13 December 2012
EMA/778608/2012
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Adasuve

loxapine

On 13 December 2012, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Adasuve, 4.5 mg, 9.1 mg, inhalation powder, pre-dispensed, intended for the rapid control of mild-to-moderate agitation in adult patients with schizophrenia or bipolar disorder. The applicant for this medicinal product is Alexza UK Ltd. They may request a re-examination of any CHMP opinion, provided they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

The active substance of Adasuve is loxapine, a psycholeptic, antipsychotic (N05AH01). The efficacy of loxapine is proposed to be mediated through high affinity antagonism of dopamine D2 receptors and serotonin 5-HT2A receptors. Loxapine binds with noradrenergic, histaminergic, and cholinergic receptors. Its interaction with these systems may influence the spectrum of its pharmacological effects that are associated with calming effects and suppression of aggressive behaviour.

The benefits with Adasuve are its ability to rapidly reduce the agitation in mild to moderate patients with schizophrenia or bipolar disorder. In these patients, decreased agitation was evident 10 minutes after the first dose, the first assessment time, and at all subsequent assessments during the 24 hour evaluation period, for both 4.5 mg and 9.1 mg doses. About a quarter to nearly half of the patients needed a second dose after 2 hours to reach a satisfactory effect.

The most common side effects are dysgeusia, sedation/somnolence and dizziness. In studies in agitated patients, bronchospasm was reported as an uncommon, but serious adverse reaction, while in subjects with active airways disease, bronchospasm was commonly reported and often required treatment with a short-acting beta-agonist bronchodilator.

A pharmacovigilance plan for Adasuve will be implemented as part of the marketing authorisation.

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion.

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The approved indication is: "ADASUVE is indicated for the rapid control of mild-to-moderate agitation in adult patients with schizophrenia or bipolar disorder. Patients should receive regular treatment immediately after control of acute agitation symptoms."

It is proposed that Adasuve should only be administered in a hospital-setting under the supervision of a healthcare professional. Short-acting beta-agonist bronchodilator treatment should be available for treatment of possible severe respiratory side-effects (bronchospasm).

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers there to be a favourable benefit-to-risk balance for Adasuve and therefore recommends the granting of the marketing authorisation.