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NDA 022549

ADASUVE® (loxapine) Inhalation Powder

Galen Limited

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the Adasuve REMS is to mitigate the risk of negative outcomes (respiratory distress or respiratory arrest) associated with Adasuve induced bronchospasm by:

- Ensuring that Adasuve is dispensed only in certified healthcare settings that have immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. Healthcare settings must have a short-acting bronchodilator (e.g. albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.
- Informing healthcare professionals about the serious risks associated with Adasuve, that Adasuve is contraindicated in patients with lung diseases and other conditions associated with bronchospasm, and how to monitor patients given Adasuve.

II. REMS ELEMENTS

A. Elements to Assure Safe Use

1. Adasuve will only be dispensed to patients in healthcare settings that are certified.
 - a. To become certified to dispense Adasuve, each healthcare setting must:
 - i. Designate an authorized representative to complete the certification process by submitting the completed *Healthcare Facility Enrollment Information and Form* on behalf of the healthcare setting.

- ii. Ensure that the authorized representative oversees implementation and compliance with the Adasuve REMS Program requirements by the following:
 - 1) Ensure all relevant staff involved in the prescribing, dispensing, administration and monitoring of Adasuve are trained on the Adasuve REMS Program requirements as described in the *Healthcare Provider Brochure, Steps for Safe Use of Adasuve, Order Set / Protocol Template* and *Adasuve Education Program*, and a record of training is maintained.
 - 2) Put processes and procedures in place to ensure the following requirements are completed prior to dispensing and administering Adasuve:
 - a. The healthcare setting is equipped with the necessary supplies and personnel to manage acute bronchospasm and ready access to emergency response services. Healthcare settings must have a short-acting bronchodilator (e.g. albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.
 - b. Screen patients prior to treatment with Adasuve, for a current diagnosis or history of asthma, chronic obstructive pulmonary disease (COPD) or other lung disease associated with bronchospasm, acute respiratory signs/symptoms (e.g. wheezing), and current use of medications to treat airways disease such as asthma or COPD.
 - c. Examine patients (including chest auscultation) for respiratory abnormalities.
 - d. Monitor patients at least every 15 minutes for a minimum of one hour following treatment with Adasuve for symptoms and signs of bronchospasm (i.e., vital signs and chest auscultation).
 - e. Limit administration of Adasuve to a single dose per patient within a 24-hour period.
 - f. Adasuve is not dispensed for use outside of the authorized representative's certified healthcare setting.
 - g. Do not sell, loan, or transfer any Adasuve inventory to any other pharmacy, institution, distributor, or prescriber.

- 3) Report any adverse events of bronchospasm that require emergency response services, in addition to any fatalities that occur following Adasuve treatment. To report suspected adverse events contact Adasuve Medical Information at 800-284-0062 or email customer.services@galen-pharma.com. Adverse events may also be reported to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch/report.htm.
 - 4) Maintain appropriate documentation that all processes and procedures are in place and are being followed for the Adasuve REMS Program and provide such documentation upon request to Galen, FDA, or a third party acting on behalf of Galen or FDA.
 - 5) Comply with audits by Galen, FDA, or a third party acting on behalf of Galen or FDA to ensure that all training, processes and procedures are in place and are being followed for the Adasuve REMS Program.
- b. As a condition of certification:
- i. The certified healthcare settings must recertify in the Adasuve REMS Program within three years from the date of initial certification, every three years thereafter, and if the healthcare setting designates a new authorized representative.
- c. Galen must:
- i. Ensure that healthcare settings that dispense Adasuve are certified, in accordance with the requirements described above.
 - ii. Provide all the following mechanisms for healthcare settings to complete enrollment for the Adasuve REMS Program: online, by e-mail, and by fax.
 - iii. Ensure that the *Adasuve REMS Education Program* will be available as an in-service or online.
 - iv. Ensure that the healthcare settings are notified when they have been certified by the Adasuve REMS Program.
 - v. Verify every three years that the authorized representative's name and contact information correspond to those of the current designated authorized representative for the certified healthcare setting. If different, the healthcare setting must be required to re-certify with a new authorized representative.

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

- *Healthcare Facility Enrollment Information and Form*

- *Healthcare Provider Brochure*
 - *Steps for Safe Use of ADASUVE*
 - *Order Set / Protocol Template*
 - *ADASUVE Education Program*
 - *ADASUVE REMS Website (www.adasuverems.com)*
2. Adasuve must be dispensed to patients only in certain healthcare settings specifically healthcare settings that have immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. Healthcare settings must have a short-acting bronchodilator (e.g. albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.

Galen must ensure that Adasuve must only be available to be dispensed in healthcare settings that have immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. Healthcare settings must have a short-acting bronchodilator (e.g. albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.

B. Implementation System

1. Galen must ensure that Adasuve is only distributed to certified healthcare settings by:
 - a. Ensuring that wholesalers/distributors who distribute Adasuve comply with program requirements for wholesalers/distributors. The wholesalers/distributors must:
 - i. Put processes and procedures in place to verify, prior to distributing Adasuve, that the healthcare settings are certified.
 - ii. Train all relevant staff on the Adasuve REMS Program requirements.
 - iii. Comply with audits by Galen, FDA, or a third party acting on behalf of Galen or FDA to ensure that all processes and procedures are in place and are being followed for the Adasuve REMS Program. In addition, wholesalers/distributors must maintain appropriate documentation and make it available for audits.
 - iv. Provide distribution data to Galen to verify compliance with the REMS.
 - b. Ensuring that wholesalers/distributors maintain distribution records of all shipments of Adasuve and provide the data to Galen.
2. Galen must monitor distribution data to ensure all the processes and procedures are in place and functioning to support the requirements of the Adasuve REMS Program.

3. Galen must audit the wholesalers/distributors within one year after the wholesaler/distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the Adasuve REMS Program. Thereafter, at least one wholesaler/distributor must be audited every calendar year. Corrective action must be instituted by Galen if noncompliance is identified.
4. Galen must maintain a validated, secure database of healthcare settings that are certified to dispense Adasuve in the Adasuve REMS Program. Ensure wholesalers/distributors are provided access to the database of certified healthcare settings.
5. Galen must maintain records of Adasuve distribution and dispensing, certified health care settings, and authorized wholesalers/distributors to meet REMS requirements.
6. Galen must maintain a Adasuve REMS Program Call Center (855-755-0492) and Adasuve REMS Program Website (www.adasuverems.com). The REMS Program Website must include the capability to review the *Adasuve Education Program* online, complete healthcare setting certification online, and the option to print the PI and Adasuve REMS materials. The Adasuve product website must include a prominent REMS-specific link to Adasuve REMS Program Website.
7. Galen must ensure that within 60 calendar days of approval of the REMS modification, the Adasuve REMS Program Website is fully operational and the REMS materials listed in or appended to the Adasuve REMS document are available through the Adasuve REMS Program Website and by calling the Adasuve REMS Program Call Center.
8. Galen must monitor on an ongoing basis the certified healthcare settings to ensure the requirements of the Adasuve REMS Program are being met. Galen must institute corrective action if noncompliance is identified and decertify healthcare settings that do not maintain compliance with the REMS requirements.
9. Galen must audit 10% of the certified healthcare settings annually to ensure that all processes and procedures are in place and functioning to support the requirements of the Adasuve REMS Program. Galen must institute corrective action if noncompliance is identified.
10. Galen must take reasonable steps to improve implementation of and compliance with the requirements in the Adasuve REMS Program based on monitoring and evaluation of the Adasuve REMS Program.

III. TIMETABLE FOR SUBMISSION OF ASSESSMENTS

The sponsor must submit REMS assessments to the FDA at 6 and 12 months, and then annually from the date of the initial approval of the REMS (12/21/2012). 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. Galen must submit each assessment so that it will be received by the FDA on or before the due date.

HOW TO ENROLL IN THE ADASUVE® REMS PROGRAM (Risk Evaluation and Mitigation Strategy)



HEALTHCARE FACILITY ENROLLMENT INFORMATION

ADASUVE is only distributed to certified healthcare settings (HCS) through a restricted distribution system. A healthcare facility (HCF) that wants to administer ADASUVE must enroll in the ADASUVE REMS Program to order and receive ADASUVE.

3 STEPS TO HEALTHCARE FACILITY ENROLLMENT

For each healthcare facility, an **authorized healthcare facility representative** is required to complete and sign the *Healthcare Facility Enrollment Form* acknowledging that the enrolled HCF meets specific requirements. This representative may be a pharmacist, or another healthcare professional with the appropriate level of responsibility within the healthcare facility, who is authorized to act on behalf of the facility.

REVIEW	COMPLETE AND SIGN	SUBMIT
<p>The authorized healthcare facility representative must review the following:</p> <ul style="list-style-type: none">• <i>Healthcare Facility Enrollment Form</i> to become familiar with the enrollment requirements for healthcare facilities• <i>ADASUVE REMS Education Program</i> to become familiar with the safe use conditions for ADASUVE	<p>The healthcare facility representative completes the <i>Healthcare Facility Enrollment Form</i> online at www.adasuverems.com/enrollment, or prints the form and then completes and signs it.</p> <p>By signing the form, the representative is attesting that the healthcare facility will meet all the ADASUVE REMS Program requirements prior to ordering ADASUVE.</p>	<p>If the form was completed online, follow the instructions to submit online.</p> <p>OR</p> <p>Submit completed, signed form via fax at: 855-755-0493</p> <p>OR</p> <p>Scan completed, signed form and submit via e-mail at: Enrollment@ AdasuveREMSProgram.com</p>

Note Healthcare facilities must re-enroll every 3 years. You will be notified by fax or e-mail 60 days prior to your re-enrollment date.

ORDERING ADASUVE®

- Once the completed enrollment form is received by the ADASUVE REMS Program, it will be entered into the ADASUVE REMS Program database, which is a secured database and is accessed only by the wholesaler/distributor and Galen US Inc
- When you place an order for ADASUVE through your wholesaler/distributor, they will check the database to confirm that your healthcare facility is enrolled. Once enrollment is confirmed, the wholesaler/distributor is allowed to ship ADASUVE to your facility



Enrollment must be complete to order and receive ADASUVE from your wholesaler/distributor.

