

DSEN ABSTRACT

A Network Meta-Analysis of Cardiovascular Risk Associated with Stalevo (levodopa/carbidopa/entacapone)

Summary

A systematic review and network meta-analysis of the safety evidence of Stalevo for the treatment of Parkinson's Disease with the aim to discover if patients treated with Stalevo are at an increased risk for myocardial infarction, stroke, or cardiovascular death compared to those taking carbidopa/levodopa alone.

Key messages

No increase in stroke or cardiovascular death were associated with Stalevo.

A small increase in cardiovascular risk (a composite of all outcomes) and myocardial infarction were associated with Stalevo, but the limited data available precludes any definite conclusions that can be drawn from these analyses.

Further study assessment of Stalevo in patients with Parkinson's Disease is suggested to assess the risk of potential harms. A subsequent cohort study found no association.

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What is the issue?

- Stalevo is the brand name for an anti-parkinsonian dopaminergic agent containing three active substances (levodopa, carbidopa, and entacapone) that is indicated in adult patients with idiopathic Parkinson's disease who experience end-of-dose "wearing off".
- In 2010, the United States Food and Drug Administration (FDA) issued a Drug Safety Communication warning that Stalevo may be associated with increased risk of myocardial infarction (MI), stroke, and cardiovascular death.
- However, due to the inconsistent findings in the internal FDA study, further exploration of this safety signal was warranted.

What was the aim of the study?

- To review the evidence on the safety of Stalevo in patients with Parkinson's disease.

How was the study conducted?

- We undertook a systematic review of randomized controlled trials followed by meta-analysis and Bayesian network meta-analysis for the following outcomes: all-cause stroke or systemic embolism, cardiovascular death, MI, and cardiovascular risk (composite of all cause stroke or systemic embolism, cardiovascular mortality, MI).

What did the study find?

- The literature search identified 34 randomized controlled trials (RCT). Eleven of the 34 RCTs were excluded from analysis because data was not reported for at least one of the cardiovascular risk outcomes.
- Results showed a small significant increase in cardiovascular risk (composite) and MI; however, these results should be interpreted with caution due to the significant limitations of the available data.
- No statistically significant differences were detected for other outcomes.
- We suggest further assessment of safety outcomes using non-randomized studies. NOTE: Following completion of this report, a large administrative database cohort study of patients with Parkinson's Disease found no association between Stalevo and risk of stroke, MI or death.

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Link to technical report: [Wells et al. 2013](#)