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 and 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, on-site resources to manage bronchospasm and/or respiratory distress.

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

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 equipment and personnel trained to manage acute bronchospasm, including advanced airway management (intubation and mechanical ventilation).

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 (eg, 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 asthma, COPD, or other lung disease and/or check medical records.

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 patient if patient is taking medication to treat asthma or COPD and/or check medical records
- Examine patients (including chest auscultation) for respiratory signs (eg, 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 (eg, albuterol)
- If medically necessary, provide additional therapy for bronchospasm per asthma guidelines, including intubation and mechanical ventilation as needed

These risks do not constitute a complete list of all the risks associated with ADASUVE. Please see the Full Prescribing Information, including Boxed Warning, for more information regarding the risks associated with ADASUVE.
ADASUVE® REMS Program Enrollment

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

The healthcare facility requirements include having the following:

• Immediate access onsite to equipment and personnel trained to provide advanced airway management, including intubation and mechanical ventilation

• Immediate access onsite to a metered-dose inhaled and nebulized form of a short-acting beta-agonist bronchodilator (eg, albuterol)

• 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

ADASUVE Wholesaler/Distributor Enrollment

ADASUVE is only available to enrolled wholesalers/distributors that agree to the following requirements:

• Will only distribute ADASUVE to healthcare facilities in which enrollment in the ADASUVE REMS Program has been validated

• Agree to cooperate with periodic audits or noncompliance investigations to ensure that ADASUVE is distributed in accordance with the program requirements

• Understand that wholesalers/distributors are required to renew enrollment in the ADASUVE REMS Program every three (3) years

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/s/

MITCHELL V Mathis
12/09/2013