New Enrollment

Re-Enrollment (Required every 3 years)

To be enrolled in the ADASUVE REMS Program, complete this form and do one of the following:

Fax

855-755-0493 (Fax both pages)

Scan and e-mail to

Enrollment@AdasuveREMSProgram.com

Submit online at

www.adasuverems.com/enrollment

HEALTHCARE FACILITY INFORMATION

Healthcare Facility Name _____

Facility DEA or NPI Number _____

Facility Type Medical Hospital Psychiatric Hospital Other (describe) _____

Facility Address _____

City _____ State _____ ZIP _____

Phone _____ Fax _____

AUTHORIZED HEALTHCARE FACILITY REPRESENTATIVE INFORMATION

First Name _____ Last Name _____

Position/Title _____

Phone _____ Fax _____

E-mail _____

Preferred communication method E-mail Fax

HEALTHCARE FACILITY AGREEMENT

As an authorized representative for this facility, I acknowledge that:

- i. I am authorized to complete enrollment on behalf of this healthcare facility.
- ii. I have reviewed the ADASUVE REMS Education Program and understand that treatment with ADASUVE can cause bronchospasm that has the potential to lead to respiratory distress and respiratory arrest.
- iii. I understand that ADASUVE is contraindicated in patients with a current diagnosis or history of asthma, chronic obstructive pulmonary disease (COPD) or other lung disease associated with bronchospasm, and patients with acute respiratory signs/symptoms (e.g., wheezing) or who are taking medications to treat airways disease, such as asthma or COPD.

HEALTHCARE FACILITY AGREEMENT (cont'd)

- iv. This healthcare facility must be able to provide:
- Immediate access on site to supplies and personnel trained to manage acute bronchospasm, and ready access to emergency response services. This healthcare facility must have a short-acting bronchodilator (e.g., albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm
 - Medical/psychiatric (physicians, nurses, etc.) staff on site at all times (24 hours a day/7 days a week) trained to manage acute bronchospasm
- v. This healthcare facility must establish procedures, protocols and/or order sets that are subject to audit, to help ensure compliance with the safe use conditions required in the ADASUVE REMS including the following:
- Screening patients, prior to treatment with ADASUVE, for a current diagnosis or history of asthma, COPD and other lung disease associated with bronchospasm, acute respiratory signs or symptoms (e.g., wheezing), and current use of medications to treat airways disease such as asthma or COPD; and examine patients (including chest auscultation) for respiratory abnormalities
 - Monitoring patients at least every 15 minutes for a minimum of one hour following treatment with ADASUVE for signs or symptoms of bronchospasm (i.e., vital signs and chest auscultation)
 - Limiting administration of ADASUVE to a single dose per patient within a 24-hour period
- vi. This healthcare facility must train relevant staff (e.g., staff involved in prescribing, dispensing or administering ADASUVE and monitoring patients after ADASUVE administration) on the safe use of ADASUVE, as described in the ADASUVE REMS Education Program. This training and ongoing training must be documented and is subject to audit.
- vii. This healthcare facility must not dispense ADASUVE for outpatient use.
- viii. I understand this healthcare facility must renew its enrollment in the ADASUVE REMS Program within three years from the date of initial enrollment, and every three years thereafter.
- ix. I understand that this healthcare facility must not sell, loan or transfer any ADASUVE inventory to any other pharmacy, institution, distributor, or prescriber.
- x. The representative understands the importance of reporting events of bronchospasm that require emergency response services, in addition to any fatalities that occur following ADASUVE treatment. To report suspected adverse events, contact ADASUVE Medical Information at **800-284-0062** or email **customer.services@galen-pharma.com**. Adverse events may also be reported to FDA at **1-800-FDA-1088** or **www.fda.gov/medwatch/report.htm**.

I confirm that the information above is correct. I understand that this information will be used to document healthcare facilities that are eligible to receive ADASUVE. I also understand that this information may be shared with government agencies.

Authorized Healthcare Facility Representative (**Signature**)

Date

Authorized Healthcare Facility Representative (**Print**)

Title

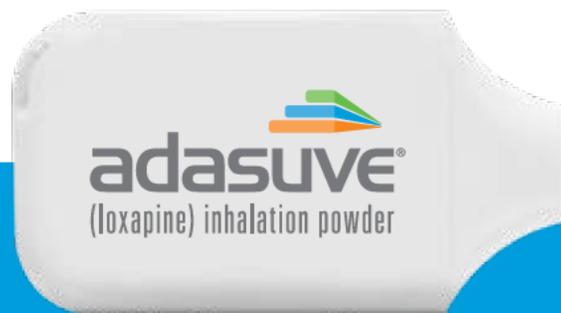
ADASUVE® (loxapine) Inhalation Powder

ADASUVE

Risk Evaluation and Mitigation Strategy (REMS) Program Healthcare Provider Brochure

This brochure includes information about:

- The risk of bronchospasm
- Recommendations for safe use of ADASUVE
- What to communicate to your patients
- Instructions for Healthcare Facility enrollment



Please share this Healthcare Provider Brochure with anyone in your healthcare setting involved in prescribing, dispensing, or administering ADASUVE or who monitors patients after treatment with ADASUVE.

Questions about ADASUVE?

Contact ADASUVE Medical Information at **800-284-0062**
or email customer.services@galen-pharma.com.

Please see Prescribing Information, including Boxed Warning.

About This Brochure

The Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of ADASUVE® outweigh the risk of bronchospasm that has the potential to lead to respiratory distress and respiratory arrest. Patients with asthma, chronic obstructive pulmonary disease (COPD), or other pulmonary diseases are at increased risk of bronchospasm after taking ADASUVE. This brochure contains information for providers on the risks and safe use of ADASUVE, as well as information on healthcare facility enrollment requirements of the ADASUVE REMS Program; ADASUVE can only be distributed to and administered in healthcare facilities that are enrolled in the ADASUVE REMS Program.

Indications and Usage

ADASUVE is a typical antipsychotic indicated for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults.

“Psychomotor agitation” is defined in DSM-IV as “excessive motor activity associated with a feeling of inner tension.” Patients experiencing agitation often manifest behaviors that interfere with their care (eg, threatening behaviors, escalating or urgently distressing behavior, self-exhausting behavior), leading clinicians to the use of rapidly absorbed antipsychotic medications to achieve immediate control of the agitation.

The efficacy of ADASUVE was established in one study of acute agitation in patients with schizophrenia and one study of acute agitation in patients with bipolar I disorder.

Limitations of Use:

As part of the ADASUVE REMS Program to mitigate the risk of bronchospasm, ADASUVE must be administered only in an enrolled healthcare facility.

Important Safety Information

Contraindications

ADASUVE® is contraindicated in patients with the following:

- Current diagnosis or history of asthma, COPD, or other lung disease associated with bronchospasm
- Acute respiratory symptoms or signs (eg, wheezing)
- Current use of medications to treat airways disease, such as asthma or COPD
- History of bronchospasm following ADASUVE treatment
- Known hypersensitivity to loxapine or amoxapine (eg, serious skin reaction)



Boxed Warning for ADASUVE®

WARNING: BRONCHOSPASM and INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Bronchospasm

ADASUVE can cause bronchospasm that has the potential to lead to respiratory distress and respiratory arrest.

Administer ADASUVE only in an enrolled healthcare facility that has immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. Facilities must have a short-acting bronchodilator (eg, albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.

Prior to administering ADASUVE, screen patients regarding a current diagnosis, history, or symptoms of asthma, COPD, and other lung diseases and examine (including chest auscultation) patients for respiratory signs. Monitor for signs and symptoms of bronchospasm following treatment with ADASUVE.

Restricted Use to Mitigate Bronchospasm

Because of the risk of bronchospasm, ADASUVE is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ADASUVE REMS. Under the ADASUVE REMS Program, healthcare facilities and distributors must enroll in the program.

Increased Mortality In Elderly Patients With Dementia-related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ADASUVE is not approved for the treatment of patients with dementia-related psychosis.

These risks do not constitute a complete list of all the risks associated with ADASUVE. Please see the enclosed Prescribing Information for more information regarding the risks associated with ADASUVE.

Steps for the Safe Use of ADASUVE®

This poster is available to enrolled healthcare facilities to reinforce how to use ADASUVE safely. Healthcare facilities are encouraged to post this where ADASUVE will be administered. Additional copies can be ordered at www.adasuverems.com or by calling 855-755-0492.

ADASUVE is indicated for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults.

ADASUVE can cause bronchospasm that has the potential to lead to respiratory distress and respiratory arrest. Patients with asthma, chronic obstructive pulmonary disease (COPD), or other lung disease associated with bronchospasm are at increased risk of bronchospasm.

Steps for Safe Use of ADASUVE	
 SCREEN	<ul style="list-style-type: none"> Ask if patient is taking medication to treat asthma or COPD and/or check medical records Ask if patient has a current diagnosis or history of asthma, COPD, or other lung disease, and/or check medical records Examine patients (including chest auscultation) for respiratory abnormalities (e.g., wheezing)
	<p>Do not use in patients with acute respiratory signs or symptoms; with a current diagnosis or history of asthma, COPD, or other lung disease associated with bronchospasm; or with current use of medications to treat airways disease, such as asthma or COPD</p>
	<ul style="list-style-type: none"> Counsel patient/caregiver on potential for bronchospasm that may occur after dosing and the need for them to report symptoms immediately
 MONITOR	<ul style="list-style-type: none"> Monitor patient every 15 minutes for at least 1 hour after treatment for signs and symptoms of bronchospasm including chest auscultation Ask patient every 15 minutes about any difficulty breathing
	<ul style="list-style-type: none"> Treat bronchospasm with an inhaled short-acting beta-agonist bronchodilator (e.g., albuterol) If medically necessary, provide additional therapy for bronchospasm per asthma guidelines
 If bronchospasm occurs MANAGE	

Reporting Adverse Events

Healthcare professionals should understand the importance of reporting events of bronchospasm that require emergency response services, in addition to any fatalities that occur following ADASUVE treatment. To report suspected adverse events, contact ADASUVE Medical Information at 800-284-0062 or email customer.services@galen-pharma.com. Adverse events may also be reported to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch/report.htm.



Patient Counseling

Discuss the risks associated with ADASUVE® therapy with patients and their caregivers, including the safe use of ADASUVE.

Helping Patients and Caregivers Understand the Risks

- Explain that in certain patients, ADASUVE may cause narrowing of the airways (bronchospasm) and may cause them to wheeze, cough, feel chest tightness, or have shortness of breath
- Ask patients to tell you if they are currently taking any medications to treat asthma, COPD, or a breathing problem or have a history of asthma, COPD, or other respiratory conditions
- Inform patients that other serious side effects may occur, such as neuroleptic malignant syndrome, tardive dyskinesia, orthostatic hypotension, or seizures
- Inform patients about other common side effects that may include dysgeusia (taste) and sleepiness

Helping Patients and Caregivers Report the Signs and Symptoms of Bronchospasm

- Ask patients to tell you immediately if they experience difficulty breathing or feel chest tightness or wheezing after they have received a treatment
- Tell patients you have a medicine available to treat any breathing problems that might occur

ADASUVE is provided with a Medication Guide. If practical, please review the Medication Guide with your patient or their caregiver before administering the product.

