Efficacy and Safety of Piribedil in Early Combination with L-dopa in the Treatment of Parkinson’s Disease: A 6-month Open Study

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Background : Piribedil is a non-ergot D2/D3 dopamine agonist with antagonistic effect on α2-adrenoceptors and lack of agonist properties at 5-HT2A/2C receptors. Previous studies indicated its efficacy in monotherapy as well as in combination with L-dopa in treating Parkinson’s disease patients.

Objective : To assess the efficacy and acceptability of the dopamine agonist piribedil, in reducing motor symptoms of Parkinson’s disease in L-dopa-treated parkinsonian patients.

Patients and Method : A 6-month, open-labeled, multicenter study was conducted in Thai Parkinsonian patients who were insufficiently controlled by L-dopa (< 600 mg/day). Piribedil 50 mg in retard form was titrated upward to 150 mg/day (50 mg tid) by the 5th week and up to 6 months as an add-on treatment. L-dopa daily dose was kept stable until the 3rd month and could be adjusted afterwards.

The main efficacy parameter was the change in UPDRS part III score versus baseline over Full Analysis Set, score variation, and percentage of responders defined by at least 30% decrease from baseline of total UPDRS part III score. The secondary efficacy criteria were changes in L-dopa dose between the third month and the end of the study, UPDRS part II score variation, Hoehn and Yahr stage variation and Schwab and England Activities of Daily Living Scale variation.

The acceptability of piribedil was assessed by physical examination, weight, blood pressure and heart rate as well as the reported adverse events.

Results : Twenty-nine patients (55.2% male) with the mean age of 64.0 ± 7.2 years and mean duration of disease of 18.3 ± 8.2 months were recruited. The mean UPDRS part III score at baseline was 19.8 ± 11.4. After 6-month treatment with piribedil, mean UPDRS part III score significantly decreased to 6.6 ± 4.7 (p < 0.0001) with mean score variation of 13.3 ± 10.3. Twenty-seven patients (93.1%) were responders. Mean UPDRS part II score was significantly decreased from 7.2 ± 5.4 at baseline to 2.7 ± 2.1 at the end of 6 months (p < 0.0001). Hoehn and Yahr stage and Schwab and England Activities of Daily Living Scale were also significantly improved. Reported adverse events were mainly gastrointestinal symptoms. Blood pressure and heart rate were not significantly changed during the study period. Peak dose dyskinesia was reported only in one patient. Two patients (6.9%) were withdrawn because of adverse events.

Conclusion : Piribedil was effective on motor symptoms during a 6-month treatment in early parkinsonian patients insufficiently controlled by L-dopa and it was well tolerated.

Keywords : Piribedil, Dopamine agonist, Non-ergot, Parkinson’s disease

J Med Assoc Thai 2004; 87(11): 1293-300
Full text. e-Journal: http://www.medassocthai.org/journal

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Parkinson’s disease is one of the most common neurodegenerative disorders of middle, and late life characterized clinically by resting tremor, muscle rigidity, bradykinesia/akinesia, and postural instability. Neurochemically, depletion of the neurotransmitters dopamine, synthesized by the pigmented neurons in the substantia nigra and released primarily in the basal ganglia, is seen (1). 

L-dopa is the gold standard for treatment of Parkinson’s disease. Use of this drug usually results in a dramatic response, but after 5 years, half of the patients begin to experience motor fluctuations. The most common and earliest pattern is the wearing off phenomenon (2). As the disease progresses, that pattern becomes less predictable with some doses giving delayed or no responses, which leads to increasing disability and a progressive deduction in quality of life. The definitive cause of motor fluctuations is not fully known.

Increasing evidence indicates that such problems are related to abnormal pulsatile stimulation of striatal dopamine receptors and that treatment providing more continuous stimulation reduces the risk that they will occur (3). As a consequence, many physicians now initiate Parkinson’s disease therapy with a dopamine agonist (4), which directly stimulates striatal dopamine receptors, an approach that offers several potential advantages (5,6). They are more selective in their actions compared with L-dopa and may exhibit relative selectivity for different subtypes of dopamine receptors (7). Most of them have a substantially longer duration of action than L-dopa and often improve dose-related motor fluctuations (8).

