTA. Transaminase levels and total bilirubin should be followed monthly for 6 months after the last dose of ZINBRYTA.
- In case of elevation in transaminases or total bilirubin, treatment interruption or discontinuation may be required.

Evaluating Monthly Lab Tests

Lab values

ALT or AST >5x ULN
OR
Total bilirubin >2x ULN
OR
ALT or AST ≥ 3 but <5x ULN and total bilirubin >1.5 but <2x ULN

Recommendations

Interrupt ZINBRYTA therapy and investigate for other etiologies of abnormal lab values

If no other etiologies are identified, then discontinue ZINBRYTA

If other etiologies are identified, re-assess the overall risk-benefit profile of ZINBRYTA in the patient and consider whether to resume ZINBRYTA when both AST or ALT are <2x ULN and total bilirubin is \leq ULN*

Monitoring and Evaluation

- Liver failure can occur at any time during treatment with ZINBRYTA even with monthly liver enzyme monitoring indicating normal values prior to each dose. Liver injury has been reported up to 5 months after the last dose of ZINBRYTA.
- Monitor patients for signs and symptoms of hepatic injury. If a patient develops clinical signs or symptoms suggestive of hepatic dysfunction (eg, unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine), promptly measure serum transaminases and total bilirubin and interrupt or discontinue treatment with ZINBRYTA, as appropriate.
- In patients with prolonged elevations of serum transaminases, evaluate for other possible causes, such as infection, and a specialist should evaluate the patient.
- Discontinue ZINBRYTA if autoimmune hepatitis is suspected. Treatment of autoimmune hepatitis with systemic corticosteroids and other immunosuppressant drugs may be required. Some patients may need long-term immunosuppression.

* In clinical trials, permanent discontinuation of therapy was required if the patient had liver test abnormalities resulting in suspension of study treatment for at least 8 consecutive weeks.

ULN=upper limit of normal.



Upon Initiation of ZINBRYTA: *Monitoring for Immune-Mediated Disorders*

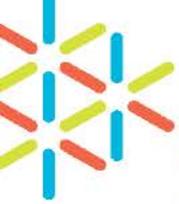
Monitoring and Evaluation

- For suspected immune-mediated disorders, ensure adequate evaluation to confirm etiology or to exclude other causes.
- Monitor for signs and symptoms such as fever, a serious diffuse or inflammatory rash, lymphadenopathy, signs or symptoms of autoimmune hemolytic anemia (eg, pallor, fatigue, dark urine, jaundice, shortness of breath), symptoms of colitis (eg, abdominal pain, fever, prolonged diarrhea, bloody stools) and other organ-specific symptoms.
- Some patients required invasive procedures for diagnosis (eg, colonoscopy, liver biopsy, kidney biopsy, lung biopsy), hospitalization for fluid replacement or blood transfusion, or prolonged treatment with systemic corticosteroids or immunosuppressant drugs. Some of these events did not resolve after stopping ZINBRYTA during study follow-up.
- If a patient develops a serious immune-mediated disorder consider stopping ZINBRYTA and refer the patient to a specialist to ensure comprehensive diagnostic evaluation and appropriate treatment.



Introduction to the ZINBRYTA REMS Program



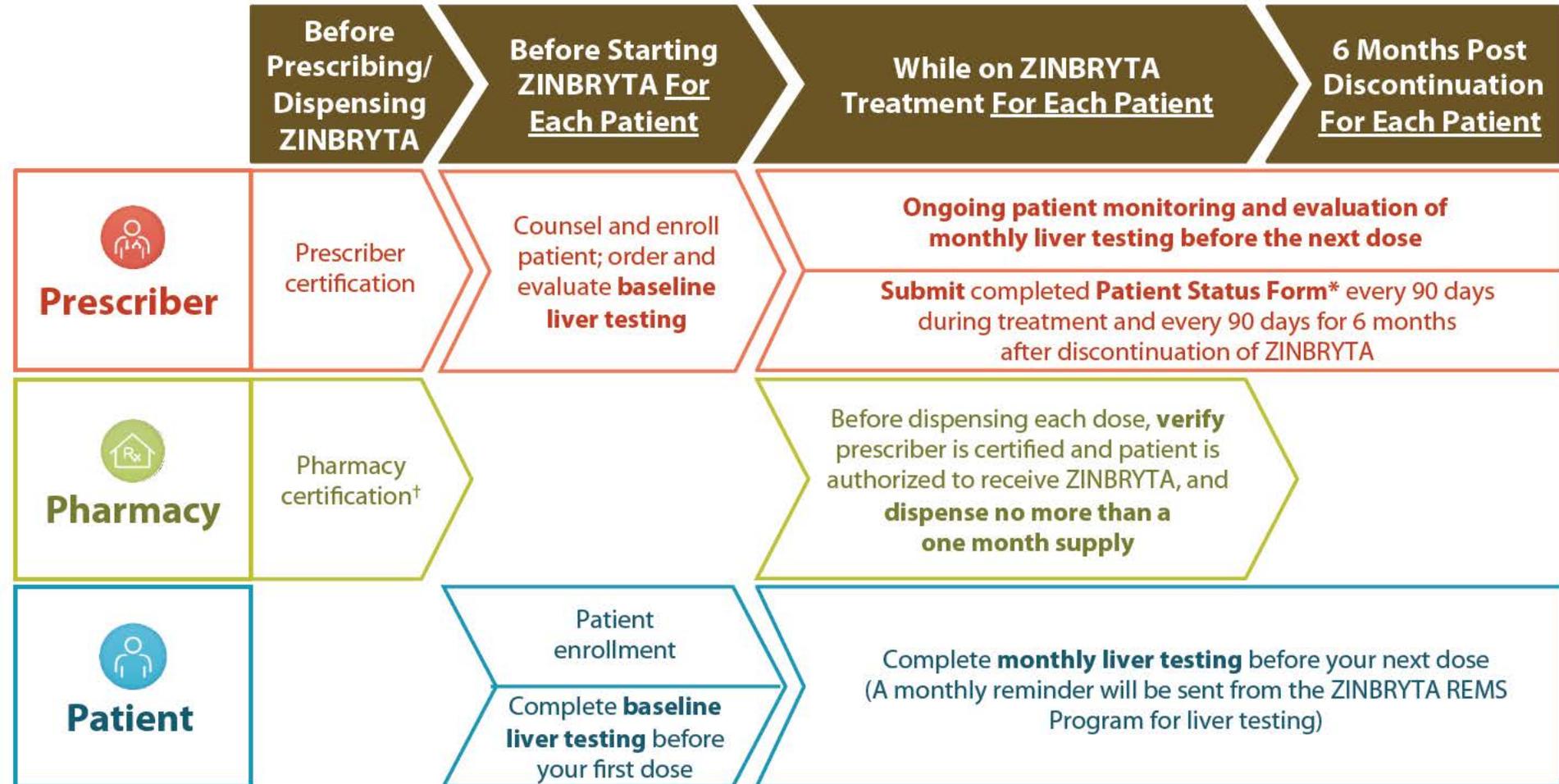


What Is the ZINBRYTA REMS Program?

- A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug continue to outweigh its risks.
- **Due to the risks of severe and fatal liver injury, including autoimmune hepatitis and liver failure, and other immune-mediated disorders such as skin reactions, lymphadenopathy, immune-mediated colitis, and other serious conditions, ZINBRYTA is available only through a restricted program called the ZINBRYTA REMS Program.**



How Does the ZINBRYTA REMS Program Work?



* Every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA, the ZINBRYTA REMS Program will send an individualized Patient Status Form to the certified prescriber for completion.

† Recertify if there is a change in authorized representative.

 **Zinbryta**[®]
(daclizumab)
150 mg Subcutaneous Injection



Requirements and Roles of Prescribers, Pharmacies, and Patients





What Are the Requirements of the ZINBRYTA REMS Program?

Prescribers



To prescribe ZINBRYTA:

1. **Become certified** by completing a one-time certification process
2. As you start patients on ZINBRYTA, **counsel and enroll** them into the ZINBRYTA REMS Program, complete the prescription, and order and evaluate baseline liver testing
3. **Perform** ongoing patient monitoring, evaluate **monthly liver testing** prior to each patient's next dose, and complete the ZINBRYTA REMS Program Patient Status Forms for each patient every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA

Pharmacies



To dispense ZINBRYTA:

1. **Designate an authorized representative, become certified,** and **recertify** if there is a change in the authorized representative
2. **Train** staff and **comply** with REMS requirements
3. Before dispensing each dose, **verify** prescriber is certified and patient is authorized to receive ZINBRYTA, and **dispense no more than a one month supply**

Patients



To receive ZINBRYTA:

1. **Understand the risks** associated with ZINBRYTA
2. **Enroll** in the ZINBRYTA REMS Program by completing the ZINBRYTA REMS Program Patient Enrollment Form with your doctor
3. **Complete** baseline liver testing before your first dose and monthly liver testing before your next dose of ZINBRYTA. A monthly reminder will be sent from the ZINBRYTA REMS Program for liver testing

- Prescribers and Pharmacies must report any adverse events suggestive of severe hepatic injury and serious immune-mediated disorders to the ZINBRYTA REMS Program



How Do I Communicate With the ZINBRYTA REMS Program?