About ADASUVE®

Administration of ADASUVE

- ADASUVE is only administered by oral inhalation
- ADASUVE must be administered only by a healthcare professional, in an enrolled healthcare facility
- Administer only a single dose per patient within a 24-hour period

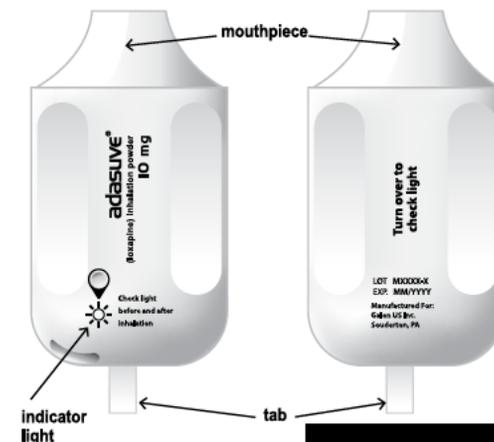
Required Examination Prior to Dosing

Prior to administering ADASUVE, screen all patients for current use of medications to treat asthma or COPD, a history of asthma, COPD, or other lung disease, and examine patients (including chest auscultation) for respiratory abnormalities (eg, wheezing).

Becoming Familiar With ADASUVE

- ADASUVE is provided in a sealed pouch
- The indicator light is off when ADASUVE is removed from the pouch
- The indicator light turns on (green) when the tab is pulled out. The inhaler is then ready for use
- The indicator light turns off after the patient inhales. This indicates that the dose has been delivered
- If the indicator light does NOT turn off, the dose has NOT been delivered. See Instructions for Use

The pictures below show the important features of the ADASUVE product (both sides shown).



Important Administration Instructions



1. Open the pouch.

When ready to use, tear open the foil pouch and remove the inhaler from the package.

When the ADASUVE® inhaler is removed from the pouch, the indicator light is off.



2. Pull tab.

Firmly pull the plastic tab from the rear of the inhaler. Check that the green light turns on. This indicates that the inhaler is ready for use. Use the inhaler within 15 minutes after removing the tab to prevent automatic deactivation of the inhaler. The green light will turn off, indicating that the inhaler is not usable. Discard the inhaler after one use.

3. Explain procedures to the patient.

Explain the administration procedures to the patient prior to use, and advise the patient that it is important to follow the instructions. Inform the patient that the inhaler may produce a flash of light and a clicking sound, and it may become warm during use. These are normal.



4. Instruct the patient to exhale.

Instruct the patient to hold the inhaler away from the mouth and breathe out fully to empty the lungs.



5. Instruct the patient to inhale.

Instruct the patient to put the mouthpiece of the inhaler between the lips, close the lips, and inhale through the mouthpiece with a steady deep breath. Check that the green light turns off indicating that the dose has been delivered.



6. Instruct the patient to hold breath.

Instruct the patient to remove the mouthpiece from the mouth and hold the breath for as long as possible, up to 10 seconds.

IMPORTANT

If the green light remains on after the patient inhales, the dose of ADASUVE has NOT been delivered. Instruct the patient to repeat Step 4, Step 5, and Step 6 up to 2 additional times. If the green light still does not turn off, discard the inhaler and use a new one.

Monitoring to Assess Safety

Monitor the patient for signs and symptoms of bronchospasm after ADASUVE administration. Perform a physical examination, including chest auscultation, at least every 15 minutes for at least 1 hour after ADASUVE administration.

Prescribing and Administering ADASUVE® at Your Healthcare Facility

- ADASUVE will be dispensed only to patients in certain healthcare facilities that are enrolled in the ADASUVE REMS Program
- Wholesalers/distributors will ship ADASUVE only to enrolled healthcare facilities

Healthcare Facility Qualifications for Enrollment

Each healthcare facility must be able to provide:

- Immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. This healthcare facility must have a short-acting bronchodilator (e.g., albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm
- Medical/psychiatric (physicians, nurses, etc) staff on site at all times (24 hours a day/7 days a week) trained to manage acute bronchospasm
- Procedures, protocols, and/or order sets to ensure the following:
 - Patients are screened, prior to treatment with ADASUVE, for a history of pulmonary disease and for acute respiratory signs and symptoms by physical exam, including taking vital signs and chest auscultation, and inquiring if patient is taking medication to treat asthma or COPD
 - Patients are monitored at least every 15 minutes for a minimum of one hour following treatment with ADASUVE for signs and symptoms of bronchospasm, including taking vital signs and chest auscultation
 - Administration of ADASUVE is limited to 1 dose per patient within 24 hours
- Healthcare providers within the facility (prescribers, nurses, monitoring staff, or pharmacists) who are trained on safe use of ADASUVE using the ADASUVE REMS Education Program



Prescribing and Administering ADASUVE® at Your Healthcare Facility (cont'd)

Authorized Healthcare Facility Representative

For each healthcare facility, an *authorized healthcare facility representative* is required to review the [ADASUVE REMS Education Program](#), and complete and sign the [Healthcare Facility Enrollment Form](#) acknowledging that the enrolled healthcare facility meets specific requirements. This representative may be a pharmacist or another healthcare professional with the appropriate level of responsibility within the healthcare facility, who is authorized to act on behalf of the facility.

To enroll your healthcare facility, please read and complete the Healthcare Facility Enrollment Form that is available at www.adasuverems.com.

For questions about the ADASUVE REMS Program, please call 855-755-0492.

ADASUVE® REMS Materials for Enrolled Healthcare Facilities

The following materials are part of the ADASUVE REMS Program and will assist enrolled healthcare facilities in complying with ADASUVE REMS requirements. They are available to review, order, or print at www.adasuverems.com or by calling 855-755-0492.

1. ADASUVE REMS Education Program

Must be reviewed by all healthcare providers within an enrolled healthcare facility who will be prescribing or administering ADASUVE, or observing patients after ADASUVE is administered.

2. Steps for Safe Use of ADASUVE Poster

Should be posted where ADASUVE is administered within enrolled healthcare facilities.

3. Order Set/Protocol Template

For use by enrolled healthcare facilities to assist with designing procedures, protocols, and/or order sets that meet the requirements of the ADASUVE REMS Program.

4. ADASUVE Healthcare Provider Brochure

Contains information for providers on the risks and safe use of ADASUVE, as well as information on healthcare facility enrollment requirements of the ADASUVE REMS Program.

Other resources are available at www.adasuverems.com

- Healthcare Facility Enrollment Information and Form
- Prescribing Information
- ADASUVE Instructions for Use
- ADASUVE Medication Guide

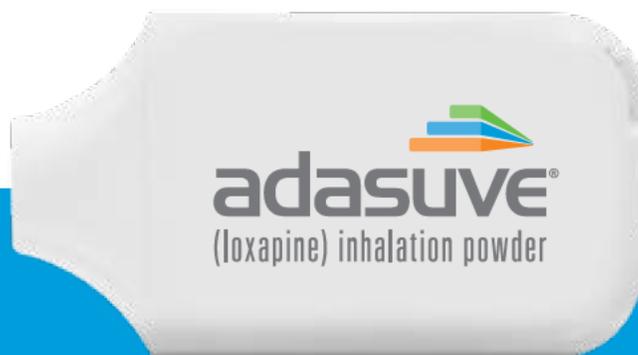


Reporting Adverse Events

Healthcare professionals should report suspected adverse events associated with ADASUVE® treatment to ADASUVE Medical Information at **800-284-0062** or email **customer.services@galen-pharma.com**. In addition, adverse events may be reported to the FDA MedWatch Reporting System by the following methods:

- Online at **www.fda.gov/medwatch/report.htm**
- Phone at **1-800-FDA-1088**
- Fax at **1-800-FDA-0718**, using the MedWatch Form 3500 (available at **www.fda.gov/medwatch/getforms.htm**)

The Prescribing Information and Medication Guide are also available from your local sales representative or by calling **800-284-0062** or email **customer.services@galen-pharma.com**.



Please share this Healthcare Provider Brochure with anyone in your healthcare facility who is involved in prescribing, dispensing, or administering ADASUVE or who monitors patients after treatment with ADASUVE.

Please see Prescribing Information, including Boxed Warning.



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PMR-JUN-2017-0014. August 2017.

Steps for Safe Use of ADASUVE®

ADASUVE is indicated for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults.

ADASUVE can cause bronchospasm that has the potential to lead to respiratory distress and respiratory arrest. Patients with asthma, chronic obstructive pulmonary disease (COPD), or other lung disease associated with bronchospasm are at increased risk of bronchospasm.



Steps for Safe Use of ADASUVE	
 SCREEN	<ul style="list-style-type: none"> <input type="checkbox"/> Ask if patient is taking medication to treat asthma or COPD and/or check medical records <input type="checkbox"/> Ask if patient has a current diagnosis or history of asthma, COPD, or other lung disease, and/or check medical records <input type="checkbox"/> Examine patients (including chest auscultation) for respiratory abnormalities (e.g., wheezing) <input type="checkbox"/> Do not use in patients with acute respiratory signs or symptoms; with a current diagnosis or history of asthma, COPD, or other lung disease associated with bronchospasm; or with current use of medications to treat airways disease, such as asthma or COPD
 COUNSEL	<ul style="list-style-type: none"> <input type="checkbox"/> Counsel patient/caregiver on potential for bronchospasm that may occur after dosing and the need for them to report symptoms immediately
 MONITOR	<ul style="list-style-type: none"> <input type="checkbox"/> Monitor patient every 15 minutes for at least 1 hour after treatment for signs and symptoms of bronchospasm including chest auscultation <input type="checkbox"/> Ask patient every 15 minutes about any difficulty breathing
 If bronchospasm occurs MANAGE	<ul style="list-style-type: none"> <input type="checkbox"/> Treat bronchospasm with an inhaled short-acting beta-agonist bronchodilator (e.g., albuterol) <input type="checkbox"/> If medically necessary, provide additional therapy for bronchospasm per asthma guidelines

Phone 855-755-0492 Fax 855-755-0493 www.adasuverems.com



ORDER SET/PROTOCOL TEMPLATE



This template is to be used as a guideline for developing procedures, protocols, and/or order sets around the use of ADASUVE® to ensure that REMS requirements are being met.

