OPINION RELATIVE TO MEDICINAL PRODUCTS

aripiprazole

ABILIFY MAINTENA 300 mg
ABILIFY MAINTENA 400 mg

Powder and solvent for prolonged-release suspension for injection

Re-evaluation

Adopted by the Transparency Committee on 20 July 2022

SUMMARY

The legally binding text is the original French opinion version

- **Schizophrenia**
- **Sectors: Retail and hospital**

Key points

Favourable opinion for reimbursement in the maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.

What therapeutic improvement?

A therapeutic improvement over XEPLION (paliperidone palmitate) in the maintenance treatment of schizophrenia.

Role in the care pathway?

Antipsychotics are the standard pharmacological treatment for schizophrenia. They are used in the treatment of the acute phase and as maintenance therapy in the prevention of relapses.

The choice of antipsychotic takes into account response to previous treatments, the safety profile of antipsychotics and the patient's individual susceptibility to adverse reactions. Second-generation antipsychotics are recommended as first-line treatment since they have a better tolerance than first-generation antipsychotics. Antipsychotic monotherapy should be favoured.

A multidimensional approach is necessary for patients with schizophrenia. Medicinal treatments should be combined with individual or group psychotherapy sessions, institutional or family care and social interventions.

The prescription of a long-acting injectable form may be considered when the patient expresses a preference for this type of treatment and/or when a patient adequately stabilised by oral treatment during the initial treatment phase has difficulty maintaining compliance with their treatment.

In its 2015 opinion on inclusion renewal[2], the Committee had maintained the role of ABILIFY MAINTENA (aripiprazole LP) administered as a monthly intramuscular injection as a therapeutic alternative to the other long-acting injectable antipsychotics in the maintenance treatment of schizophrenia in patients stabilised with oral aripiprazole.

Role of the medicinal product in the care pathway

Considering:

- data from the initial inclusion having demonstrated the non-inferiority of ABILIFY MAINTENA (prolonged-release aripiprazole) as a monthly injection *versus* oral aripiprazole in terms of efficacy on the exacerbation of psychotic symptoms in patients stabilised with oral aripiprazole and its superiority *versus* placebo on the time to relapse,
- new comparative quality of life data from a single-blind study (primary endpoint assessed under blind conditions by the investigator) having demonstrated the non-inferiority and superiority of the maintenance treatment strategy under ABILIFY MAINTENA (prolonged-release aripiprazole) as monthly injections *versus* paliperidone palmitate as monthly injections (XEPLION) with a modest effect size over a short treatment duration of 28 weeks (difference of 4.7 points on a 126-point scale; $CI_{95\%}$ [0.32; 9.02]; p=0.036),
- new data from indirect comparisons (Ostuzzi et al. network meta-analysis, 2021) having reported a superiority in terms of acceptability (defined as the percentage of treatment discontinuations for all causes) of prolonged-release aripiprazole compared to five prolonged-release injectable antipsychotics, including monthly paliperidone palmitate,
- and its known safety profile,

the Committee considers that ABILIFY MAINTENA (prolonged-release aripiprazole) as monthly injections is a preferential alternative to XEPLION (paliperidone palmitate) as monthly injections in terms of acceptability and quality of life in the maintenance treatment strategy of patients having been initially stabilised under oral antipsychotics in accordance with their respective MAs. However, it highlights the fact that the superiority in terms of efficacy compared to other second-generation long-acting injectable antipsychotics has not been demonstrated.

Special recommendations

Taking into account the MA for ABILIFY MAINTENA restricting its use to patients stabilised patients stabilised with oral aripiprazole, the Committee raises the question of whether it might be appropriate to revise the prescription conditions defined in the MA and to restrict prescription to psychiatric specialists and departments, in line with several other second-generation injectable antipsychotics also indicated in the same clinical situation: ZYPADHERA (olanzapine pamoate monohydrate), XEPLION and TREVICTA (paliperidone palmitate).

Committee's conclusions

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

- Schizophrenia is a severe disease in terms of the disability it causes, the age of onset (late adolescence, young adulthood) and its personal, social, family or professional impact. It usually has a chronic course, due to residual symptoms or relapses, which are common in the disease. It is often associated with numerous psychiatric and somatic comorbidities.
- ABILIFY MAINTENA (prolonged-release aripiprazole) 400 mg and 300 mg administered as a monthly intramuscular injection is a maintenance treatment for schizophrenia in adult patients stabilised with oral aripiprazole.
- The efficacy/adverse effects ratio of ABILIFY MAINTENA (aripiprazole) 300 mg and 400 mg in the maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole is high.
- ABILIFY MAINTENA (prolonged-release aripiprazole) as monthly injections is a first-line treatment for schizophrenia in adult patients stabilised with oral aripiprazole.
- There are medicinal alternatives in the care pathway for the maintenance treatment of patients having been initially stabilised with oral antipsychotics.

Public health benefit

Considering:

- the seriousness and high prevalence of schizophrenia,
- the partially met medical need,
- the partial response to the identified need, with:
  - the absence of an additional impact on morbidity and mortality,
  - a modest impact demonstrated on quality of life versus prolonged-release paliperidone palmitate as a monthly injection in the single-blind QUALIFY study and over a short period of time (28 weeks),
- the lack of data on an additional impact on the organisation of care,

ABILIFY MAINTENA (prolonged-release aripiprazole) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ABILIFY MAINTENA (aripiprazole) is substantial in the MA indication.

The Committee issues a favourable opinion for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and at the MA dosages.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- Data from the first registration having demonstrated the non-inferiority of Abilify Maintena (aripiprazole LP) in monthly injection versus oral aripiprazole in terms of efficacy on exacerbation of psychotic symptoms in patients stabilised on oral aripiprazole and its superiority versus placebo over relapse time,
- New comparative quality of life data from a single-blind study (main judgment criterion assessed blindly by investigator) having demonstrated the non-inferiority and superiority of the maintenance treatment strategy under Abilify Maintena in monthly injection versus ABILIFY paliperidone palmitate in monthly injection (XEPLION) with a modest amount of effect over a short treatment period of 28 weeks (difference of 4.7 points on a 126-point scale; IC95% [0.32; 9.02]; p=0.036),
- New data from indirect comparisons (Ostuzzi and al. 2021) having reported a superiority in terms of acceptability (defined as the stop-study percentage for all causes) of aripiprazole LP compared to 5 injectable antipsychotics LP, including paliperidone palmitate monthly,
- and its known tolerance profile,

the Transparency Commission deems that Abilify Maintena (aripiprazole), within the framework of the strategy of stabilizing the patient with the same oral molecule beforehand, provides a minor clinical added value (CAV IV) compared to paliperidone palmitate in monthly injection (XEPLION) in the maintenance treatment strategy of schizophrenia in of patients who were initially stabilised on oral antipsychotics in accordance with their respective MAs.