Online



ZINBRYTA Program Portal
www.zinbrytarems.com

Phone



1-800-456-2255
Monday-Friday

Paper



Fax: 1-855-474-3067



How Does a Prescriber Become Certified in the Program?



Before prescribing ZINBRYTA

- Review** the following educational materials on ZINBRYTA to understand the risks of severe and life-threatening hepatic injury including autoimmune hepatitis, and serious immune-mediated disorders, and the REMS Program:
 - **ZINBRYTA Prescribing Information**
 - **ZINBRYTA REMS Program Overview**
 - **ZINBRYTA REMS Program Prescriber Training**
- Complete** and **submit** the ZINBRYTA REMS Program Prescriber Knowledge Assessment and the ZINBRYTA REMS Program Prescriber Enrollment Form, using the submission details at the end of this presentation
- Once completed, the ZINBRYTA REMS Program will notify you to finish certification. Within 2 business days upon receipt of your form, you will receive correspondence from the ZINBRYTA REMS Program. Correspondence will include:
 - How to retake the **ZINBRYTA REMS Program Prescriber Knowledge Assessment**, if necessary
 - OR*
 - A confirmation of your enrollment and certification in the ZINBRYTA REMS Program



How Does a Prescriber Enroll Appropriate Patients in the Program?



Before starting each patient on ZINBRYTA

- Counsel** your patient about the risks associated with ZINBRYTA and the need for baseline and monthly liver testing before the next dose and share the resources below
 - **ZINBRYTA REMS Program Patient Guide**
 - **ZINBRYTA REMS Program Patient Wallet Card**
- Order and evaluate** the baseline liver testing before each patient's first dose of ZINBRYTA
- Submit** a completed ZINBRYTA REMS Program Patient Enrollment Form and prescription for each patient, store a copy in the patient's records. Your patient can expect to be contacted by the ZINBRYTA REMS Program



What Are the Monitoring Requirements for Prescribers After Starting a Patient on ZINBRYTA?

Become Certified
(One-time)

Enroll Your
Patients

Monitor Your
Patients

Once your patient is on ZINBRYTA

- 1. Monitor** your ZINBRYTA patients on an ongoing basis. Test transaminase levels and total bilirubin monthly, and assess before the next dose of ZINBRYTA. Transaminase levels and total bilirubin should be followed monthly for 6 months after the last dose of ZINBRYTA
- 2. Submit** a completed ZINBRYTA REMS Program Patient Status Form* for each patient **every 90 days** during treatment and **every 90 days for 6 months after discontinuation** of ZINBRYTA using the submission details at the end of this presentation
- 3. Report** any adverse events suggestive of hepatic injury including autoimmune hepatitis, and other immune-mediated disorders to the ZINBRYTA REMS Program. You will be contacted for more information about these events
- 4. Inform** the ZINBRYTA REMS Program if a patient is no longer under your care or has discontinued ZINBRYTA

* Every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA, the ZINBRYTA REMS Program will send an individualized Patient Status Form to the certified prescriber for completion.



Overview of ZINBRYTA REMS Program Forms





Prescribers Must Enroll Each Patient in the ZINBRYTA REMS Program

ZINBRYTA REMS Program Patient Enrollment Form For Patients

ZINBRYTA is available only through the ZINBRYTA REMS Program, a restricted distribution program. Only prescribers, pharmacies, and patients enrolled in the program are able to prescribe, dispense, and receive ZINBRYTA. Your certified healthcare provider will help you complete this form and provide you with a copy. Fields marked with * are required.

Please submit this completed form to the ZINBRYTA REMS Program via online using the ZINBRYTA Program Portal, fax, or mail:
www.zinbrytarems.com | 1 855 474 3067 | 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709
If you have any questions regarding the ZINBRYTA REMS Program please visit www.zinbrytarems.com or call: 1 800 456 2255

Zinbryta®
(daclizumab)
150mg Subcutaneous Injection

PATIENT INFORMATION (PLEASE PRINT)

First Name* [] Last Name* [] Date of Birth* [] Gender* Male Female
Address* [] City* [] State* [] ZIP* []
Email [] Primary Phone* [] Secondary Phone []
Preferred method(s) of contact: Primary Phone Email
In addition, I give permission and allow for the sharing of my health information to the designated individual named below. Biogen may contact the individual designated below to discuss my enrollment in the ZINBRYTA REMS Program.
Designated Individual [] Relationship []
Email Address [] Phone Number []

PRESCRIBER INFORMATION (PLEASE PRINT)

First Name* [] Last Name* [] Phone Number* [] Prescriber NPI Number* []

PATIENT AGREEMENT

By signing this form, I understand and acknowledge that:

- I have received, read, and understand the ZINBRYTA REMS Program Patient Guide that my doctor has given me.
- In order to receive ZINBRYTA, I am required to enroll in the ZINBRYTA REMS Program, and my information will be stored in a secure database of all patients who receive ZINBRYTA in the United States. After enrolling, my doctor will provide me with a signed copy of this enrollment form.
- ZINBRYTA can cause serious side effects. It can cause serious liver problems (including autoimmune-related problems) that may lead to death. ZINBRYTA can also cause other immune system problems. These complications can be identified through monthly testing and awareness of side effects, reactions, or symptoms. My doctor has reviewed with me the risks of treatment with ZINBRYTA.
- I must complete liver testing before my first dose of ZINBRYTA, every month (before my next dose) during ZINBRYTA treatment, and for 6 months after discontinuation of ZINBRYTA. It is important that I complete these monthly blood tests to check my liver, even if I am feeling well.
- I will not be able to receive ZINBRYTA if I do not complete the required monthly liver testing.
- I will tell my doctor if I have any side effects, reactions, or symptoms after receiving ZINBRYTA.
- My doctor has counseled and given me the ZINBRYTA REMS Program Patient Wallet Card, which I will carry with me at all times. I will show this card to all my doctors involved in my medical treatment, even if it is not for my MS.
- I will tell all of my doctors that I have been treated with ZINBRYTA.
- I will tell the ZINBRYTA REMS Program right away if I change my ZINBRYTA doctor, if my contact information changes, or if I discontinue ZINBRYTA.
- I give permission to Biogen and its agents to use and share my personal health information for the purposes of enrolling me into and administering the ZINBRYTA REMS Program, coordinating the dispensing of ZINBRYTA, and releasing my personal health information to the Food and Drug Administration (FDA), as necessary.
- Biogen and its agents may contact me via phone, mail, or email to support administration of the ZINBRYTA REMS Program.

PATIENT ACKNOWLEDGMENT

Patient/Patient Representative Signature [] Print Name [] Relationship to Patient [] Date []

PRESCRIBER ACKNOWLEDGMENT

I have reviewed and discussed the risks of ZINBRYTA and the requirements of the ZINBRYTA REMS Program with this patient, and baseline liver testing will be completed prior to this patient's first dose of ZINBRYTA.

Prescriber Signature [] Date []

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- Form includes:
 - Patient information and acknowledgment of REMS requirements.
 - Prescriber information, acknowledgment that this patient was counseled on the risks associated with ZINBRYTA, and that baseline testing will be completed prior to patient's first dose of ZINBRYTA.

- Missing information will prompt a follow-up from the ZINBRYTA REMS Program.
- Prescriber will be notified upon successful enrollment of each patient.





ZINBRYTA REMS Program Patient Status Form: To Be Completed by Prescriber Every 90 Days While on Therapy and Every 90 Days for 6 Months Post Discontinuation

- Prescribers will receive an individualized ZINBRYTA REMS Program Patient Status Form for completion every 90 days during treatment and every 90 days for 6 months post discontinuation of ZINBRYTA.
- A ZINBRYTA certified prescriber or delegate may complete and submit this form on behalf of the certified Prescriber of record. The certified Prescriber of record is responsible for compliance with the ZINBRYTA REMS Program requirements, including monitoring, evaluation, and management of each patient under his/her care.