INDICATION

- Agitation associated with bipolar I disorder
- Agitation associated with schizophrenia

PATIENT SCREENING

PRIOR TO DOSING:

Assess for acute respiratory symptoms

- wheezing cough
- dyspnea other: _____

Assess for respiratory signs
(include chest auscultation)

- wheezing other: _____

Inquire and/or check medical records for:

- current diagnosis or history of asthma, COPD, or other lung disease associated with bronchospasm
- current use of medications to treat airways disease, such as asthma or COPD
- history of bronchospasm following ADASUVE treatment
- known hypersensitivity (e.g., serious skin reaction) to loxapine or amoxapine

If any of the above screening is positive, DO NOT USE ADASUVE. ADASUVE is contraindicated in these patients.

DOSE ADMINISTERED

TIME: _____

Limit ADASUVE use to a single dose per patient within a 24-hour period.

POST-TREATMENT OBSERVATION/MONITORING

Patient must be monitored every 15 minutes for at least 1 hour after treatment for signs/symptoms of bronchospasm.

MONITORING

TIME: _____

- Heart rate (rate per minute): _____
- Respiratory rate (rate per minute): _____
- Chest auscultation (clear/other) _____
- Check for respiratory signs/symptoms
 - wheezing cough
 - dyspnea chest tightness
 - other: _____

TIME: _____

- Heart rate (rate per minute): _____
- Respiratory rate (rate per minute): _____
- Chest auscultation (clear/other) _____
- Check for respiratory signs/symptoms
 - wheezing cough
 - dyspnea chest tightness
 - other: _____

TIME: _____

- Heart rate (rate per minute): _____
- Respiratory rate (rate per minute): _____
- Chest auscultation (clear/other) _____
- Check for respiratory signs/symptoms
 - wheezing cough
 - dyspnea chest tightness
 - other: _____

TIME: _____

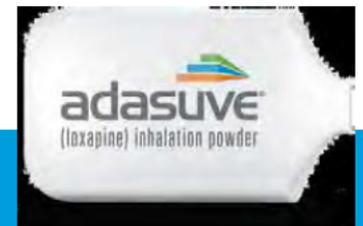
- Heart rate (rate per minute): _____
- Respiratory rate (rate per minute): _____
- Chest auscultation (clear/other) _____
- Check for respiratory signs/symptoms
 - wheezing cough
 - dyspnea chest tightness
 - other: _____

Note: Treat bronchospasm with inhaled short-acting beta-agonist bronchodilator (e.g., albuterol) and other measures as clinically indicated.

ADASUVE[®] **(LOXAPINE) INHALATION POWDER**

EDUCATION PROGRAM for HEALTHCARE PROFESSIONALS

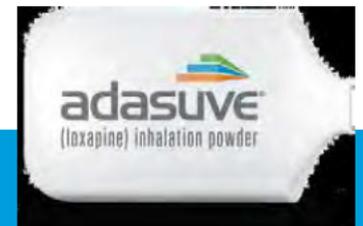
August 2017



ADASUVE[®] Risk Evaluation and Mitigation Strategy (REMS) Education Program Content

At the end of this education program, you should understand:

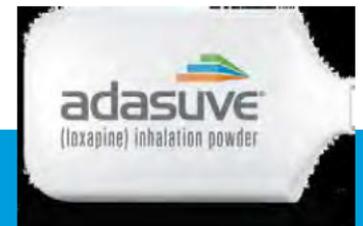
- ADASUVE REMS Program Requirements
- ADASUVE Product Information
 - Indication
 - Dose
- Important Safety Information
 - Risk of bronchospasm with ADASUVE
 - Use of albuterol rescue treatment to treat bronchospasm in asthma and COPD patients
 - Decreased forced expiratory volume in 1 second (FEV₁) in asthma and COPD patients
 - Safety of ADASUVE in agitation trials
 - Administer only a single dose of ADASUVE per patient within any 24-hour period



ADASUVE[®] Risk Evaluation and Mitigation Strategy (REMS) Education Program Content

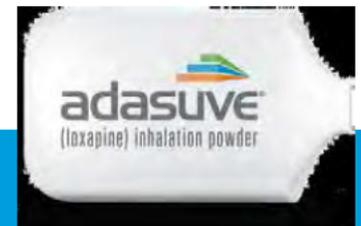
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- How to use ADASUVE safely
 - Appropriate patient selection
 - Dosage and administration
 - Observation and management of patient
- How to enroll in the ADASUVE REMS Program



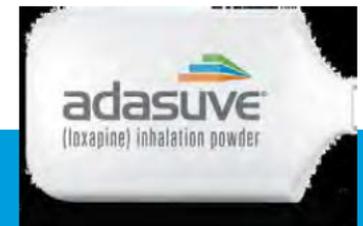
ADASUVE[®] REMS Program

- The purpose of the ADASUVE REMS Program is to mitigate the risk of bronchospasm that has the potential to lead to respiratory distress and respiratory arrest
- To mitigate the risk, the ADASUVE REMS Program requires that ADASUVE is administered only in enrolled healthcare facilities:
 - With immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services
- The REMS Program will inform healthcare professionals about:
 - The risk of bronchospasm after ADASUVE administration
 - Appropriate patient selection
 - Monitoring patients after ADASUVE administration
 - Management of ADASUVE-induced bronchospasm



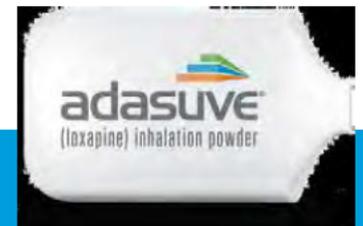
Risk of Bronchospasm

- ADASUVE[®] can cause bronchospasm that has the potential to lead to respiratory distress and respiratory arrest
- Administer ADASUVE only in an enrolled healthcare facility that has:
 - Immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. This healthcare facility must have a short-acting bronchodilator (e.g., albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm
 - Medical/psychiatric (physicians, nurses, etc.) staff on site at all times (24 hours a day/7 days a week) trained to manage acute bronchospasm
- Prior to administering ADASUVE, ask patients regarding:
 - A history or symptoms of asthma, COPD, and other lung diseases
 - Examine (including chest auscultation) patients for respiratory abnormalities (e.g., wheezing)
- Following treatment with ADASUVE, monitor for signs and symptoms of bronchospasm



Contraindications

- ADASUVE® is contraindicated in patients with the following:
 - Current diagnosis or history of asthma, COPD, or other lung disease associated with bronchospasm
 - Acute respiratory signs or symptoms (e.g., wheezing)
 - Current use of medications to treat airways disease, such as asthma or COPD
 - History of bronchospasm following ADASUVE treatment
 - Hypersensitivity to loxapine or amoxapine (e.g., serious skin reaction)



ADASUVE[®]: Product Information

ADASUVE is a typical antipsychotic indicated for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults.

- The efficacy of ADASUVE was established in one study of acute agitation in patients with schizophrenia and one study of acute agitation in patients with bipolar I disorder

Dosing and Administration

- ADASUVE is a single-use disposable product that delivers an aerosol of loxapine in a single inhalation
 - ADASUVE is administered only by oral inhalation
 - ADASUVE must be administered only by a healthcare professional, in an enrolled healthcare facility
 - Recommended dose of ADASUVE is 10 mg
 - Only a single dose per patient should be administered in any 24-hour period



Pulmonary Safety Studies in Patients With Asthma and COPD

Albuterol Rescue Treatment After Administration of ADASUVE®

- Dedicated pulmonary safety studies were performed in subjects with mild-to-moderate persistent asthma or mild-to-severe COPD
- After receiving ADASUVE (Dose 1 and Dose 2):
 - 54% of patients with asthma required treatment with albuterol to treat pulmonary adverse events
 - 23% of patients with COPD required treatment with albuterol

Do not use in patients with acute respiratory signs and symptoms; with a current diagnosis or history of asthma, COPD and other lung disease associated with bronchospasm; or with current use of medications to treat airways disease, such as asthma or COPD.



Pulmonary Safety Studies in Patients With Asthma and COPD – Use of Rescue Albuterol

Asthma	Placebo (n=26)	ADASUVE® (n=26)
Number of subjects receiving albuterol rescue at any time	3/26 (12%)	14/26 (54%)
Number receiving rescue after Dose 1	1/26 (4%)	7/26 (27%)
Number receiving rescue after Dose 2	2/25 (8%)	7/17 (41%)
COPD	Placebo (n=27)	ADASUVE® (n=26)
Number of subjects receiving albuterol rescue at any time	4/27 (15%)	6/26 (23%)
Number receiving rescue after Dose 1	1/27 (4%)	2/26 (8%)
Number receiving rescue after Dose 2	3/26 (12%)	4/19 (21%)

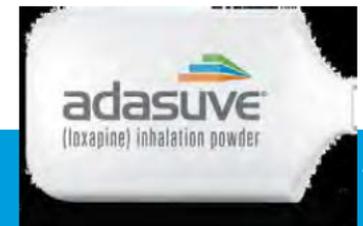


Pulmonary Safety Studies in Patients With Asthma and COPD

Decreased Forced Expiratory Volume in One Second (FEV₁) After ADASUVE® Administration

- Dedicated pulmonary safety studies were performed in subjects with mild-to-moderate persistent asthma or mild-to-severe COPD
- There were significantly more asthma and COPD patients who experienced a decrease in FEV₁ of >10%, >15%, and >20% in the ADASUVE-treated patients compared with the placebo-treated patients

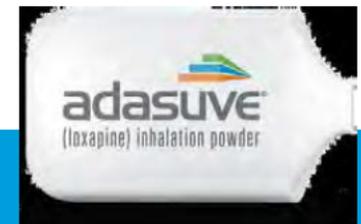
Do not use in patients with acute respiratory signs and symptoms; with a current diagnosis or history of asthma, COPD and other lung disease associated with bronchospasm; or with current use of medications to treat airways disease, such as asthma or COPD.



