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# Refusal of the marketing authorisation for Nouryant (istradefylline)

## Re-examination confirms refusal

After re-examining its initial opinion, the European Medicines Agency has confirmed its recommendation to refuse marketing authorisation for the medicine Nouryant. The medicine was intended for the treatment of Parkinson's disease.

The Agency issued its opinion after re-examination on 11 November 2021. The Agency had issued its initial opinion on 22 July 2021. The company that applied for authorisation of Nouryant is Kyowa Kirin Holdings B.V.

### What is Nouryant and what was it intended for?

Nouryant was developed as a medicine to treat adults with Parkinson's disease (a progressive brain disease that causes shaking and muscle stiffness and slows movement).

Nouryant was intended to be used in addition to treatment based on levodopa (a medicine commonly used to treat the symptoms of Parkinson's disease) to treat patients who are experiencing 'off' periods. 'Off' periods are when the patient has difficulty moving about and occur when the effect of the last dose of levodopa wears off.

Nouryant contains the active substance istradefylline and was to be available as tablets to be taken by mouth once a day.

### How does Nouryant work?

The active substance in Nouryant, istradefylline, is an adenosine $A_{2A}$ receptor antagonist and works in a different way to levodopa. It attaches to and blocks the activity of adenosine $A_{2A}$ receptors which are found on certain brain cells and are involved in controlling movement. When the effect of levodopa wears off, dopamine levels drop, leading to an increase in symptoms. Nouryant is intended to balance this effect by blocking the $A_{2A}$ receptors.

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## What did the company present to support its application?

The company presented the results of eight main studies involving 3,245 patients with Parkinson's disease who were receiving treatment based on levodopa and were experiencing 'off' time on this treatment. The studies compared the effect of Nouryant with that of placebo (a dummy treatment) and, in one study, entacapone (another Parkinson's disease medicine) in reducing the 'off' time when given in addition to levodopa-based treatment.

## What were the main reasons for refusing the marketing authorisation?

At the time of the initial evaluation, the Agency considered that the results of the studies were inconsistent and did not satisfactorily show that Nouryant was effective at reducing the 'off' time. Only four out of the eight studies showed a reduction in 'off' time, and the effect did not increase with an increased dose of Nouryant. The Agency also noted that no effect was seen in the two studies that included patients from EU populations, including the most recent study which involved patients who were receiving the maximum and optimal treatment for their Parkinson's disease.

The initial refusal was confirmed after re-examination. The Agency looked at the data from the company again and confirmed that efficacy cannot be considered established based on the available results. Therefore, the Agency concluded that the benefits of Nouryant did not outweigh its risks and maintained the previous recommendation that the medicine be refused marketing authorisation.

## Does this refusal affect patients in clinical trials?

The company informed the Agency that there are no ongoing clinical trials with Nouryant.