Is the above-named patient still under the care of the prescriber identified above? Yes No
If No, please indicate the name of the prescriber now responsible for this patient's care

Prescriber Name Prescriber Phone Number Unknown

PATIENT STATUS

1. This patient has completed required liver testing during the last 90 days: Yes No

2. Has this patient been diagnosed with any of the following that you have *not already* reported to Biogen in the last 90 days?

a. Hepatic injury Yes No
· May include elevated liver enzymes and/or total bilirubin:
- ALT or AST >5x ULN **OR**
- Total bilirubin >2x ULN **OR**
- ALT or AST ≥3x ULN but <5x ULN **and** total bilirubin >1.5x ULN but <2x ULN
· Or a suspected or confirmed diagnosis (e.g. autoimmune hepatitis)

b. Immune-mediated disorders Yes No
· May include skin reactions, lymphadenopathy, autoimmune hemolytic anemia, immune-mediated colitis or other suspected or newly diagnosed single or multi-organ immune-mediated disorder or systemic inflammatory reaction

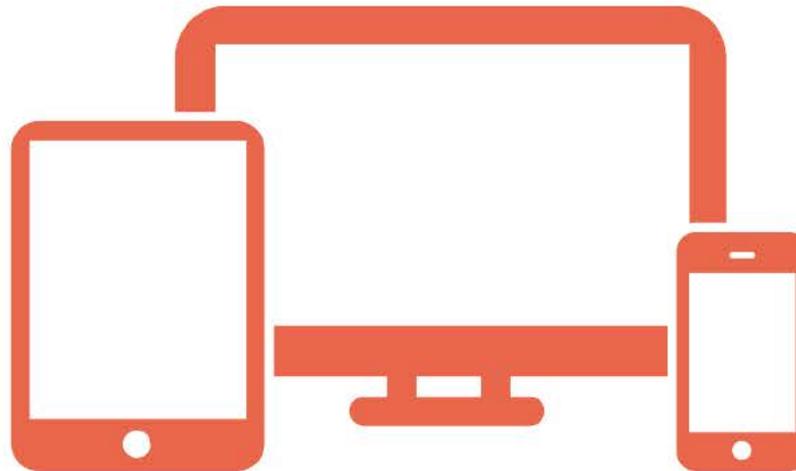
3. (On-therapy patients only) This patient will continue to receive ZINBRYTA: Yes No
*If no, ZINBRYTA REMS will begin the disenrollment process for the patient, the patient **will not be eligible to receive ZINBRYTA**, and you will be contacted for patient status information every 90 days for 6 months post-therapy discontinuation.*

- Prescribers will be contacted to obtain missing information, based on responses provided, or if the form is not received.
- Please note that if the prescriber does not submit the form, it may result in a delay of the patient receiving ZINBRYTA.



ZINBRYTA Program Portal Overview

- ZINBRYTA Program Portal is a web-based tool designed to:
 - Provide real-time access to ZINBRYTA patient data
 - Maintain compliance with the ZINBRYTA REMS Program
 - Streamline communication to/from prescribers
- ZINBRYTA Program Portal is now available for prescribers to instantly enroll, train, certify, and manage their patients online.
- ZINBRYTA Program Portal is accessed with secure user name and password.





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 **Zinbryta**[®]
(daclizumab)
150mg Subcutaneous Injection

If you have any questions regarding the ZINBRYTA REMS Program, please visit www.zinbrytarems.com or call: 1-800-456-2255.

Online: www.zinbrytarems.com

Fax: 1-855-474-3067

Mail: 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709



abbvie

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 **Zinbryta[®]**
(daclizumab)
150 mg Subcutaneous Injection

ZINBRYTA is available only through the ZINBRYTA REMS Program, a restricted distribution program. Only prescribers, pharmacies, and patients enrolled in the program are able to prescribe, dispense, and receive ZINBRYTA. Fields marked with * are required.



Instructions:

1. **Review** the ZINBRYTA Prescribing Information, the ZINBRYTA REMS Program Overview, and the ZINBRYTA REMS Program Prescriber Training
2. **Complete** and **submit** the ZINBRYTA REMS Program Prescriber Knowledge Assessment and this ZINBRYTA REMS Program Prescriber Enrollment Form
3. **Complete** all mandatory fields on this form to avoid a delay in the enrollment process. Upon completion of these steps, the ZINBRYTA REMS Program will notify you to finish certification.

Please submit this completed form to the ZINBRYTA REMS Program via online, using the ZINBRYTA Program Portal, fax, or mail:
www.zinbrytarems.com ☎ 1-855-474-3067 ✉ 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709
 If you have any questions regarding the ZINBRYTA REMS Program, please visit www.zinbrytarems.com or call: 1-800-456-2255.

PRESCRIBER INFORMATION (PLEASE PRINT)

| | | |
|---|---|--|
| <input type="text"/> Last Name* | <input type="text"/> First Name* | <input type="text"/> Email Address |
| <input type="text"/> Address* | | |
| <input type="text"/> City* | <input type="text"/> State* | <input type="text"/> ZIP* |
| <input type="text"/> Office Phone Number* | <input type="text"/> Fax Number* | <input type="text"/> Mobile Phone Number |
| <input type="text"/> Clinical/Hospital Affiliation | | |
| <input type="text"/> Prescriber NPI Number* | <input type="text"/> Practice NPI Number | Best time(s) to contact: <input type="checkbox"/> Morning <input type="checkbox"/> Afternoon <input type="checkbox"/> Evening |
| | | Preferred method(s) of contact: <input type="checkbox"/> Phone <input type="checkbox"/> Email <input type="checkbox"/> Fax |
| <input type="text"/> State License Number | <input type="text"/> Tax ID Number | |

OFFICE CONTACT INFORMATION (PLEASE PRINT)

| | | |
|---|--|--|
| <input type="text"/> Office Contact Name | <input type="text"/> Office Contact Email | <input type="text"/> Office Contact Phone |
|---|--|--|

(Continued on the next page)

PRESCRIBER AGREEMENT

By completing this form, I understand and agree that:

- ZINBRYTA is only available through the ZINBRYTA REMS Program and I must comply with the program requirements in order to prescribe ZINBRYTA.
 - I have reviewed the ZINBRYTA Prescribing Information, ZINBRYTA REMS Program Overview, and ZINBRYTA REMS Program Prescriber Training and must successfully complete the ZINBRYTA REMS Program Knowledge Assessment.
 - By completing the certification requirements and signing this ZINBRYTA REMS Program Prescriber Enrollment Form, I will be enrolled in the ZINBRYTA REMS Program and can prescribe ZINBRYTA.
 - In order to prescribe ZINBRYTA to a patient, I must enroll the patient in the ZINBRYTA REMS Program by:
 - i. Counseling each patient about the risks of severe and fatal hepatic injury and serious immune mediated disorders associated with ZINBRYTA and the need for baseline and monthly liver testing, using the ZINBRYTA REMS Program Patient Guide and ZINBRYTA REMS Program Patient Wallet Card, and providing a copy of each to the patient.
 - ii. Completing and submitting the ZINBRYTA REMS Program Patient Enrollment Form for each patient to the ZINBRYTA REMS Program, storing a copy in the patient's records, and providing a copy to the patient.
- I understand the risks of severe and fatal hepatic injury and serious immune-mediated disorders associated with the use of ZINBRYTA, and the requirement for baseline and monthly monitoring in order to identify and mitigate these risks.
 - I am responsible for ordering and evaluating serum transaminases (ALT and AST) and total bilirubin levels prior to each patient's first dose of ZINBRYTA.
 - I am responsible for ordering and evaluating ALT, AST and total bilirubin every month (prior to the next dose) during treatment and monthly for 6 months after the last dose of ZINBRYTA. A patient who does not complete the required liver testing cannot receive ZINBRYTA.
 - I will report any adverse events suggestive of hepatic injury or immune-mediated disorders to the ZINBRYTA REMS Program.
 - I will complete and submit the ZINBRYTA REMS Program Patient Status Form every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA.
 - I will notify the ZINBRYTA REMS Program if an enrolled patient is no longer under my care or if the patient discontinues treatment with ZINBRYTA.
 - If I do not maintain compliance with the requirements of the ZINBRYTA REMS Program, I will no longer be able to prescribe ZINBRYTA.
 - Biogen and its agents may contact me via phone, mail, fax, or email to support administration of the ZINBRYTA REMS Program.

PRESCRIBER SIGNATURE

By completing this form and providing my signature below, I hereby confirm that I have read, understand, and agree with the full Prescriber Agreement of this ZINBRYTA REMS Program Prescriber Enrollment Form.

Prescriber Signature

Date



ZINBRYTA REMS (Risk Evaluation and Mitigation Strategy) Program Prescriber Knowledge Assessment

To become a certified prescriber in the ZINBRYTA REMS Program, you must complete this ZINBRYTA REMS Program Prescriber Knowledge Assessment and the ZINBRYTA REMS Program Prescriber Enrollment Form. You need to answer ALL 7 questions correctly to become certified.

1. Review the following materials:
 - ZINBRYTA Prescribing Information
 - ZINBRYTA REMS Program Overview
 - ZINBRYTA REMS Program Prescriber Training
2. Complete all 7 questions and print your name and National Provider Identifier (NPI).
3. Submit your completed ZINBRYTA REMS Program Prescriber Knowledge Assessment and the ZINBRYTA REMS Program Prescriber Enrollment Form to the ZINBRYTA REMS Program via online, using the ZINBRYTA Program Portal, fax, or mail:
 - 🖱️ **Online:** www.zinbrytarems.com
 - 📠 **Fax:** 1-855-474-3067
 - ✉️ **Mail:** 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709

If completed via fax or mail, you will be notified by the ZINBRYTA REMS Program on the status of your certification within 2 business days upon receipt. When contacted, you will receive either:

- Confirmation of your certification in the ZINBRYTA REMS Program
- OR
- Instructions on how to retake the ZINBRYTA REMS Program Prescriber Knowledge Assessment, if necessary

If you have any questions regarding the ZINBRYTA REMS Program, please visit www.zinbrytarems.com or call: 1-800-456-2255.