Maximum Decrease in FEV₁ from Baseline in Healthy Volunteer, Asthma, and COPD Trials

	Maximum % FEV ↓	Healthy Volunteer		Asthma		COPD	
		Placebo n (%)	ADASUVE n (%)	Placebo n (%)	ADASUVE n (%)	Placebo n (%)	ADASUVE n (%)
After Any Dose		n=26	n=26	n=26	n=26	n=27	n=25
	≥10	7 (27%)	7 (27%)	3 (12%)	22 (85%)	18 (67%)	20 (80%)
	≥15	1 (4%)	5 (19%)	1 (4%)	16 (62%)	9 (33%)	14 (56%)
	≥20	0	1 (4%)	1 (4%)	11 (42%)	3 (11%)	10 (40%)
After Dose 1		n=26	n=26	n=26	n=26	n=27	n=25
	≥10	4 (15%)	5 (19%)	2 (8%)	16 (62%)	8 (30%)	16 (64%)
	≥15	1 (4%)	2 (8%)	1 (4%)	8 (31%)	4 (15%)	10 (40%)
	≥20	0	0	1 (4%)	6 (23%)	2 (7%)	9 (36%)
After Dose 2		n=26	n=25	n=25	n=17	n=26	n=19
	≥10	5 (19%)	6 (24%)	3 (12%)	12 (71%)	15 (58%)	12 (63%)
	≥15	0	5 (20%)	1 (4%)	9 (53%)	6 (23%)	10 (53%)
	≥20	0	1 (4%)	1 (4%)	5 (30%)	1 (4%)	5 (26%)

FEV₁ categories are cumulative, ie, a subject with a maximum decrease of 21% is included in all 3 categories.
 Patients with a >20% decrease in FEV₁ did not receive a second dose of study drug.
 Dose 1 = time 0, Dose 2 = 10 hours after time 0



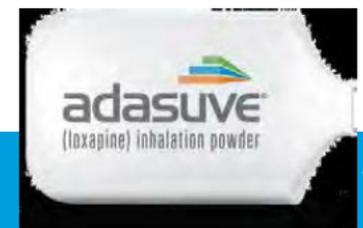
Pulmonary Safety Studies in Patients With Asthma and COPD

Increased Pulmonary Adverse Events after Dose 2 of ADASUVE®

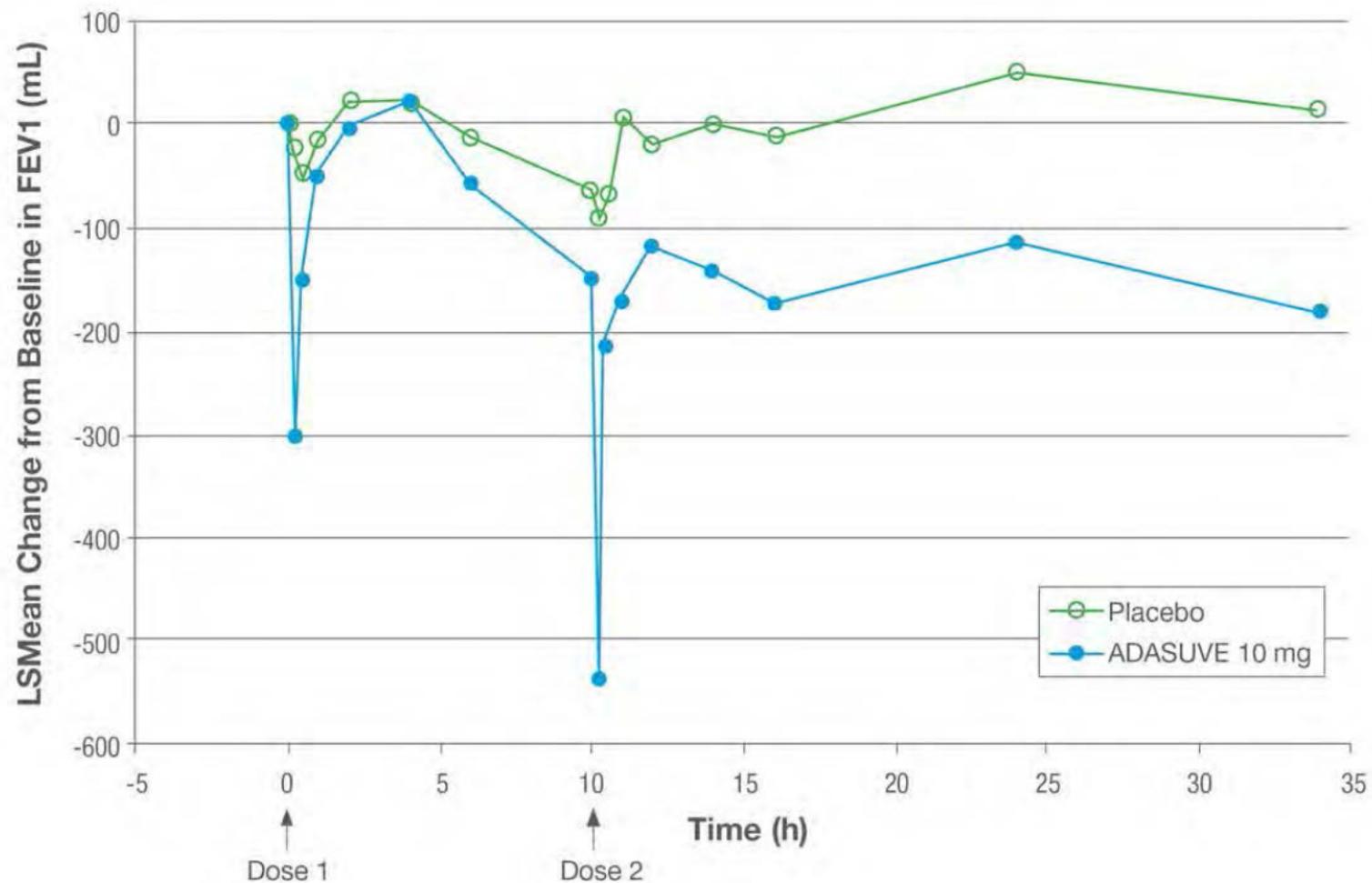
- A higher percentage of patients required albuterol treatment after Dose 2 compared with Dose 1 (Slide 9)
- A higher percentage of patients treated with ADASUVE had a decrease in FEV₁ after Dose 2 compared with Dose 1 (Slide 11)
- FEV₁s did not return to baseline up to 24 hours after administration of the second dose of ADASUVE (Slide 13)

ADASUVE may only be administered to a patient once in 24 hours.

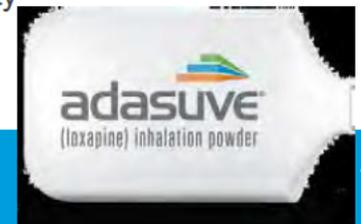
Healthcare facilities must have policies in place to limit administration of ADASUVE to a single dose per patient in a 24-hour period.



Mean Change From Baseline in FEV₁ in Patients With Asthma



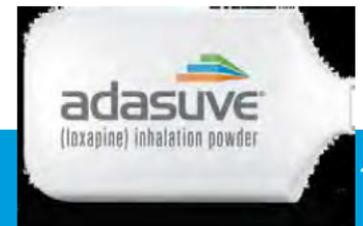
Subjects in the ADASUVE group who had a >20% decrease in FEV₁ or developed respiratory symptoms after the first dose did not receive a second dose of ADASUVE in the pulmonary safety studies. Therefore, 9 of 26 (35%) subjects in the asthma study did not receive a second dose.



Profile of Bronchospasm Occurring After a First Dose of ADASUVE[®] in Subjects With Asthma or COPD

In subjects who developed bronchospasm after a first dose of ADASUVE:

- Timing:
 - Symptoms occurred with a median time of 4 minutes in asthma subjects and 10 minutes in COPD subjects
 - In 11/12 subjects with asthma or COPD, symptoms began within 25 minutes
- Outcome:
 - When treatment was required, bronchospasm resolved with use of an inhaled bronchodilator (via metered-dose inhaler or nebulizer), without sequelae



Profile of Bronchospasm Occurring After a First Dose^a of ADASUVE[®] in Subjects With Asthma or COPD

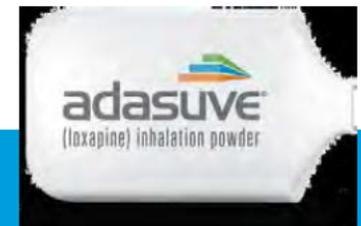
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In subjects who developed bronchospasm after a first dose of ADASUVE:

- Albuterol was used by:
 - 7/26 (26.9%) asthma subjects after ADASUVE 10 mg, compared with 1/26 (3.8%) after placebo
 - 2/26 (7.7%) COPD subjects after ADASUVE 10 mg, compared with 1/27 (3.7%) after placebo
- After albuterol treatment, FEV1^b was documented to return to within 10% of baseline in ≤1 hour
 - Asthma subjects: in 7/8 (87.5%) instances
 - COPD subjects: in 2/3 (66.7%) instances
 - At later, scheduled spirometry time points in the remaining 2 instances

a And before Dose 2 in those who received it at the 10-hour time point

b Forced expiratory volume in 1 second, as measured by spirometry

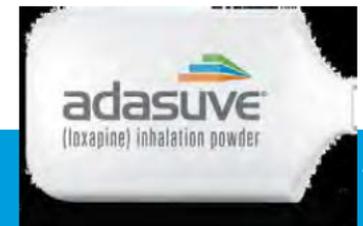


Bronchospasm in Agitation Trials

- Bronchospasm (including reports of wheezing, shortness of breath, or cough) was reported in premarketing phase 2 and 3 trials **in patients with agitation associated with schizophrenia or bipolar I disorder**

ADASUVE® 10 mg	0.8% (2/259)
Placebo	0% (0/263)

- One patient with schizophrenia, without a history of pulmonary disease, had significant bronchospasm requiring rescue treatment with a bronchodilator and oxygen

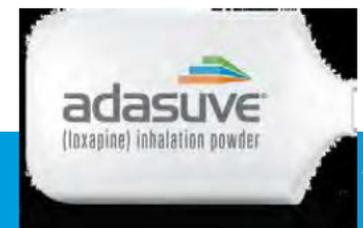


ADASUVE[®] Adverse Reactions^a in Premarketing Agitation Trials

Adverse Reactions in Short-Term, Placebo-Controlled Phase 2 and 3 Trials

Adverse Reaction	Placebo (n=263)	10 mg ADASUVE (n=259)
Dysgeusia	5%	14%
Sedation	10%	12%
Throat Irritation	0%	3%

a Adverse reactions (incidence >2% and greater than placebo) for ADASUVE 10 mg

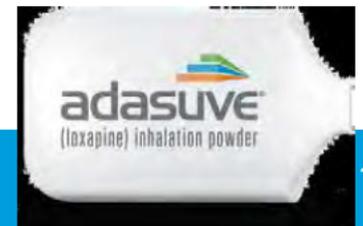


Steps to Reduce Risk of Bronchospasm

This poster is available to enrolled healthcare facilities to reinforce how to use ADASUVE® safely.