The rationale for the use of dopamine agonist monotherapy in early disease is to delay the initiation of L-dopa or to decrease the total exposure to L-dopa, thereby reducing motor complications that are often seen with long-term L-dopa therapy (4,5). Early combination therapy of dopamine agonist with L-dopa has been suggested as a strategy to improve symptoms of Parkinson’s disease while minimizing or delaying the development of motor complications and disabilities (3).

The reason for introduction of dopamine agonist is that dopamine agonist receptor remains responsive with direct stimulation even during “off” period, and the addition of dopamine agonist may improve antiparkinsonian efficacy by increasing “on” time and decreasing motor fluctuations (9).

Piribedil is a non-ergot, direct dopamine agonist with demonstrated activity on dopamine receptors in the nigrostriatal, mesolimbic, mesocortical and tubero-infundibular pathways, and on peripheral vascular dopamine receptors. It differs from other dopamine agonists by its selective affinity for D2 and D3 receptors and its non-ergot structure. It possesses a unique pattern of interaction at multiple, human monoaminergic receptors. Its antagonist properties on central α2-adrenoceptors may facilitate cognitive and motor functioning (10). Piribedil is also associated with a non-significant incidence of somnolence when compared with placebo (11). The lack of agonist properties at 5-HT2A receptors is optimizing its therapeutic efficacy and minimizing psychiatric side effects (12). In addition, piribedil’s long elimination half-life of 21 hr may ensure more stable plasma concentrations and better clinical efficacy (9). Usually 3-7 weeks are required to achieve its common therapeutic efficacy range (150-250 mg) in monotherapy and only 1-3 weeks in combination with L-dopa (8).

Piribedil can be used as an initial treatment as well as in combination with L-dopa. It is active as monotherapy on all the cardinal signs of Parkinson’s disease, and is the treatment of choice for Parkinsonian tremor (13). Its use at an early stage can also delay the need for L-dopa and hence delay the onset of iatrogenic motor disorders. Several open and blind studies have shown piribedil to be effective in reversing akinesia, rigidity and tremor in Parkinsonian patients (14).

Objective

The objective of this study was to evaluate the efficacy and safety profile of piribedil in early combination with L-dopa treatment on motor symptoms of Parkinson’s disease over 6-months.

Patients and Method

A 6-month, open labeled, multicenter study was conducted in 6 hospitals in Bangkok (Pramongkutkla, Siriraj, Rajavithi, Vajira, and Noppharatrabhathani Hospitals) and one in upcountry (Maharat Nakorn Chiang Mai Hospital). Patients, male or female, aged between 40 and 80 years old, diagnosed idiopathic Parkinson’s disease according to UK Parkinson’s Disease Society Brain Bank were recruited. All had the duration of disease from their first clinical symptoms of less than 5 years. They were required to have a minimum score of 8 on Unified Parkinson’s Disease rating Scale (UPDRS) part III (motor examination) and a stage I-III by the Hoehn and Yahr classification, but insufficiently controlled clinically by a L-dopa regimen of ≤ 600 mg/day during the past 2 years.

The non-inclusion criteria were: pure akineti-hypertonic Parkinsonism, a history of recent cardio-
vascular disease (recent acute myocardial ischemia, orthostatic hypotension, uncontrolled hypertension), a severe psychological disorder (cognitive impairment, confusion), psychiatric symptoms or chronic illness (liver or kidney failure, severe or uncontrolled diabetes, cancer), and never been treated with a type A or B monoamine oxidase inhibitor, neuroleptic or piribedil. Patients already on a non-levodopa antiparkinsonian therapy (anticholinergics, propranolol, or other dopamine agonists) underwent a 2-week washout period before final inclusion. Female patients of child-bearing potential without effective contraception were not eligible to participate in this study.