Reference ID: 4175674

 **Zinbryta**[®]
(daclizumab)
150mg Subcutaneous Injection



ZINBRYTA REMS Program Prescriber Knowledge Assessment

Questions 1-7

Select the one best answer.

QUESTION 1 (Check One)

Before starting each patient on ZINBRYTA, I should:

- Counsel them about the risks associated with ZINBRYTA and the need for baseline and monthly liver testing before the next dose, and provide the ZINBRYTA REMS Program Patient Guide and ZINBRYTA REMS Program Patient Wallet Card
- Order and evaluate baseline liver testing before each patient's first dose
- Complete the ZINBRYTA REMS Program Patient Enrollment Form
- All of the above

QUESTION 2

In order to receive ZINBRYTA, patients must enroll in the ZINBRYTA REMS Program and comply with ongoing monitoring requirements.

- True
- False

QUESTION 3

ZINBRYTA treatment initiation is not recommended in patients with pre-existing hepatic disease or hepatic impairment, including patients with ALT or AST >2 times the upper limit of normal.

- True
- False

QUESTION 4 (Check One)

I should monitor and evaluate my patient's liver testing:

- Only at baseline before the first dose
- At baseline before the first dose and every 3 months before the next dose
- At baseline before the first dose and every 6 months before the next dose
- At baseline before the first dose, monthly before the next dose during ZINBRYTA treatment, and for 6 months after discontinuation

QUESTION 5

I should submit a completed ZINBRYTA REMS Program Patient Status Form for each patient every 90 days during treatment and every 90 days for 6 months after discontinuation.

- True
- False

QUESTION 6

The most common immune-mediated reactions seen with ZINBRYTA treatment are skin reactions and lymphadenopathy.

- True
- False

QUESTION 7 (Check One)

Treatment should be interrupted for the following lab values:

- If ALT or AST is >5 times the ULN
- Total bilirubin is >2 times the ULN
- ALT or AST is ≥ 3 but <5 times the ULN and total bilirubin is >1.5 but <2 times the ULN
- All of the above

Please print your name and NPI number so we can associate your responses with your ZINBRYTA REMS Program certification.

Prescriber Name

Prescriber NPI Number

 **Zinbryta[®]**
(daclizumab)
150 mg Subcutaneous Injection

ZINBRYTA is available only through the ZINBRYTA REMS Program, a restricted distribution program. Only prescribers, pharmacies, and patients enrolled in the program are able to prescribe, dispense, and receive ZINBRYTA. Your certified healthcare provider will help you complete this form and provide you with a copy. Fields marked with * are required.



Please submit this completed form to the ZINBRYTA REMS Program via online, using the ZINBRYTA Program Portal, fax, or mail:

www.zinbrytarems.com ☎ 1-855-474-3067 ✉ 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709

If you have any questions regarding the ZINBRYTA REMS Program, please visit www.zinbrytarems.com or call: 1-800-456-2255.

PATIENT INFORMATION (PLEASE PRINT)

| | | | | |
|---|----------------------|----------------------|--|----------------------|
| <input type="text"/> | <input type="text"/> | <input type="text"/> | Gender*: <input type="checkbox"/> Male <input type="checkbox"/> Female | |
| First Name* | Last Name* | Date of Birth* | | |
| <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> |
| Address* | City* | State* | ZIP* | |
| <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> |
| Email | Primary Phone* | Secondary Phone | | |
| Preferred method(s) of contact: <input type="checkbox"/> Primary Phone <input type="checkbox"/> Email | | | | |
| In addition, I give permission and allow for the sharing of my health information to the designated individual named below. Biogen may contact the individual designated below to discuss my enrollment in the ZINBRYTA REMS Program. | | | | |
| <input type="text"/> | <input type="text"/> | | <input type="text"/> | |
| Designated Individual | Relationship | | | |
| <input type="text"/> | <input type="text"/> | | <input type="text"/> | |
| Email Address | Phone Number | | | |

PRESCRIBER INFORMATION (PLEASE PRINT)

| | | | |
|----------------------|----------------------|----------------------|------------------------|
| <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> |
| First Name* | Last Name* | Phone Number* | Prescriber NPI Number* |

PATIENT AGREEMENT

By signing this form, I understand and acknowledge that:

- I have received, read, and understand the ZINBRYTA REMS Program Patient Guide that my doctor has given me.
- In order to receive ZINBRYTA, I am required to enroll in the ZINBRYTA REMS Program, and my information will be stored in a secure database of all patients who receive ZINBRYTA in the United States. After enrolling, my doctor will provide me with a signed copy of this enrollment form.
- ZINBRYTA can cause serious side effects. It can cause serious liver problems (including autoimmune-related problems) that may lead to death. ZINBRYTA can also cause other immune system problems. These complications can be identified through monthly testing and awareness of side effects, reactions, or symptoms. My doctor has reviewed with me the risks of treatment with ZINBRYTA.
- I must complete liver testing before my first dose of ZINBRYTA, every month (before my next dose) during ZINBRYTA treatment, and for 6 months after discontinuation of ZINBRYTA. It is important that I complete these monthly blood tests to check my liver, even if I am feeling well.
- I will not be able to receive ZINBRYTA if I do not complete the required monthly liver testing.
- I will tell my doctor if I have any side effects, reactions, or symptoms after receiving ZINBRYTA.
- My doctor has counseled and given me the ZINBRYTA REMS Program Patient Wallet Card, which I will carry with me at all times. I will show this card to all my doctors involved in my medical treatment, even if it is not for my MS.
- I will tell all of my doctors that I have been treated with ZINBRYTA.
- I will tell the ZINBRYTA REMS Program right away if I change my ZINBRYTA doctor, if my contact information changes, or if I discontinue ZINBRYTA.
- I give permission to Biogen and its agents to use and share my personal health information for the purposes of enrolling me into and administering the ZINBRYTA REMS Program, coordinating the dispensing of ZINBRYTA, and releasing my personal health information to the Food and Drug Administration (FDA), as necessary.
- Biogen and its agents may contact me via phone, mail, or email to support administration of the ZINBRYTA REMS Program.

PATIENT ACKNOWLEDGMENT

| | | | |
|--|----------------------|-------------------------|----------------------|
| <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> |
| Patient/Patient Representative Signature | Print Name | Relationship to Patient | Date |

PRESCRIBER ACKNOWLEDGMENT

I have reviewed and discussed the risks of ZINBRYTA and the requirements of the ZINBRYTA REMS Program with this patient, and baseline liver testing will be completed prior to this patient's first dose of ZINBRYTA.

| | |
|----------------------|----------------------|
| <input type="text"/> | <input type="text"/> |
| Prescriber Signature | Date |

This form must be completed every 90 days for all patients treated with ZINBRYTA during treatment and every 90 days for 6 months after discontinuation. Please complete this form and return to the ZINBRYTA REMS Program by the date listed on the form. You may also be contacted for additional information in response to answers provided on this form.



Please submit this completed form to the ZINBRYTA REMS Program via online, using the ZINBRYTA Program Portal, fax, or mail:
www.zinbrytarems.com ☎ 1-855-474-3067 ✉ 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709
 If you have any questions regarding the ZINBRYTA REMS Program, please visit www.zinbrytarems.com or call: 1-800-456-2255.

| | |
|--|--|
| <input style="width: 95%;" type="text" value="<Today's Date>"/> <small>Today's Date</small> | <input style="width: 95%;" type="text" value="<Due Date>"/> <small>Due Date</small> |
|--|--|

PRESCRIBER INFORMATION (PLEASE PRINT)

| | | |
|--|--|--|
| <input style="width: 95%;" type="text" value="<Prescriber Name>"/> <small>Prescriber Name</small> | | |
| <input style="width: 95%;" type="text" value="<Prescriber Address>"/> <small>Prescriber Address</small> | | |
| <input style="width: 30%;" type="text" value="<City>"/> <small>City</small> | <input style="width: 30%;" type="text" value="<State>"/> <small>State</small> | <input style="width: 30%;" type="text" value="<ZIP>"/> <small>ZIP</small> |
| <input style="width: 95%;" type="text" value="<Prescriber Enrollment ID>"/> <small>Prescriber Enrollment ID</small> | | |

PATIENT INFORMATION (PLEASE PRINT)

| | |
|--|--|
| <input style="width: 95%;" type="text" value="<Patient Name>"/> <small>Patient Name</small> | |
| <input style="width: 60%;" type="text" value="<Patient Enrollment ID>"/> <small>Patient Enrollment ID</small> | <input style="width: 30%;" type="text" value="<DOB>"/> <small>Patient Date of Birth</small> |
| <input style="width: 95%;" type="text" value="<Patient Therapy Status>"/> <small>Patient Therapy Status</small> | |

