HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 MARCH 2022

The legally binding text is the original French opinion version

levodopa/carbidopa/entacapone
LECIGIMON 20 mg/5 mg/20 mg per ml intestinal gel

First assessment

Key points

Unfavourable opinion for reimbursement in the treatment of advanced Parkinson's disease with severe motor fluctuations and hyperkinesia or dyskinesia when available oral combinations of Parkinson medicinal products have not given satisfactory results.

Role in the care pathway?

The initial treatment strategy for the disease depends on the presence or otherwise of Parkinson's symptoms with functional impairment, with treatment only initiated in the presence of impairment. In cases of very mild impairment, treatments will be considered based on the predominant symptom and age, from monoamine oxidase B inhibitors (MAO-B inhibitors), dopamine agonists by the oral or transdermal route and anticholinergic agents.

In the event of functional effects, dopamine agonists will be preferred for patients under 65 years of age whereas L-Dopa will be preferred for elderly subjects.

After a stabilisation period of varying duration, the clinical status deteriorates due to the onset of motor complications associated with the dopaminergic treatment (motor fluctuations, on/off effects, dyskinesia) and the onset or deterioration of non-dopa-dependent symptoms specific to the disease.

A review of the medical prescription and of the associated medicines liable to impair motor and non-motor complications should be conducted, optimising the dopa therapy thereafter if necessary to target continuous dopamine stimulation (division of the daily dose, adaptation of dosing times, change of pharmaceutical form, dietary changes).

The addition of L-dopa treatment can be envisaged subsequently, with:

As first-line treatment:

* dopamine agonists administered per os or transdermally:

- non-rye ergot-derived agents as first-line treatments: ropinirole, piribedil, pramipexole, rotigotine (transdermal device).
- rye ergot-derived agonists, which require annual cardiac monitoring by ECG (risk of the development of valve disease): bromocriptine, lisuride;

* COMT inhibitors, with:

- entacapone, which has the benefit of significantly increasing the duration of ON episodes and can often make it possible to reduce L-dopa doses;
- tolcapone, if entacapone is not sufficiently effective or is poorly tolerated (treatment with tolcapone must not exceed 3 weeks in the event of inefficacy due to its toxicity, particularly hepatic, and regular assay of AST-ALT is necessary)

* MAO-B inhibitors.

A combination of these different substances may also be envisaged.

As second-line treatment:

- anticholinergic antitremor agents, only in patients with no cognitive impairment,
- amantadine remains a useful treatment option in the management of levodopa-induced dyskinesia or fluctuations. In other clinical situations in Parkinson's disease, particularly at the start of the disease, immediate-release amantadine has no role in the care pathway in view of the medicinal alternatives.
- discontinuous subcutaneous apomorphine injections indicated as an adjuvant treatment for severe dopa therapy activity fluctuations in the course of Parkinson's disease (on-off effects).

As a last resort, and in accordance with national, European (EFNS/MDS-ES) and international guidelines, invasive treatments such as deep brain stimulation, continuous subcutaneous apomorphine infusion or enteral levodopa-carbidopa administration may be envisaged for some patients.

Role of LECIGIMON (levodopa/carbidopa/entacapone) in the care pathway:

Considering:

- limited data from a pharmacokinetic study versus DUODOPA (levodopa/carbidopa) conducted in the short term (two days) on a small number of patients (n=11), not having demonstrated the clinical value of adding entacapone to levodopa/carbidopa dual therapy administered via an implantable pump;

- the fact that the implantable pump administering LECIGIMON (levodopa/carbidopa/entacapone) is different from that administering DUODOPA (levodopa/carbidopa), making it necessary to change the pump following any change of treatment,

the Committee considers that LECIGIMON (levodopa/carbidopa/entacapone) has no role in the treatment strategy for adult patients with advanced Parkinson's disease.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Parkinson's disease is a neurodegenerative disease with multisystemic involvement characterised by the insidious onset and intermittent progression of symptoms. As the disease progresses, it results in disability and a marked deterioration in quality of life.

◗ The proprietary medicinal product LECIGIMON (levodopa/carbidopa/entacapone) is a symptomatic medicinal product.

◗ Considering the limited data from a pharmacokinetic study versus DUODOPA (levodopa/carbidopa) conducted in the short term (two days) on a small number of patients (n=11), the efficacy/adverse effects report of LECIGIMON (levodopa/carbidopa/entacapone) has not been adequately established.

◗ There are medicinal and non-medicinal alternatives.

◗ LECIGIMON (levodopa/carbidopa/entacapone) has no role in the care pathway for the management of adult patients with advanced Parkinson's disease.

Public health impact

Considering:

- the seriousness of the disease in patients at an advanced stage, and its prevalence,
- the partially met medical need,
- the lack of additional response to the identified need with:
    - the absence of an additional impact on morbidity and mortality in view of the limited pharmacokinetic data in the short term relative to a small number of patients,
    - the lack of an additional impact on quality of life in the absence of data,
- the lack of an additional impact on the organisation of care in the absence of data supporting an impact on the care and life pathway,

LECIGIMON (levodopa/carbidopa/entacapone) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of LECIGIMON (levodopa/carbidopa/entacapone) is insufficient to justify its public funding cover in the MA indication.

The Committee issues an unfavourable opinion for 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 dosages.