This is a repository copy of *PND2 – A Systematic Review and Network Meta-Analysis of Pharmacological Therapies Used for Patients with Advanced Parkinson’s Disease*.

White Rose Research Online URL for this paper:
http://eprints.whiterose.ac.uk/97344/

Version: Accepted Version

**Article:**
Ren, S., Cooper, K. orcid.org/0000-0002-7702-8103, Cooper, J.A. et al. (2 more authors) (2014) *PND2 – A Systematic Review and Network Meta-Analysis of Pharmacological Therapies Used for Patients with Advanced Parkinson’s Disease*. Value in Health, 17 (7). A390-A390. ISSN 1098-3015

https://doi.org/10.1016/j.jval.2014.08.856

**Reuse**
This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can’t change the article in any way or use it commercially. More information and the full terms of the licence here: https://creativecommons.org/licenses/

**Takedown**
If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.
A Systematic Review and Network Meta-Analysis of Pharmacological Therapies Used for Patients with Advanced Parkinson’s Disease
Shijie Ren,1 Katy Cooper,1 James Cooper,2 Helen Smith,2 Soraya Shaikh2

1 School of Health and Related Research, University of Sheffield, Sheffield, United Kingdom
2 GlaxoSmithKline, Brentford, Middlesex, United Kingdom

Objectives
To assess the relative efficacy and safety of modified-release levodopa (IPX066), controlled-release levodopa and add-on therapy to immediate-release levodopa (including dopamine agonists, monoamine oxidase-B inhibitors (MAOBI), and catechol-O-methyl transferase inhibitors (COMTI)) using network meta-analysis (NMA).

Methods
A systematic literature search was conducted in MEDLINE, MEDLINE In-Process, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, DARE and HTA. A random effects NMA was used to determine the relative efficacy and safety of treatments on off-time reduction, three Unified Parkinson’s Disease Rating Scale (UPDRS) scores, patient withdrawals, and six adverse events in WinBUGS. An additional analysis was conducted to assess treatment class effects. Node-splitting approach was used to assess the assumption of consistency when direct and indirect evidence was combined.

Results
Forty-three trials with 9,453 patients were identified. Immediate-release levodopa plus pramipexole produced the greatest reduction in off-time relative to immediate-release levodopa plus placebo (-1.71 hours a day; 95% CrI: -2.11, -1.35), followed by IPX066 (-1.40; 95% CrI: -2.19, -0.67). The greatest improvement on UPDRS ADL score was given by add-on ropinirole (-2.33 points; 95% CrI: -3.53, -1.06); on UPDRS motor and total score was given by add-on pramipexole (-5.88 points; 95% CrI: -7.22, -4.63 and -10.09 points; 95% CrI: -13.75, -6.56, respectively). Dyskinesia was increased with IPX066 and adjuvant therapy classes except for MAOBI. Patient withdrawals were also increased with IPX066 and controlled-release levodopa.
Conclusions
The NMA showed that all treatments except controlled-release levodopa were associated with a statistically significant reduction in off-time. Dopamine agonist class as adjunctive to levodopa therapy had the greatest reduction. IPX066 was broadly comparable with add-on dopamine agonists on off-time reduction, and comparable with add-on MAOBIs and COMTIs on UPDRS scores. However, the treatments were associated with an increase in the risk of having dopaminergic side effects, particularly dyskinesia.