Is the above-named patient still under the care of the prescriber identified above? Yes No
 If No, please indicate the name of the prescriber now responsible for this patient's care

| | | |
|--|--|----------------------------------|
| <input style="width: 95%;" type="text"/> <small>Prescriber Name</small> | <input style="width: 95%;" type="text"/> <small>Prescriber Phone Number</small> | <input type="checkbox"/> Unknown |
|--|--|----------------------------------|

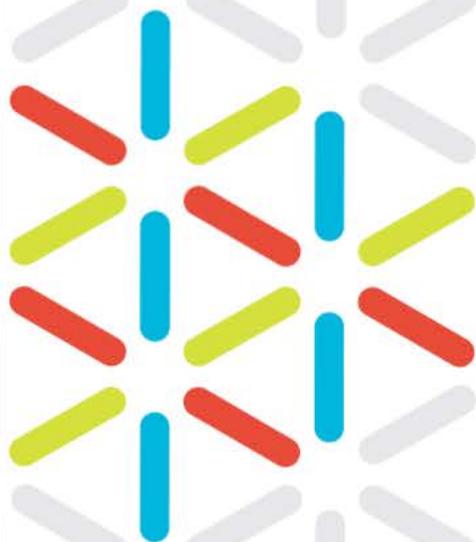
PATIENT STATUS

1. This patient has completed required liver testing during the last 90 days: Yes No
2. Has this patient been diagnosed with any of the following that you have not already reported to Biogen in the last 90 days?
 - a. Hepatic injury Yes No
 - May include elevated liver enzymes and/or total bilirubin:
 - ALT or AST >5x ULN **OR**
 - Total bilirubin >2x ULN **OR**
 - ALT or AST ≥3x ULN but <5x ULN and total bilirubin >1.5x ULN but <2x ULN
 - Or a suspected or confirmed diagnosis (e.g. autoimmune hepatitis)
 - b. Immune-mediated disorders Yes No
 - May include skin reactions, lymphadenopathy, autoimmune hemolytic anemia, immune-mediated colitis or other suspected or newly diagnosed single or multi-organ immune-mediated disorder or systemic inflammatory reaction
3. (On-therapy patients only) This patient will continue to receive ZINBRYTA: Yes No
 If no, ZINBRYTA REMS will begin the disenrollment process for the patient, the patient **will not be eligible to receive ZINBRYTA**, and you will be contacted for patient status information every 90 days for 6 months post-therapy discontinuation.

ZINBRYTA CERTIFIED PRESCRIBER OR DELEGATE SIGNATURE

| | |
|---|---|
| <input style="width: 95%;" type="text"/> <small>Signature</small> | <input style="width: 95%;" type="text"/> <small>Date</small> |
| <input style="width: 95%;" type="text"/> <small>Print name</small> | |

Please note: A ZINBRYTA certified prescriber or delegate may complete and submit this form on behalf of the certified prescriber of record. The certified prescriber of record is responsible for compliance with the ZINBRYTA REMS Program requirements, including monitoring, evaluation, and management of each patient under his/her care. If you have questions on this information, please call 1-800-456-2255.



ZINBRYTA REMS (Risk Evaluation and Mitigation Strategy) Program Patient Guide

Patients: Your doctor will go over this patient guide with you. It is important to ask any questions you might have. Keep this guide for important safety information about the serious risks of ZINBRYTA.

Healthcare Providers: Review this patient guide with your patient, and provide your patient a copy to take home.

To learn more about ZINBRYTA, please talk to your doctor and visit www.zinbrytarems.com. You can also call us at **1-800-456-2255**.

 **Zinbryta**[®]
(daclizumab)
150 mg Subcutaneous Injection



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What is ZINBRYTA?

ZINBRYTA is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS). Because of its risks, ZINBRYTA is generally used in people who have tried 2 or more MS medicines that have not worked well enough.

What are the most serious risks of ZINBRYTA?

ZINBRYTA can cause serious liver problems (including autoimmune-related liver problems) that may lead to death. It can also cause other immune system problems. **Contact your doctor right away and seek emergency medical care if you have any of the following symptoms:**

Liver problems. Symptoms include:

- Nausea or vomiting
- Stomach pain
- Unusual tiredness
- Not wanting to eat
- Yellowing of the skin or whites of your eyes
- Dark urine

Immune system problems. Some people using ZINBRYTA develop immune mediated disorders (a condition where the body's immune cells attack other cells or organs in the body) and other immune system problems. Symptoms include:

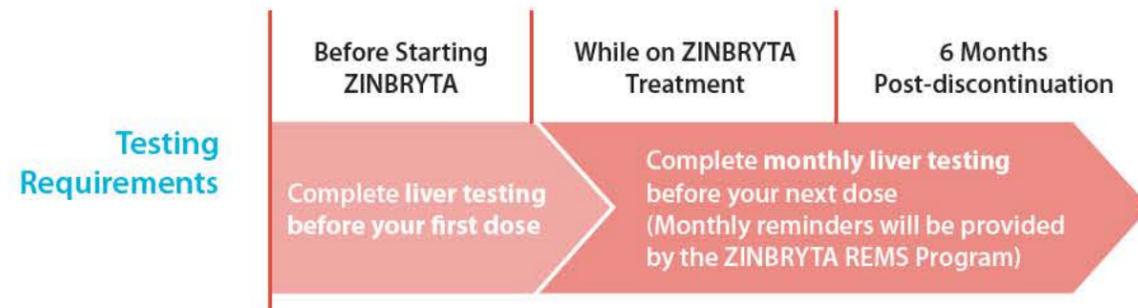
- Skin reactions such as rash or skin irritation
- Tender, painful, or swollen lymph nodes
- Symptoms of low red blood cell counts which can include looking very pale, feeling more tired than usual, dark urine, shortness of breath, or yellowing of the skin or whites of your eyes
- Intestinal problems (colitis). Symptoms can include fever, stomach pain, blood in your stools, or diarrhea that does not go away
- Any new and unexplained symptoms affecting any part of your body





What is the ZINBRYTA REMS Program?

- A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug continue to outweigh its risks.
- Because of the risk of serious liver problems (including autoimmune-related liver problems) and other immune system problems, ZINBRYTA is only available through a restricted program called the ZINBRYTA Risk Evaluation and Mitigation (REMS) Program.
- The ZINBRYTA REMS Program educates patients and doctors about these risks associated with ZINBRYTA.
- Requirements of the ZINBRYTA REMS Program include the following:
 - You and your doctor must be enrolled in the ZINBRYTA REMS Program in order to receive and prescribe ZINBRYTA.
 - ZINBRYTA is only available from pharmacies that participate in the ZINBRYTA REMS Program.
- Your doctor will do blood tests to check your liver before you start using ZINBRYTA, every month while you are using ZINBRYTA, and for 6 months after you stop using ZINBRYTA. Your doctor will check your test results before your next dose.



It is very important that you complete these monthly blood tests to check your liver, even if you are feeling well.

How do I enroll in the ZINBRYTA REMS Program and what is required of me?

Before starting ZINBRYTA:

- Discuss** with your doctor and understand:
 - The risk of serious liver problems and immune system problems.
 - The required monthly liver testing.
- Receive and read:**
 - This **ZINBRYTA REMS Program Patient Guide**.
 - The **ZINBRYTA REMS Program Patient Wallet Card** (fill in your name and your doctor's information).
- Complete** the **ZINBRYTA REMS Program Patient Enrollment Form** with your doctor.
- Complete liver testing** before your first dose of ZINBRYTA.



How do I enroll in the ZINBRYTA REMS Program and what is required of me? (cont'd)

Your doctor will help you fill out the ZINBRYTA REMS Program Patient Enrollment Form mentioned on the previous page. You will be asked to acknowledge the following:

- I have received, read, and understand the ZINBRYTA REMS Program Patient Guide that my doctor has given me.
- In order to receive ZINBRYTA, I am required to enroll in the ZINBRYTA REMS Program, and my information will be stored in a secure database of all patients who receive ZINBRYTA in the United States. After enrolling, my doctor will provide me with a signed copy of this enrollment form.
- ZINBRYTA can cause serious side effects. It can cause serious liver problems (including autoimmune-related liver problems) that may lead to death. ZINBRYTA can also cause other immune system problems. These complications can be identified through monthly testing and awareness of side effects, reactions, or symptoms. My doctor has reviewed with me the risks of treatment with ZINBRYTA.
- I must complete liver testing before my first dose of ZINBRYTA, every month (before my next dose) during ZINBRYTA treatment, and for 6 months after discontinuation of ZINBRYTA. It is important that I complete these monthly blood tests to check my liver, even if I am feeling well.
- I will not be able to receive ZINBRYTA if I do not complete the required monthly liver testing.
- I will tell my doctor if I have any side effects, reactions, or symptoms after receiving ZINBRYTA.
- My doctor has counseled and given me the ZINBRYTA REMS Program Patient Wallet Card, which I will carry with me at all times. I will show this card to all my doctors involved in my medical treatment, even if it is not for my MS.
- I will tell all of my doctors that I have been treated with ZINBRYTA.
- I will tell the ZINBRYTA REMS Program right away if I change my ZINBRYTA doctor, if my contact information changes, or if I discontinue ZINBRYTA.
- I give permission to Biogen and its agents to use and share my personal health information for the purposes of enrolling me into and administering the ZINBRYTA REMS Program, coordinating the dispensing of ZINBRYTA, and releasing my personal health information to the Food and Drug Administration (FDA), as necessary.
- Biogen and its agents may contact me via phone, mail, or email to support administration of the ZINBRYTA REMS Program.

