Medicines & Healthcare products Regulatory Agency

MHRA

# Public Assessment Report

# National Procedure

# Lecigon 20 mg/ml + 5 mg/ml + 20 mg/ml intestinal gel

# (levodopa, carbidopa monohydrate and entacapone)

# PL 53856/0001

# LobSor Pharmaceuticals AB

# LAY SUMMARY

## Lecigon 20 mg/ml + 5 mg/ml + 20 mg/ml intestinal gel (levodopa, carbidopa monohydrate and entacapone)

This is a summary of the Public Assessment Report (PAR) for Lecigon 20 mg/ml + 5 mg/ml + 20 mg/ml intestinal gel. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Lecigon in this lay summary for ease of reading.

For practical information about using Lecigon, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

**What is Lecigon and what is it used for?**
This product has been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA) for the United Kingdom, using the MR/DC Decision Reliance Procedure. This procedure takes into account the outcome of mutual recognition (MR) procedures in European Union Member States (and/or Iceland, Liechtenstein, Norway) on 24 September 2019 and 15 September 2020: SE/H/1986/001/MR and SE/H/1986/001/E/001, respectively).

This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indication.

Lecigon is used for the treatment of Parkinson's disease. It is used in advanced cases when oral medicines (medicines taken by mouth) no longer produce sufficient effect.

**How does Lecigon work?**
Lecigon is a gel for continuous delivery that is supplied through a pump and tube directly into the small intestine. Lecigon contains three active substances:
• levodopa
• carbidopa (in the form of carbidopa monohydrate)
• entacapone.

In a person with Parkinson's disease, the levels of dopamine in the brain are low. Levodopa is converted into dopamine in the brain, thereby relieving the symptoms of Parkinson's disease. Carbidopa and entacapone improve the effect that levodopa has on Parkinson's disease.

**How is Lecigon used?**
The pharmaceutical form of this medicine is an intestinal gel.

Lecigon intestinal gel is contained in cartridges and the gel is administered using a portable pump (Crono LECIG) and tube directly into the upper part of the intestine. The pump is connected to a tube that has been surgically positioned in the intestine via the abdominal wall.

The pump gives the patient a small dose throughout the day. This means that the level of the medicine in the blood stays the same. It also means that some side effects, like those affecting movement, are lower compared to medicines taken by mouth.

Before the tube is inserted into the small intestine, the doctor may choose to check whether treatment with Lecigon works for the patient. In such cases, the gel is given via a tube that passes through the nose, throat and stomach to the small intestine.

A manual with instructions for using the pump is supplied with the pump.

**Dosage**
The doctor adjusts the doses to the patient individually based on previous medication. It may be necessary to fine-tune the dose during the first few weeks of treatment.

A larger dose (called a bolus dose) is usually given in the morning when treatment is started so the medicine reaches the right levels in the blood quickly. After this, a continuous maintenance dose is given during the waking hours (usually about 16 hours). If necessary, the patient's doctor can decide to give Lecigon up to 24 hours a day.

Extra doses can also be given as needed.

Some individuals may also need to increase or decrease the continuous maintenance dose during the day. How and when the patient takes the extra doses or adjust the dose during the day will be decided by the doctor after consulting with their patient.

The total daily dose, including morning dose (bolus dose), maintenance dose and extra doses may not exceed 100 ml (which corresponds to 2000 mg levodopa, 500 mg carbidopa and 2000 mg entacapone).

If the user has dementia, the doctor may decide that the pump may only be handled by a healthcare professional or relative. The pump can be locked to prevent the daily recommended dose from being exceeded accidentally.

**Opened cartridge**
The cartridge of medicine is for single use only, and must not be used for more than 24 hours, even if there is medicine left. The dosage pump with installed cartridge can be worn close to the body for up to 16 hours. During overnight treatment, the pump should not be worn next to the body but can, for example, be kept on the bedside table. If there is a break in treatment during the night, the patient can continue using the opened cartridge the next day, but only for up to 24 hours after it was first opened. The patient/carer should not remove the cartridge from the pump until the patient has finished using it (i.e. either after 24 hours have passed since it was opened or when it is empty, whichever occurs first).

The gel may become slightly yellow/reddish towards the end of its shelf life. This does not impact the effect of the treatment.

For further information on how Lecigon is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the MHRA website.

This medicine can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

**What benefits of Lecigon have been shown in studies?**
Data from several studies and clinical experience predicted Lecigon to be effective in the treatment of advanced Parkinsons´s disease when oral combination of the substances have not given satisfactory results.

**What are the possible side effects of Lecigon?**
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk/ or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

**Why was Lecigon approved?**
Based on the results from data described above the MHRA was of the opinion that Lecigon's benefits are greater than its risks in patients with advanced disease where oral medicines no longer provide a satisfactory result and recommended Lecigon to be approved for use.

**What measures are being taken to ensure the safe and effective use of Lecigon?**
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Lecigon. The RMP details the important risks of Lecigon, how these risks can be minimised, any uncertainties about Lecigon (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Lecigon:

| Summary of safety concerns | |
|---|---|
| Important identified risks | • Myocardial infarction and other ischaemic heart disease |
| Important potential risks | • None |
| Missing information | • Use in pregnancy and breast-feeding<br>• Clinical relevance of hydrazine content |

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Lecigon are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

**Other information about Lecigon**
A Marketing Authorisation was granted in the United Kingdom on 18 May 2022.

The full PAR for Lecigon follows this summary.

This summary was last updated in July 2022.

