

Initial REMS approval: 12/21/2012

Last modified/revised: 10/2017

NDA 022549

ADASUVE® (loxapine) Inhalation Powder

Galen Limited

Seagoe Industrial Estate,
Craigavon, BT63 5UA,
United Kingdom

Phone: +44 (0)28 3833 4974

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.