After enrolling, what are the next steps? And how will I receive ZINBRYTA?

Upon enrollment:

1. A Biogen representative from the ZINBRYTA REMS Program will contact you to get you started.
2. The pharmacy will call you to schedule a shipment of ZINBRYTA that will come right to your home.
 - ZINBRYTA is only available from pharmacies that participate in the ZINBRYTA REMS Program.
 - The pharmacy will dispense only a one month supply at a time.
3. Once you start taking ZINBRYTA, it will be important for you to complete your liver testing every month before your next dose.

After starting ZINBRYTA:

- Complete** monthly liver testing (before your next dose) during ZINBRYTA treatment and for 6 months after discontinuation.
- Inform your doctor** if you have any side effects, reactions or symptoms after receiving ZINBRYTA.
- Show** the **ZINBRYTA REMS Program Patient Wallet Card** to your doctor when you have any medical treatment, even if it is not for your MS.
- Notify** the ZINBRYTA REMS Program if you **change your ZINBRYTA doctor**, if your **contact information changes**, or if you **discontinue treatment with ZINBRYTA**.

If you have any questions regarding the ZINBRYTA REMS Program,
visit www.zinbrytarems.com or call: 1-800-456-2255

Fax: 1-855-474-3067

Mail: 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709



 **Zinbryta[®]**
(daclizumab)

150mg Subcutaneous Injection

ZINBRYTA REMS Program

Patient Wallet Card

Carry this card with you at all times and show it to any doctor involved in your health care.

Reference ID: 4175674



Emergency contact info

Patient Name

ZINBRYTA Doctor Name

ZINBRYTA Doctor's Phone Number

Reference ID: 4175674



Important Safety Information for Patients taking ZINBRYTA

ZINBRYTA can cause serious liver problems (including autoimmune-related liver problems) that may lead to death. It can also cause other immune system problems.

Be sure to get monthly blood tests as scheduled by your doctor.



Contact your doctor right away and seek emergency medical care if you have any of the following symptoms:

 **Zinbryta**[®]

Reference ID: 4175674
(daclatasvir)

150 mg Subcutaneous Injection

Liver problems:

- Nausea or vomiting
- Stomach pain
- Unusual tiredness
- Not wanting to eat
- Yellowing of the skin or whites of your eyes
- Dark urine

→ **OPEN TO CONTINUE**



Contact your doctor right away and seek emergency medical care if you have any of the following symptoms:

 **Zinbryta**
Reference ID: 4175674
(daclizumab)
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Immune system problems:

- Skin reactions such as rash or skin irritation
- Tender, painful, or swollen lymph nodes
- Symptoms of low red blood cell counts which can include

looking very pale, feeling more tired than usual, dark urine, shortness of breath, or yellowing of the skin or whites of your eyes

- Intestinal problems (colitis). Symptoms can include fever, stomach pain, blood in your stools, or diarrhea that does not go away

- Any new and unexplained symptoms affecting any part of your body



**Important
Information
for the Treating
Physician**


Reference ID: 4175674

150 mg Subcutaneous Injection

This patient has been prescribed ZINBRYTA for the treatment of relapsing multiple sclerosis (MS). ZINBRYTA increases the risk of serious liver problems and immune system problems.

- If these conditions are suspected, please contact the ZINBRYTA prescribing physician as soon as possible.
- For more information about ZINBRYTA, please see the Prescribing Information, including

BOXED WARNING, at www.zinbrytarems.com.

- Please report any adverse events to the ZINBRYTA REMS Program at 1-800-456-2255.



Zinbryta[®]

(daclizumab)

150 mg Subcutaneous Injection



Biogen. abbvie

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Reference ID: 4175074

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ZINBRYTA is available only through the ZINBRYTA REMS Program, a restricted distribution program. Only prescribers, pharmacies, and patients enrolled in the program are able to prescribe, dispense, and receive ZINBRYTA. An authorized representative of the pharmacy must enroll the pharmacy in the ZINBRYTA REMS Program. Fields marked with * are required.



Submit the completed form to the ZINBRYTA REMS Program using the submission details below. ZINBRYTA REMS Program will notify the pharmacy upon successful certification.

Please submit this completed form to the ZINBRYTA REMS Program via fax or mail:
 📠 1-855-474-3067 📧 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709
 If you have any questions regarding the ZINBRYTA REMS Program, call: 1-800-456-2255.

New Certification Recertification With New Authorized Representative (REMS ID # _____) Other Mandatory Field Changes (REMS ID # _____)

PHARMACY INFORMATION (PLEASE PRINT)

| | | |
|------------------------------------|-------------|----------------|
| Name of Pharmacy* | | |
| NCPDP Number* | NPI Number* | DEA Number* |
| Address* | | |
| City* | State* | ZIP* |
| Name of Authorized Representative* | Title* | |
| Phone Number* | Fax Number* | Email Address* |

PHARMACY AGREEMENT

I am the authorized representative designated by my Pharmacy to coordinate the activities of the ZINBRYTA REMS Program. By signing this form, I agree, on behalf of myself and Pharmacy, to comply with the following program requirements:

- I will oversee implementation of and ensure my pharmacy's compliance with the ZINBRYTA REMS Program requirements.
- I have reviewed the ZINBRYTA REMS Program Overview and will ensure that all relevant staff involved in the dispensing of ZINBRYTA are trained on the ZINBRYTA REMS Program requirements (as described in the ZINBRYTA REMS Program Overview) and that a record of training is maintained.
- I understand that upon completing the certification requirements and signing this ZINBRYTA REMS Program Pharmacy Enrollment Form, this pharmacy will be enrolled in the ZINBRYTA REMS Program, upon confirmation from the ZINBRYTA REMS Program. I understand that my pharmacy will only dispense ZINBRYTA if certified by the ZINBRYTA REMS Program.
- I will ensure that prior to dispensing ZINBRYTA, my pharmacy will verify that the prescriber is certified and the patient is authorized to receive ZINBRYTA by contacting the ZINBRYTA REMS Program.

- This pharmacy will ensure that no more than a one month supply of ZINBRYTA is dispensed.
- This pharmacy will ensure any adverse events suggestive of hepatic injury or immune-mediated disorders are reported by Pharmacy to the ZINBRYTA REMS Program.
- This pharmacy will maintain and make available appropriate documentation reflecting that all processes and procedures are in place and are being followed for the ZINBRYTA REMS Program and provide copies of such documentation (including, without limitation, patient-specific information), upon request to Biogen, FDA, or any third party acting on behalf of Biogen or FDA.
- This pharmacy will comply with audits by Biogen, FDA, or a third party acting on behalf of Biogen or FDA to ensure compliance with the ZINBRYTA REMS Program.
- This pharmacy will confirm the authorized representative annually and must recertify in the ZINBRYTA REMS Program if there is a personnel change for that authorized representative.
- I understand that non-compliance with the requirements of the ZINBRYTA REMS Program will result in decertification of my Pharmacy and termination of the authorization to dispense ZINBRYTA.

AUTHORIZED REPRESENTATIVE SIGNATURE

| | |
|-------------------------------------|------|
| Authorized Representative Signature | Date |
| Print Name | |



ZINBRYTA Program Portal

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[PATIENTS](#)

[FORMS AND RESOURCES](#)

ZINBRYTA REMS Program

What is the ZINBRYTA (daclizumab) Risk Evaluation and Mitigation Strategy (REMS) Program?