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# I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Lecigon 20 mg/ml + 5 mg/ml + 20 mg/ml intestinal gel (PL 53856/0001) could be approved.

The product is approved for the following indication:

- 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.

Lecigon 20 mg/ml + 5 mg/ml + 20 mg/ml intestinal gel is a combination of levodopa, carbidopa monohydrate and entacapone (ratio 4:1:4) in a gel for continuous intestinal infusion.

According to current knowledge, the symptoms of Parkinson's disease are related to the lack of dopamine in the corpus striatum. Dopamine does not cross the blood-brain barrier.

Levodopa, a metabolic precursor of dopamine, crosses the blood-brain barrier and relieves the symptoms of the disease. Since levodopa is extensively metabolised peripherally in tissues, only a small proportion of the given dose reaches the central nervous system when levodopa is administered without metabolic enzyme inhibitors.

Carbidopa is a peripheral decarboxylation with dopadecarboxylase (DDC) inhibitor which reduces the peripheral metabolism of levodopa to dopamine, thereby making more levodopa available to the brain. When decarboxylation of levodopa is reduced through co-administration of a DDC inhibitor, a lower dose of levodopa can be used and the incidence of adverse events such as nausea may be reduced.

When decarboxylase is inhibited with a DDC inhibitor, catechol-O-methyltransferase (COMT) becomes the dominant peripheral metabolic pathway. Entacapone is a reversible, specific and mainly peripherally-acting COMT inhibitor designed for co-administration with levodopa. Entacapone reduces clearance of levodopa from the blood, resulting in an increased AUC in the pharmacokinetic profile of levodopa. Consequently, the clinical response of levodopa is prolonged.

This product has authorised by the MHRA for the United Kingdom using the MR/DC Decision Reliance Procedure. This procedure takes into account the outcome of mutual recognition (MR) procedures in European Union Member States (and/or Iceland, Liechtenstein, Norway) on 24 September 2019 and 15 September 2020 with Sweden as the Reference Member State (RMS) [SE/H/1986/001/MR and SE/H/1986/001/E/001, respectively].

For the scientific discussion of the quality, non-clinical and clinical assessment conducted during the MR procedures, please refer to the RMS Public Assessment Report, available on the RMS regulatory agency website or on the Heads of Medicines Agencies website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a full product specific waiver (P/0011/2019).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A Marketing Authorisation was granted on 18 May 2022.

## II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

## PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

## LABEL

The labelling is in line with current guidelines and is satisfactory.

## III. QUALITY ASPECTS

The MHRA considered that the quality data submitted for this application is satisfactory,

The grant of a Marketing Authorisation is recommended.

## IV. NON-CLINICAL ASPECTS

The MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of  a Marketing Authorisation is recommended.

## V. CLINICAL ASPECTS

The MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a Marketing Authorisation is recommended.

## VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulations 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

## VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

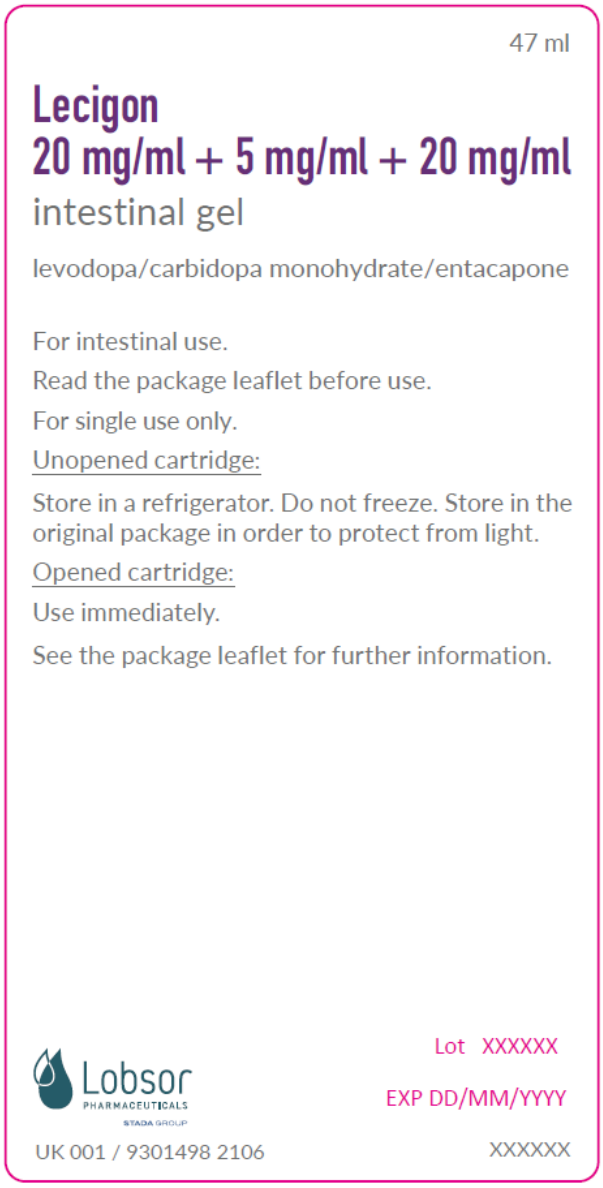
## VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The SmPC, PIL and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided below.



UK Lecigon label 001_8.pdf

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the Marketing Authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

| **Application type** | **Scope** | **Product information affected** | **Date of grant** | **Outcome** | **Assessment report attached Y/N** |
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