Healthcare facilities are encouraged to post this where ADASUVE will be administered.

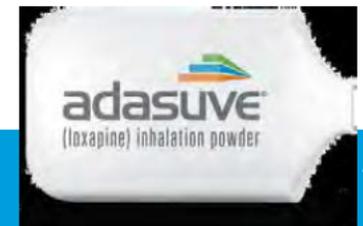
Additional copies can be ordered at www.adasuverems.com or by calling 855-755-0492.



Steps for Safe Use of ADASUVE®



- Ask if patient is taking medication to treat asthma or COPD and/or check medical records
- Ask if patient has a current diagnosis or history of asthma, COPD, or other lung disease and/or check medical records
- Examine patients (including chest auscultation) for respiratory abnormalities (e.g., wheezing)
- **Do not use in patients with acute respiratory signs or symptoms, with a current diagnosis or history of asthma, COPD or other lung disease associated with bronchospasm; or with current use of medications to treat airways disease, such as asthma or COPD**
- Counsel patient/caregiver on potential for bronchospasm that may occur after dosing and the need to report symptoms immediately
- Monitor patients every 15 minutes for at least 1 hour after treatment for signs or symptoms of bronchospasm including chest auscultation
- Ask patient every 15 minutes about any difficulty breathing
- Treat bronchospasm with an inhaled short-acting beta-agonist bronchodilator (e.g., albuterol)
- If medically necessary, provide additional therapy for bronchospasm per asthma guidelines

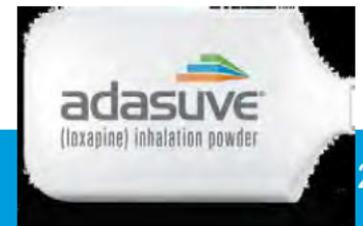


Reporting Adverse Events Associated With ADASUVE®

Healthcare professionals should understand the importance of reporting events of bronchospasm that require emergency response services, in addition to any fatalities that occur following ADASUVE treatment.

Suspected adverse events may be reported by the following methods:

- ADASUVE Medical Information at 800-284-0062 or email customer.services@galen-pharma.com
- FDA at 1-800-FDA-1088
- FDA at www.fda.gov/medwatch/report.htm



Patient Counseling

Discuss the risks associated with ADASUVE® treatment with patients and their caregivers, including the safe use of ADASUVE.

Helping Patients and Caregivers Understand Risks

- Explain that patients may have bronchospasm after using ADASUVE
- Ask patients to tell you if they are **currently taking medications** to treat asthma, COPD, other breathing problems
- Inform patients of other common side effects that may occur with ADASUVE (taste and sleepiness)
- Inform patients of other serious side effects that can occur with antipsychotics, in general

Helping Patients Report Signs/Symptoms of Bronchospasm

- Ask patients to tell you **immediately** if they experience:
 - Difficulty breathing
 - Chest tightness
 - Wheezing
- Tell patients you have a medicine available to treat breathing problems that might occur

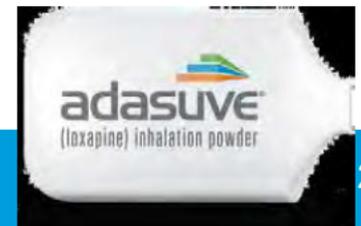


Administration of ADASUVE®

- ADASUVE is only administered by oral inhalation
- Administer only a single dose within any 24-hour period
- ADASUVE must be administered only by a healthcare professional, in an enrolled healthcare facility

Required Examination Prior to Dosing:

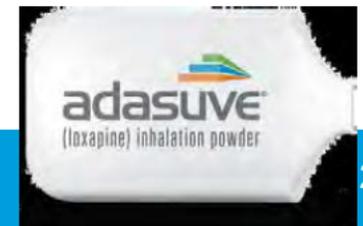
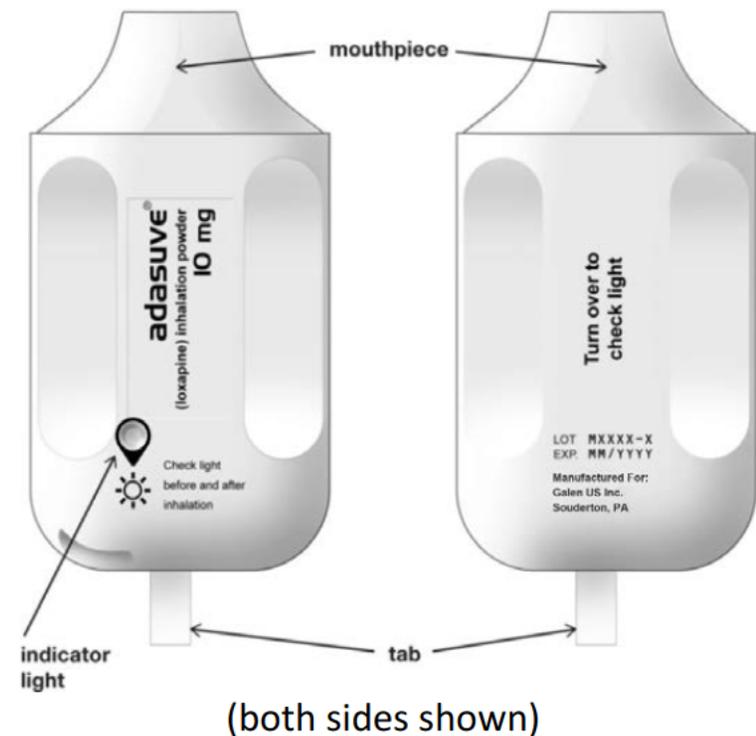
- Prior to administering ADASUVE, screen all patients for:
 - Current use of medications to treat asthma or COPD
 - History of asthma, COPD or other pulmonary disease
 - Examine patients (including chest auscultation) for respiratory abnormalities (e.g., wheezing)



Becoming Familiar With ADASUVE®

- ADASUVE is provided in a sealed pouch
- The indicator light is off when ADASUVE is removed from the pouch
- The indicator light turns on (green) when the tab is pulled out. The product is then ready for use
- The indicator light turns off after the patient inhales. This indicates that the dose has been delivered
- If the indicator light does NOT turn off, the dose has NOT been delivered

The pictures below show the important features of the ADASUVE product



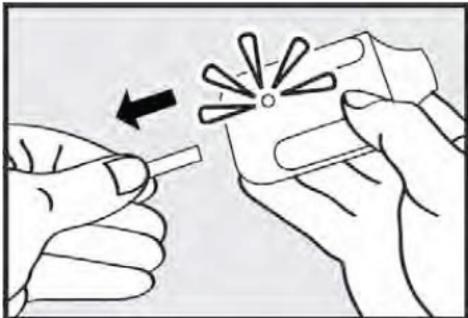
ADASUVE[®]: Important Administration Instructions

Before administering ADASUVE:



- 1. Open the pouch.** When ready to use, tear open the foil pouch and remove the inhaler from the package.

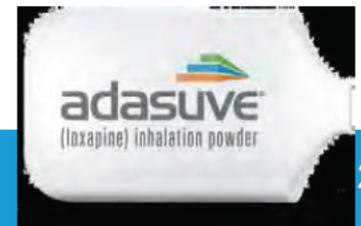
When the ADASUVE inhaler is removed from the pouch, the indicator light is off.



- 2. Pull tab.** Firmly pull the plastic tab from the rear of the inhaler. Check that the green light turns on. This indicates that the inhaler is ready for use.

Use the inhaler within 15 minutes after removing tab to prevent automatic deactivation of the inhaler.

The green light will turn off, indicating that the inhaler is not usable. Discard the inhaler after one use.

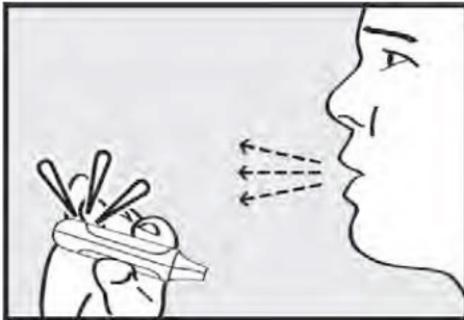


ADASUVE®: Important Administration Instructions

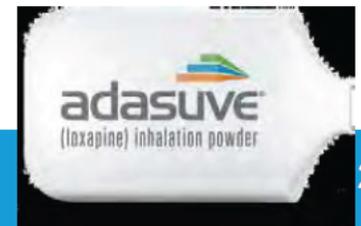
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- 3. Explain procedures to the patient.** Explain the administration procedures to the patient prior to use, and advise the patient that it is important to follow the instructions.

Inform the patient that the inhaler may produce a flash of light and a clicking sound, and it may become warm during use. These are normal.

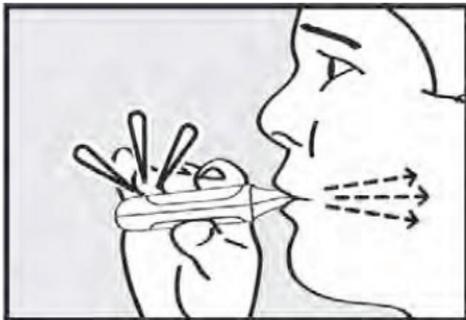


- 4. Instruct the patient to exhale.** Instruct the patient to hold the inhaler away from the mouth and breathe out fully to empty the lungs.



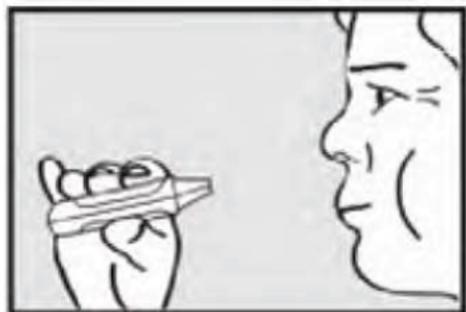
ADASUVE®: Important Administration Instructions

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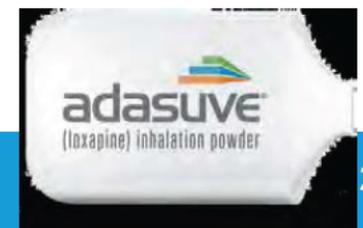
- 5. Instruct the patient to inhale.** Instruct the patient to put the mouthpiece of the inhaler between the lips, close the lips, and inhale through the mouthpiece with a steady deep breath.