A REMS is a strategy to manage known or potential serious risks associated with a drug product and is required by the FDA to ensure the benefits of a drug outweigh its risks. **Due to the risks of severe and fatal liver injury, including autoimmune hepatitis and liver failure, and other immune-mediated disorders such as skin reactions, lymphadenopathy, immune-mediated colitis, and other serious conditions, ZINBRYTA is available only through a restricted program called the ZINBRYTA REMS Program.**

Prescribers



Click here to learn how to prescribe ZINBRYTA:

1. **Become certified** by completing a one-time certification process
2. As you start patients on ZINBRYTA, **counsel and enroll** them into the ZINBRYTA REMS Program, complete the prescription, and order and evaluate baseline liver testing
3. **Perform** ongoing patient monitoring, evaluate **monthly liver testing before each patient's next dose**, and complete the ZINBRYTA REMS Program Patient Status Forms for each patient every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA

Pharmacies



Click here to learn how to dispense ZINBRYTA:

1. **Designate an authorized representative, become certified, and recertify** if there is a change in the authorized representative
2. **Train** staff and **comply** with REMS requirements
3. Before dispensing each dose, **verify** prescriber is certified and patient is authorized to receive ZINBRYTA, and **dispense no more than a one month supply**

Patients



Click here to learn how to receive ZINBRYTA:

1. **Understand the risks** associated with ZINBRYTA
2. **Enroll** in the ZINBRYTA REMS Program by completing the ZINBRYTA REMS Program Patient Enrollment Form with your doctor
3. **Complete** baseline liver testing before your first dose and **monthly liver testing** before your next dose of ZINBRYTA. A monthly reminder will be sent from the ZINBRYTA REMS Program for liver testing

ZINBRYTA is not available to all pharmacies. If you have any questions about the ZINBRYTA REMS Program or need help enrolling, call **1-800-456-2255.*

Indication

ZINBRYTA is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of ZINBRYTA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

Please see [Prescribing Information](#), including **BOXED WARNING**, for additional information.

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Zinbryta[®]
(daclizumab)
150mg Subcutaneous Injection

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ZINBRYTA REMS Program: For Prescribers - Available Online

Prescribers

Prescribers are now able to use the ZINBRYTA Program Portal to instantly enroll, train, certify, and manage their patients all online. If you are already a certified ZINBRYTA REMS Program prescriber, click **Create Account**. If you need to become certified, click **Enroll Here**.

Already Certified?
Create an online account to manage ZINBRYTA patients
[Create Account](#)

Begin Certification
Create an online account and become ZINBRYTA REMS Program certified
[Enroll Here](#)

To enroll in the ZINBRYTA REMS Program via fax or mail, [click here](#) for the required forms.

The requirements for treating with ZINBRYTA (daclizumab)

Please complete this **3-step process** to prescribe ZINBRYTA.

Step 1. Become certified:

Complete the certification process before you prescribe ZINBRYTA [>](#)

Step 2. Before you start your patients on ZINBRYTA:

Enroll the patient in the ZINBRYTA REMS Program [>](#)

Step 3. Once a patient starts on ZINBRYTA:

Perform monthly monitoring and evaluation [>](#)

*If you have any questions about the ZINBRYTA REMS Program or need help enrolling, call **1-800-456-2255**.*

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Already Certified?
Create an online account to manage ZINBRYTA patients

[Create Account](#)

Begin Certification
Create an online account and become ZINBRYTA REMS Program certified

[Enroll Here](#)

To enroll in the ZINBRYTA REMS Program via fax or mail, [click here](#) for the required forms.

The requirements for treating with ZINBRYTA (daclizumab)

Please complete this 3-step process to prescribe ZINBRYTA.

Step 1. Become certified:

Complete the certification process before you prescribe ZINBRYTA

1. **Register** online to create a prescriber account and to access the ZINBRYTA Program Portal.

2. **Review** the following educational materials on ZINBRYTA to understand the risks of severe and fatal liver injury, including autoimmune hepatitis and liver failure, and serious immune-mediated disorders, and the ZINBRYTA REMS Program. Download the:



ZINBRYTA Prescribing Information



ZINBRYTA REMS Program Overview



ZINBRYTA REMS Program Prescriber Training

3. **Complete** the ZINBRYTA REMS Program Prescriber Knowledge Assessment and the ZINBRYTA REMS Program Prescriber Enrollment Form online, using the [ZINBRYTA Program Portal](#), or via paper. You must answer all questions in the ZINBRYTA REMS Program Prescriber Knowledge Assessment correctly to become certified. Download the:



ZINBRYTA REMS Program Prescriber Knowledge Assessment



ZINBRYTA REMS Program Prescriber Enrollment Form

4. **Submit** the ZINBRYTA REMS Program Prescriber Knowledge Assessment and the ZINBRYTA REMS Program Prescriber Enrollment Form online, using the [ZINBRYTA Program Portal](#). Alternatively, the completed forms may also be faxed to the ZINBRYTA REMS Program at 1-855-474-3067, or mailed to the ZINBRYTA REMS Program at 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709. You will be notified by the ZINBRYTA REMS Program within 2 business days upon receipt. When notified, you will receive either:

- A confirmation of your certification in the ZINBRYTA REMS Program

OR

- If necessary, instructions on how to retake the ZINBRYTA REMS Program Prescriber Knowledge Assessment

Once this one-time step has been completed, the ZINBRYTA REMS Program will contact you to finish certification.

Step 2. Before you start your patients on ZINBRYTA:

Enroll the patient in the ZINBRYTA REMS Program

1. **Counsel** your patient about the risks associated with ZINBRYTA and the need for baseline and monthly liver testing before the next dose and share the resources provided below. Download the:



ZINBRYTA REMS Program Patient Guide



ZINBRYTA REMS Program Patient Wallet Card

2. **Order and evaluate** the baseline liver testing before each patient's first dose of ZINBRYTA.

3. **Complete** the ZINBRYTA REMS Program Patient Enrollment Form and prescription with your patient online, using the [ZINBRYTA Program Portal](#), or via paper and provide them with a copy of the finished form. Download the:



ZINBRYTA REMS Program Patient Enrollment Form

4. **Submit** the completed ZINBRYTA REMS Program Patient Enrollment Form online, using the [ZINBRYTA Program Portal](#), and store a copy in the patient's record. Completed forms can also be faxed to the ZINBRYTA REMS Program at 1-855-474-3067, or mailed to the ZINBRYTA REMS Program at 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709. Your patient can expect to be contacted by the ZINBRYTA REMS Program.

Step 3. Once a patient starts on ZINBRYTA:

Perform monthly monitoring and evaluation

1. **Monitor** your ZINBRYTA patients on an ongoing basis. Test transaminase levels and total bilirubin monthly and assess before the next dose of ZINBRYTA. Transaminase levels and total bilirubin should be followed monthly for 6 months after the last dose of ZINBRYTA. The patient will be contacted by the ZINBRYTA REMS Program each month to remind them to complete their liver testing.

If there are changes in the test results, adjust the monitoring and treatment with ZINBRYTA as follows:

| Lab values | Recommendations |
|---|---|
| ALT or AST >5x ULN OR Total bilirubin >2x ULN OR ALT or AST ≥3 but <5x ULN and total bilirubin >1.5 but <2x ULN | Interrupt ZINBRYTA therapy and investigate for other etiologies of abnormal lab values If no other etiologies are identified, then discontinue ZINBRYTA If other etiologies are identified, re-assess the overall risk-benefit profile of ZINBRYTA in the patient and consider whether to resume ZINBRYTA when both AST or ALT are <2x ULN and total bilirubin is ≤ to ULN* |

*In clinical trials, permanent discontinuation of therapy was required if the patient had liver test abnormalities resulting in suspension of study treatment for at least 8 consecutive weeks.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

2. **Submit** a completed ZINBRYTA REMS Program Patient Status Form online, using the [ZINBRYTA Program Portal](#) or send a completed form via fax or mail, **every 90 days** during treatment and **every 90 days for 6 months after discontinuation** of ZINBRYTA. Every 90 days, the ZINBRYTA REMS Program will send an individualized Patient Status Form to the certified prescriber for completion. Download the:



ZINBRYTA REMS Program Patient Status Form

3. **Report** any adverse events suggestive of hepatic injury including autoimmune hepatitis, and other immune-mediated disorders to the ZINBRYTA REMS Program at 1-800-456-2255. You will be contacted for more information about these events.

4. **Inform** the ZINBRYTA REMS Program if the patient is no longer under your care or has discontinued ZINBRYTA.

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If you have any questions about the ZINBRYTA REMS Program or need help enrolling, call 1-800-456-2255.

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ZINBRYTA REMS Program: For Pharmacies

Pharmacies

 The requirements for dispensing ZINBRYTA (daclizumab)

ZINBRYTA is not available to all pharmacies. If you have any questions about the ZINBRYTA REMS Program or how to obtain ZINBRYTA, call **1-800-456-2255**.

Please complete this **2-step process** to dispense ZINBRYTA.

Step 1. Become certified:

Complete the certification process before you are authorized to dispense ZINBRYTA [>](#)

Step 2. Dispense ZINBRYTA to authorized patients:

Ensure compliance with the ZINBRYTA REMS Program requirements [>](#)

.....

*If you have any questions about the ZINBRYTA REMS Program
or need help enrolling, call **1-800-456-2255**.*

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ZINBRYTA REMS Program: For Pharmacies

Pharmacies

The requirements for dispensing ZINBRYTA (daclizumab)
ZINBRYTA is not available to all pharmacies. If you have any questions about the ZINBRYTA REMS Program or how to obtain ZINBRYTA, call 1-800-456-2255.

Please complete this **2-step process** to dispense ZINBRYTA.

