HAUTE AUTORITÉ DE SANTÉ

PSYCHIATRY
Focus
October 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VALDOXAN (agomelatine), antidepressant

No clinical benefit demonstrated in the treatment of major depressive episodes in adults.

Main points

- VALDOXAN has Marketing Authorisation in the treatment of major (i.e. clear) depressive episodes in adults.
- Its efficacy is modest and has been demonstrated only in the short term (6-12 weeks) versus placebo. It has not been shown to have any impact on the remission rates for depressive episodes, the primary efficacy endpoint. Its use necessitates strict monitoring of liver function before the initiation of and throughout the treatment.

Therapeutic use

Since the overall efficacy of antidepressants is similar, their selection should be based primarily on their adverse effects profile, pharmacological properties, patient preference, treatment history, risk of withdrawal symptoms and toxicity in the event of overdose.
Imipramine-type drugs and MAOIs are generally prescribed as second- or third-line options.
Antidepressant treatment should not be envisaged independently of an overall management strategy and must be combined with psychotherapy.

Role of the medicinal product in the therapeutic strategy

VALDOXAN is a second-line treatment option:

Clinical data

- In a meta-analysis of randomised trials, the short-term efficacy (6-12 weeks) of agomelatine was demonstrated by comparison with placebo. The standardised mean difference between the change in depression scores by comparison with baseline was 0.24 points 95% CI [0.12; 0.35] and on average 25% more patients responded to treatment compared with placebo RR = 1.25 95% CI [1.11; 1.45]. In terms of remission rates, agomelatine is no different to placebo RR = 1.22 95% CI [0.97; 1.53].
- The superiority of agomelatine by comparison with other antidepressants in terms of the probability of a short-term response to treatment was not demonstrated in a meta-analysis of randomised trials RR = 1.01 95% CI [0.95; 1.08] by comparison with selective serotonin reuptake inhibitors (SSRIs) and RR = 1.06 95% CI [0.98; 1.16] compared with venlafaxine.
- As regards long-term efficacy in the prevention of relapses (24-52 weeks), a meta-analysis did not demonstrate the superiority of agomelatine by comparison with placebo RR = 0.78 99% CI [0.41; 1.48].
- In terms of safety, agomelatine was no different to placebo, either in all-cause discontinuation of treatment: RR 0.92 [0.78; 1.08] or in the discontinuation of treatment due to an adverse event: RR 1.03 [0.75; 1.41]. However, compared with other antidepressants, the results were, overall, inconclusive for these endpoints.
- The risk of hepatotoxicity is a major concern. The use of VALDOXAN necessitates strict monitoring of liver function before its initiation and throughout treatment, in accordance with the SPC data.

Benefit of the medicinal product

- The actual benefit* of VALDOXAN is low.
- VALDOXAN does not provide clinical added value** (CAV V) in the therapeutic strategy for the treatment of major depressive episodes.
- Recommends continued inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 21 October 2015 (CT-14029) and is available at **www.has-sante.fr**

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[i] * The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".