Check that the green light turns off, indicating that the dose has been delivered.



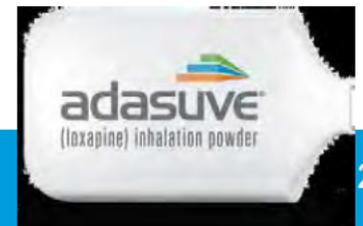
- 6. Instruct the patient to hold breath.** Instruct the patient to remove the mouthpiece from the mouth and hold the breath for as long as possible, up to 10 seconds.

Important: If the green light remains on after the patient inhales, the dose of ADASUVE has NOT been delivered. Instruct the patient to repeat Step 4, Step 5, and Step 6 up to 2 additional times. If the green light still does not turn off, discard the inhaler and use a new one.



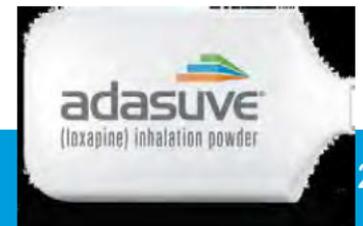
ADASUVE[®]: Monitoring to Assess Safety

- Monitor the patient for signs or symptoms of bronchospasm after ADASUVE administration
- Perform a physical examination, including chest auscultation, at least every 15 minutes for at least one hour after ADASUVE administration



How to Enroll in the ADASUVE® REMS Program

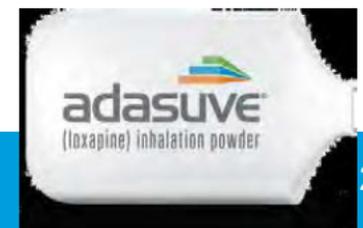
- **ADASUVE will be dispensed to patients only in certain healthcare facilities that are enrolled in the ADASUVE REMS Program**
- **Wholesalers/Distributors will ship ADASUVE only to enrolled healthcare facilities**
- Each healthcare facility must be able to provide:
 - Immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. This healthcare facility must have a short-acting bronchodilator (e.g., albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm
 - Medical/psychiatric (physicians, nurses, etc.) staff on site at all times (24 hours a day/7 days a week) trained to manage acute bronchospasm
 - Healthcare providers within the facility (prescribers, nurses, monitoring staff, or pharmacists) who are trained on safe use of ADASUVE using the ADASUVE Education Program
 - Procedures, protocol and/or order sets guiding safe use of ADASUVE



Procedures, Protocols, Order Sets for Safe Use of ADASUVE[®]

Procedures, protocols, and/or order sets to ensure the following:

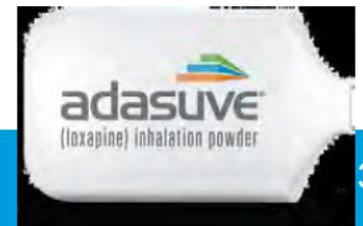
- Patients are screened, prior to treatment with ADASUVE:
 - For a history of pulmonary disease
 - For acute respiratory signs and symptoms by physical exam, including taking vital signs and chest auscultation
 - Inquiring if patient is taking medication to treat asthma or COPD
- Patients are monitored at least every 15 minutes for a minimum of one hour following treatment with ADASUVE for signs and symptoms of bronchospasm
 - Taking vital signs
 - Chest auscultation
- Administration of ADASUVE is limited to one dose per patient within 24 hours



Designate an Authorized Healthcare Facility Representative

For each facility, an authorized healthcare facility representative is required to:

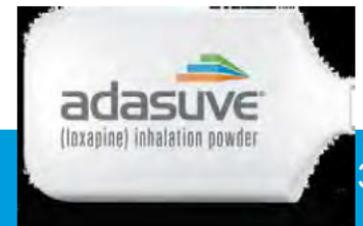
- Review the ***ADASUVE® Education Program***
- Complete and sign the ***Healthcare Facility Enrollment Information and Form***
 - Acknowledging that the enrolled healthcare facility meets specific requirements
- Healthcare Facility Representative:
 - May be a Pharmacist or another healthcare professional with appropriate level of responsibility within the facility
 - Authorized to act on behalf of the facility



Authorized Healthcare Facility Representative Actions

- Review the ***Healthcare Facility Enrollment Information and Form*** to become familiar with the enrollment requirements
- Review the ***ADASUVE REMS Education Program*** to become familiar with safe use conditions for ADASUVE
- Complete and sign the ***Healthcare Facility Enrollment Form***
- Submit the completed form on-line, via fax, via email

The ***Healthcare Facility Enrollment Information and Form*** are available at www.adasuverems.com or by calling 855-755-0492



ADASUVE[®] REMS Materials for Enrolled Healthcare Facilities

The following materials are part of the ADASUVE REMS Program and will assist enrolled healthcare facilities in complying with ADASUVE REMS requirements. They are available to review, order or print at www.adasuverems.com or by calling 855-755-0492.

1. ADASUVE REMS Education Program

- Must be reviewed by all healthcare providers within an enrolled healthcare facility who will be prescribing or administering ADASUVE, or observing patients after ADASUVE is administered

2. Steps for Safe Use of ADASUVE Poster

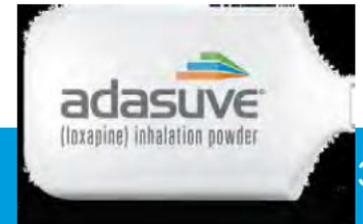
- Should be posted where ADASUVE is administered within enrolled healthcare facilities

3. Order Set/Protocol Template

- For use by enrolled healthcare facilities to assist with designing procedures, protocols and/or order sets that meet the requirements of the ADASUVE REMS Program

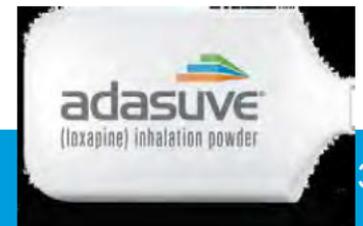
4. ADASUVE Healthcare Provider Brochure

- Contains information for providers on the risks and safe use of ADASUVE
- Information on healthcare facility enrollment requirements of the ADASUVE REMS Program



Other Resources Available at www.adasuverems.com

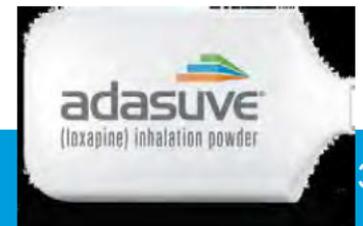
- ***Healthcare Facility Enrollment Information and Form***
- Prescribing Information
- ADASUVE® Instructions for Use
- ADASUVE® Medication Guide



ADASUVE[®] Education Program Summary

At the end of this education program, you should understand:

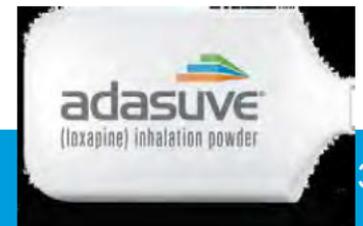
- ADASUVE REMS Program Information
 - The ADASUVE REMS Program is necessary to mitigate the risk of bronchospasm that has the potential to cause respiratory distress and respiratory arrest
- Important safety information
 - ADASUVE can cause bronchospasm
 - Patients with active airways disease (asthma, COPD) are at increased risk of bronchospasm after dosing with ADASUVE
 - It is important to report events of bronchospasm that require emergency response services, in addition to any fatalities, that occur following ADASUVE treatment
 - Administer only a single dose of ADASUVE per patient within any 24-hour period



ADASUVE[®] Education Program Summary

-continued-

- How to use ADASUVE safely
 - SCREEN patients to identify and select appropriate ADASUVE patients
 - OBSERVE and MONITOR patients every 15 minutes for at least one hour after ADASUVE treatment
 - MANAGE bronchospasm with an inhaled short-acting beta-agonist bronchodilator or if necessary, by accessing emergency response services



ADASUVE[®] Education Program Summary

-continued-

How to enroll in the ADASUVE REMS Program

- Each healthcare facility must be able to provide:
 - Immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. This healthcare facility must have a short-acting bronchodilator (e.g., albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.
 - Medical/psychiatric (physicians, nurses, etc.) staff on site at all times (24 hours a day/7 days a week) trained to manage acute bronchospasm.
- For each facility, an authorized healthcare facility representative is required to complete and sign the Healthcare Facility Enrollment Information and Form acknowledging that the enrolled healthcare facility meets specific requirements
- Find more information at www.adasuverems.com



ADASUVE Website Screen Captures

ADASUVE REMS Program

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1. Home Page



REMS Program Enrollment

ADASUVE Education Program

Healthcare Provider Brochure

Safe Use of ADASUVE

ADASUVE Instructions for Use

Sign in

ADASUVE® REMS Program

ADASUVE is a drug-device combination product that delivers an aerosol of the antipsychotic agent loxapine in a single oral inhalation. ADASUVE has been approved by the US Food and Drug Administration (FDA) for the acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults.

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for ADASUVE to ensure that the benefits of treatment outweigh the risks of bronchospasm.

The purpose of the ADASUVE REMS Program is to mitigate the risk of bronchospasm that has the potential to lead to respiratory distress and respiratory arrest.

In order to mitigate the risk, the ADASUVE REMS Program requires that ADASUVE is only administered in enrolled healthcare facilities with immediate access on site to supplies and personnel trained to manage acute bronchospasm, and ready access to emergency response services.

In addition, the REMS Program will inform healthcare professionals about:

- The risk of bronchospasm after ADASUVE administration
- Appropriate patient selection
- Monitoring patients after ADASUVE administration
- Management of bronchospasm, if it occurs

Click here to see the **REMS Program Enrollment Information for Healthcare Facilities**

Click the links below to see the **Materials for Healthcare Professionals:**

- Healthcare Provider Brochure
- Steps for Safe Use of ADASUVE
- ADASUVE Education Program
- ADASUVE Instructions for Use
- ADASUVE Order Set/Protocol Template

Important Safety Information About ADASUVE

Risk of Bronchospasm

ADASUVE can cause bronchospasm that has the potential to lead to respiratory distress and respiratory arrest.

Administer ADASUVE only in an enrolled healthcare facility that has immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. Facilities must have a short-acting bronchodilator (e.g., albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.

ADASUVE is contraindicated in patients with a current diagnosis or history of asthma, chronic obstructive pulmonary disease (COPD), or other lung disease associated with bronchospasm because they are at increased risk of bronchospasm.