Step 1. Become certified:

Complete the certification process before you are authorized to dispense ZINBRYTA

- 1. Designate** an authorized representative for the pharmacy. He or she will need to review the ZINBRYTA REMS Program Overview and will oversee implementation and ensure compliance with the ZINBRYTA REMS Program requirements. Download the:
 [ZINBRYTA REMS Program Overview](#)
- 2. Have the authorized representative complete** the ZINBRYTA REMS Program Pharmacy Enrollment Form. Download the:
 [ZINBRYTA REMS Program Pharmacy Enrollment Form](#)
- 3. Submit** the completed form to the ZINBRYTA REMS Program. Completed forms should be faxed to the ZINBRYTA REMS Program at **1-855-474-3067**, or mailed to the ZINBRYTA REMS Program at **5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709**. You will be contacted by the ZINBRYTA REMS Program to complete certification.
- 4. Have the authorized representative ensure** that all relevant staff involved in the dispensing of ZINBRYTA are trained on the ZINBRYTA REMS Program requirements and that a record of training is maintained by the pharmacy.

Step 2. Dispense ZINBRYTA to authorized patients:

Ensure compliance with the ZINBRYTA REMS Program requirements

- Before dispensing each dose, **verify** that the prescriber is certified and the patient is authorized to receive ZINBRYTA by calling the ZINBRYTA REMS Program at **1-800-456-2255**. **Do not dispense more than a one month supply per patient.**
- Ensure** that the pharmacy complies with the procedures required by the ZINBRYTA REMS Program:
 - **Report** any adverse events suggestive of hepatic injury including autoimmune hepatitis, and other immune-mediated disorders to the ZINBRYTA REMS Program at **1-800-456-2255**. You may be contacted for more information about these events.
 - **Maintain** appropriate documentation that all processes and procedures are in place and are being followed so that it can be provided upon request to Biogen, the FDA, or a third party acting on behalf of Biogen or the FDA.
 - **Comply** with potential audits conducted by Biogen, FDA, or a third party acting on behalf of Biogen or the FDA to ensure that all processes and procedures are in place and are being followed.
- Recertify** in the ZINBRYTA REMS Program if a new authorized representative is designated by completing and submitting the ZINBRYTA REMS Program Pharmacy Enrollment Form.

Adobe® Reader® is required to view all of these PDFs. If you do not have it installed, download it free [here](#).

If you have any questions about the ZINBRYTA REMS Program or need help enrolling, call 1-800-456-2255.

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ZINBRYTA REMS Program: For Patients

Patients

The requirements for receiving treatment with ZINBRYTA (daclizumab)
Work with your doctor to complete this **2-step process** so you can start treatment on ZINBRYTA.

Step 1. Complete enrollment:

Enroll, understand the risks, and complete liver testing before starting treatment [>](#)

Step 2. Continue treating your relapsing MS:

Complete monthly liver testing before your next dose and report side effects [>](#)

.....

*If you have any questions about the ZINBRYTA REMS Program
or need help enrolling, call **1-800-456-2255**.*

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ZINBRYTA REMS Program: For Patients

Patients

The requirements for receiving treatment with ZINBRYTA (daclizumab)
Work with your doctor to complete this 2-step process so you can start treatment on ZINBRYTA.

Step 1. Complete enrollment:

Enroll, understand the risks, and complete liver testing before starting treatment

- 1. Discuss** the following with your doctor and make sure you understand:
 - The risks of ZINBRYTA including serious liver problems that may lead to death and immune system problems.
 - The baseline liver testing required before your first dose and monthly liver testing required before your next dose.

.....

- 2. Receive and read** the ZINBRYTA REMS Program Patient Guide and the ZINBRYTA REMS Program Patient Wallet Card.
 - The ZINBRYTA REMS Program Patient Guide is your comprehensive guide to understanding treatment with ZINBRYTA.
 - The ZINBRYTA REMS Program Patient Wallet Card, which is provided for you to carry during treatment and for up to 6 months after stopping treatment, can be shared with your other doctors.Download the:
 -  ZINBRYTA REMS Program Patient Guide
 -  ZINBRYTA REMS Program Patient Wallet Card

.....

- 3. Complete** the ZINBRYTA REMS Program Patient Enrollment Form with your doctor who will provide you with a copy of this form. You can expect to be contacted by the ZINBRYTA REMS Program.

.....

- 4. Complete** baseline liver testing before your first dose to ensure ZINBRYTA is safe for you to use, as guided by your doctor. You can expect to be contacted by the ZINBRYTA REMS Program each month to remind you to complete your lab tests.

Step 2. Continue treating your relapsing MS:

Complete monthly liver testing before your next dose and report side effects

- 1. Complete** your monthly liver testing before your next dose during treatment with ZINBRYTA and for 6 months after you discontinue treatment with ZINBRYTA.

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- 2. Inform** your doctor of any side effects, reactions, or symptoms you experience after receiving ZINBRYTA.

.....

- 3. Carry** your ZINBRYTA REMS Program Patient Wallet Card and tell any of your other doctors that you have been treated with ZINBRYTA.

.....

- 4. Notify** the ZINBRYTA REMS Program right away if you change your ZINBRYTA doctor, if your contact information changes, or if you discontinue treatment with ZINBRYTA.

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If you have any questions about the ZINBRYTA REMS Program or need help enrolling, call 1-800-456-2255.

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ZINBRYTA REMS Program: Forms and Resources

Below are downloadable forms required to become certified and enrolled in the ZINBRYTA (daclizumab) REMS Program.

Prescribers

Materials for Prescribers

[Click here](#) to learn more about these resources. Download the:

- Prescriber Education and Certification**
 - [ZINBRYTA Prescribing Information](#)
 - [ZINBRYTA REMS Program Overview](#)
 - [ZINBRYTA REMS Program Prescriber Training](#)
 - [ZINBRYTA REMS Program Prescriber Knowledge Assessment](#)
 - [ZINBRYTA REMS Program Prescriber Enrollment Form](#)
 - [ZINBRYTA REMS Program Letter for Healthcare Providers](#)
- Patient Enrollment**
 - [ZINBRYTA REMS Program Patient Enrollment Form](#)
- Continuing Enrolled Patients on Treatment**
 - [ZINBRYTA REMS Program Patient Status Form](#)

Pharmacies

Materials for Pharmacies

[Click here](#) to learn more about these resources. Download the:

- [ZINBRYTA REMS Program Overview](#)
- [ZINBRYTA REMS Program Pharmacy Enrollment Form](#)

Patients

Materials for Patient Counseling

[Click here](#) to learn more about these resources. Download the:

- [ZINBRYTA REMS Program Patient Guide](#)
- [ZINBRYTA REMS Program Patient Wallet Card](#)

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ZINBRYTA REMS Program

5000 Davis Drive
PO Box 13919
Research Triangle Park, NC 27709
Phone: 1-800-456-2255
Fax: 1-855-474-3067

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ZINBRYTA REMS Program

What is the ZINBRYTA (daclizumab) Risk Evaluation and Mitigation Strategy (REMS) Program?

A REMS is a strategy to manage known or potential serious risks associated with a drug product and is required by the FDA to ensure the benefits of a drug outweigh its risks. Due to the risks of severe liver injury, including life-threatening events, liver failure, and autoimmune hepatitis, and other immune-mediated disorders such as skin reactions, lymphadenopathy, and non-infectious colitis, ZINBRYTA is available only through a restricted program called the ZINBRYTA REMS Program.

 Close

You are now leaving the ZINBRYTA[®] (daclizumab) REMS Program website.

[Cancel](#) [CONTINUE >](#)

Prescribers:

1. Become certified by completing a one-time certification process.
2. As you start patients on ZINBRYTA, counsel and enroll them into the ZINBRYTA REMS Program, complete the prescription, and order and evaluate baseline liver testing.
3. Perform ongoing patient monitoring, evaluate monthly liver testing before each patient's next dose, and complete the ZINBRYTA REMS Program Patient Status Forms for each patient every 90 days during treatment and every 90 days for 6 months after discontinuation of ZINBRYTA.

Pharmacies:

1. Designate an authorized representative, become certified, and recertify if there is a change in the authorized representative.
2. Train staff and comply with REMS requirements.
3. Before dispensing each dose, verify prescriber is certified and patient is authorized to receive ZINBRYTA, and dispense no more than a one month supply.

Patients:

1. Understand the risks associated with ZINBRYTA.
2. Enroll in the ZINBRYTA REMS Program by completing the ZINBRYTA REMS Program Patient Enrollment Form with your doctor.
3. Complete baseline liver testing before your first dose and monthly liver testing before your next dose of ZINBRYTA. A monthly reminder will be sent from the ZINBRYTA REMS Program for liver testing.

**ZINBRYTA is not available to all pharmacies. If you have any questions about the ZINBRYTA REMS Program or need help enrolling, call 1-800-456-2255.*

Indication

ZINBRYTA is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of ZINBRYTA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ALICE HUGHES
11/01/2017