ADASUVE is also contraindicated in patients with acute respiratory signs/symptoms (e.g., wheezing) or who are currently taking medications to treat airways disease, such as asthma or COPD.

ADASUVE is contraindicated in patients with a history of bronchospasm following ADASUVE treatment.

Prior to administering ADASUVE, screen patients regarding a current diagnosis or history of symptoms of asthma, COPD and other lung diseases, and examine (including chest auscultation) patients for respiratory signs. Monitor for signs and symptoms of bronchospasm following treatment with ADASUVE.

The Use of ADASUVE Should Be Accompanied by a 4-step Process of: Screening, Counseling, Monitoring, and Management

Steps for Safe Use of ADASUVE	
SCREEN	Ask if patient is taking medication to treat asthma or COPD and/or check medical records
	Ask if patient has a current diagnosis or history of asthma, COPD or other lung disease and/or check medical records
	Examine patients (including chest auscultation) for respiratory abnormalities (e.g., wheezing)
COUNSEL	Do not use in patients with acute respiratory signs or symptoms; with a current diagnosis or history of asthma, COPD or other lung disease associated with bronchospasm; or with current use of medications to treat airways disease, such as asthma or COPD
	Counsel patient/caregiver on potential for bronchospasm that may occur after dosing and the need for them to report symptoms immediately
MONITOR	Monitor patient every 15 minutes for at least 1 hour after treatment for signs and symptoms of bronchospasm including chest auscultation
	Ask patient every 15 minutes about any difficulty breathing
MANAGE	Treat bronchospasm with an inhaled short-acting beta-agonist bronchodilator (e.g., albuterol)
	If medically necessary, provide additional therapy for bronchospasm per asthma guidelines

These risks do not constitute a complete list of all the risks associated with ADASUVE. Please see the [Prescribing Information](#), including Boxed Warning, for more information regarding the risks associated with ADASUVE.



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2. REMS Program Enrollment Page



REMS Program Enrollment

ADASUVE Education Program

Healthcare Provider Brochure

Safe Use of ADASUVE

ADASUVE Instructions for Use

[Sign in](#)

ADASUVE® REMS Program Enrollment

HEALTHCARE FACILITY

- Enrolls in ADASUVE REMS Program
- Authorized healthcare facility representative attests to certain criteria required for receipt of ADASUVE order

[CLICK HERE TO ENROLL](#)

[Click here to enroll as a Healthcare Facility in the ADASUVE REMS Program](#)

Click on a link below to view, print or order the corresponding material intended for healthcare professionals in enrolled Healthcare Facilities:

[Schedule ADASUVE Education Program In-service](#)

[View or print ADASUVE Education Program online](#)

[View, print, or order Steps for Safe Use of ADASUVE](#)

[View or print Healthcare Facility Enrollment Information Form](#)

[View or print ADASUVE Order Set/ Protocol Template](#)

To order any of the above materials, contact Galen at 855-755-0492

ADASUVE Healthcare Facility Enrollment

ADASUVE will be dispensed only to patients in healthcare facilities that are enrolled in the ADASUVE REMS Program.

Authorized Healthcare Facility Representative

For each healthcare facility, an **authorized healthcare facility representative** is required to complete and sign the Healthcare Facility Enrollment Form acknowledging that the enrolled healthcare facility meets specific requirements. This representative may be a pharmacist, or another healthcare professional with the appropriate level of responsibility within the healthcare facility, who is authorized to act on behalf of the facility.

Healthcare Facility Qualifications for Enrollment

Each healthcare facility must be able to provide:

- Immediate access on site to supplies and personnel trained to manage acute bronchospasm and ready access to emergency response services. This healthcare facility must have a short-acting bronchodilator (e.g. albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.
- Medical/psychiatric (physicians, nurses, etc.) staff on site at all times (24 hours a day/7 days a week) trained to manage acute bronchospasm.
- Procedures, protocols, and/or order sets to ensure the following:
 - Patients are screened, prior to treatment with ADASUVE, for a history of pulmonary disease and for acute respiratory signs and symptoms by physical exam, including taking vital signs and chest auscultation, and inquiring if patient is taking medication to treat asthma or COPD
 - Patients are monitored at least every 15 minutes for a minimum of 1 hour following treatment with ADASUVE for signs and symptoms of bronchospasm, including taking vital signs and chest auscultation
 - Administration of ADASUVE is limited to 1 dose per patient within 24 hours
- Healthcare providers within the facility (prescribers, nurses, monitoring staff, or pharmacists) who are trained on the safe use of ADASUVE using the ADASUVE Education Program

These risks do not constitute a complete list of all the risks associated with ADASUVE. Please see the [Prescribing Information](#), including Boxed Warning, for more information regarding the risks associated with ADASUVE.

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3. ADASUVE Education Program Page

adasuve
(loxapine) inhalation powder

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REMS Program Enrollment | **ADASUVE Education Program** | Healthcare Provider Brochure | Safe Use of ADASUVE | ADASUVE Instructions for Use

[Sign in](#)

ADASUVE Education Program

The **ADASUVE Education Program** must be reviewed by all healthcare providers within an enrolled healthcare facility who will be prescribing or administering ADASUVE or observing patients after ADASUVE is administered. It ensures they understand the REMS Program requirements, ADASUVE product information, Important Safety Information, how to use ADASUVE safely, and how to enroll in the ADASUVE REMS Program.

Download the ADASUVE Education Program

To schedule an ADASUVE Education Program In-Service, call 855-755-0492

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4. Healthcare Provider Brochure

adasuve
(loxapine) inhalation powder

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REMS Program Enrollment | ADASUVE Education Program | **Healthcare Provider Brochure** | Safe Use of ADASUVE | ADASUVE Instructions for Use

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ADASUVE Healthcare Provider Brochure

The **Healthcare Provider Brochure** contains information about ADASUVE, as well as information on healthcare facility enrollment requirements of the ADASUVE REMS Program.

Download the ADASUVE Healthcare Provider Brochure

To order the ADASUVE Healthcare Provider Brochure, contact Galen at 855-755-0492

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5. Safe Use of ADASUVE



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[REMS Program Enrollment](#)

[ADASUVE Education Program](#)

[Healthcare Provider Brochure](#)

[Safe Use of ADASUVE](#)

[ADASUVE Instructions for Use](#)

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Steps for Safe Use of ADASUVE

A healthcare facility that wants to administer ADASUVE must enroll in the ADASUVE REMS Program, and the **Steps for Safe Use of ADASUVE** poster should then be posted where ADASUVE is administered within the enrolled healthcare facility.



[Download the Steps for Safe Use of ADASUVE](#)

To order Steps for Safe Use of ADASUVE, call 855-755-0492

ADASUVE Order Set/Protocol Template

The **Order Set/Protocol Template** should be used as a guideline for developing procedures, protocols, and/or order sets around the use of ADASUVE to ensure that REMS requirements are being met.



[Download the ADASUVE Order Set/Protocol Template](#)

To order the ADASUVE Order Set/Protocol Template, call 855-755-0492

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6. ADASUVE Instructions for Use

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[REMS Program Enrollment](#) | [ADASUVE Education Program](#) | [Healthcare Provider Brochure](#) | [Safe Use of ADASUVE](#) | [ADASUVE Instructions for Use](#)

[Sign in](#)

ADASUVE Instructions for Use

ADASUVE is only administered by oral inhalation and must be administered only by a healthcare professional in an enrolled healthcare facility.

[Download the ADASUVE Instructions for Use](#)



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7. Access your Account

The screenshot shows the Adasuve website's account access page. At the top left is the Adasuve logo (toxapine) Inhalation powder. To the right are links for Prescribing Information, Medication Guide, and Contact Us. Below this is a navigation bar with buttons for REMS Program Enrollment, ADASUVE Education Program, Healthcare Provider Brochure, Safe Use of ADASUVE, and ADASUVE Instructions for Use. A Sign in button is located on the right side of the navigation bar. The main content area is titled "Access your Account" and contains a login form with fields for Username and Password, a Sign in button, and links for Need an Account?, Forgot Username?, and Forgot Password?. Below the form is a note: "For assistance, please contact the ADASUVE REMS Program at 855-755-0492". The footer includes the GALEN logo, copyright information (©2017 Galen US Inc. All rights reserved. August 2017.), and links for Site Map, Terms of Use, Privacy Policy, and Contact Us. A blue banner at the bottom contains a link: "Click here to see Prescribing Information, including Boxed Warning." and an image of the Adasuve inhalation powder container.

adasuve
(toxapine) Inhalation powder

Prescribing Information | Medication Guide | Contact Us

REMS Program Enrollment | ADASUVE Education Program | Healthcare Provider Brochure | Safe Use of ADASUVE | ADASUVE Instructions for Use

Sign in

Access your Account

Username

Password

[Need an Account?](#) [Forgot Username?](#) [Forgot Password?](#)

For assistance, please contact the ADASUVE REMS Program at 855-755-0492

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8. Request Username

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[REMS Program Enrollment](#) | [ADASUVE Education Program](#) | [Healthcare Provider Brochure](#) | [Safe Use of ADASUVE](#) | [ADASUVE Instructions for Use](#)

[Sign in](#)

Request Username

Please enter your credentials in the space provided. Your Username will be sent to your registered email address with the ADASUVE REMS Program.

First Name

Last Name

Email Address

For assistance, please contact the ADASUVE REMS Program at 855-755-0492

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9. Request Password

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[REMS Program Enrollment](#) | [ADASUVE Education Program](#) | [Healthcare Provider Brochure](#) | [Safe Use of ADASUVE](#) | [ADASUVE Instructions for Use](#)

[Sign in](#)

Request Password

Please enter your Username in the space provided. Your Username is the ID you established when creating your account and this ID was also sent to you upon completion of enrollment in the ADASUVE REMS Program.

Username

Email Address

[Submit](#)

For assistance, please contact the ADASUVE REMS Program at 855-755-0492



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10. Account Information



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[REMS Program Enrollment](#) | [ADASUVE Education Program](#) | [Healthcare Provider Brochure](#) | [Safe Use of ADASUVE](#) | [ADASUVE Instructions for Use](#)

[Registration](#) | [Enrollment Form](#) | [Attestation](#) | [My Activity](#) | [Sign in](#)

Account Information

First Name

Last Name

Email Address

Enrollment ID
(optional)
(If you enrolled via fax, please enter your enrollment confirmation ID.)

Username

Use Email Address as Username

Password
(Your new password must be at least eight (8) characters in length and contain at least one letter and one number.)

Confirm Password

For assistance, please contact the ADASUVE REMS Program at 855-755-0492

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