The study protocol was approved by the Ethical Committee of the Ministry of Public Health. All patients were informed about the purpose of the trial and how it would be conducted. Patient’s informed consents were obtained prior to the enrollment.

The eligible patients underwent a single blinded controlled period for 2 weeks to washout the effects of previous non-levodopa antiparkinsonian therapy. Treatment schedules were divided into the adjustment period from day 0 to day 42, and the active treatment period from day 42 to 6 months. Piribedil 50 mg (1 tablet) in retard form was administered as a single evening dose for 14 days before increasing by 50 mg every 2 weeks to the final dose of 150 mg/day in three divided doses during meals. Then the appropriate dose of piribedil was kept stable during the active treatment period, from the beginning of week 7 until the end of 6-months. L-dopa was administered at constant daily dosage until the end of third month and could be adjusted afterwards according to clinical efficacy. The patients were first examined at 2-week intervals for 8 weeks (including the 2 weeks washout period), then at the end of the third and the sixth month. The evaluation protocol included the following: (a) UK Parkinson’s Disease Society Brain Bank - Clinical Diagnostic Criteria at D-15; (b) physical examination, UPDRS part III score, and dose of L-dopa at each visit; (c) UPDRS part II at D-15, D00, D42, M3 and M6; (d) Hoehn and Yahr Stage and Schwab and England Activities of Daily Living Scale at visits D-15, D00 and M6; (e) routine laboratory testing including hematologic, hepatic, and renal tests at visits D-15 and M6. Any adverse events reported were recorded at each visit.

The main efficacy criteria of piribedil were assessed by the analysis of UPDRS part III score, mainly in terms of score variation from baseline at the end of the 6-month study and also in terms of percentage of responders, which was defined as a decrease of 30%, or more from baseline of total UPDRS part III score. The secondary efficacy criteria were change of L-dopa dose between the third month and the end of the study, UPDRS part II score variation, Hoehn and Yahr stage variation and Schwab and England Activities of Daily Living Scale variation. The acceptability of piribedil was assessed by physical examination, weight, blood pressure and heart rate at all visits as well as the reported adverse events.

Statistical analysis was performed on the changes between inclusion and the end of the study in Full Analysis Set (FAS).

**Results**

A total of 34 idiopathic Parkinson’s disease patients were initially recruited into the study, one patient did not come back for any visit and 4 patients had protocol violation. Therefore, 29 patients (55.2% male) were eligible for analysis. The mean age was 64.0 ± 7.2 years (range 41-76 years). Demographic data of all patients are shown in Table 1. The disease had been present for less than two years in 18 cases, and from 2 to 4 years in 11 cases with the mean duration of disease of 18.3 ± 8.2 months. No one had a family history of the disease. The first clinical symptoms were tremor in 21 cases, bradykinesia in 4 cases and 4 cases of unknown records. All of them had already been on L-dopa treatment with the mean dose of 300 ± 132 mg/day for the mean duration of 10.4 ± 6.7 months.

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male n (%)</td>
<td>16 (55.2%)</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>13 (44.8%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64.0 ± 7.2 (range 41-76 years)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.7 ± 10.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.5 ± 7.3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.6 ± 3.3</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>133.3 ± 18.3</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>80.0 ± 7.9</td>
</tr>
<tr>
<td>HR (beat/min)</td>
<td>73.1 ± 9.4</td>
</tr>
<tr>
<td>Duration of PD (months)</td>
<td>18.3 ± 8.2 (range 2-37 months)</td>
</tr>
</tbody>
</table>

**Table 1. Patient demographic data (n = 29)**
anti-parkinson drugs had been also co-prescribed: 10 cases had been receiving anticholinergics, 3 cases other dopamine agonists and 2 cases MAOI-inhibitors. These drugs were stopped 2 weeks before starting the study. Six patients had a concomitant disease, 5 cases had controlled hypertension and one case had osteoarthritis.

Two patients (6.9%) were withdrawn from the study due to adverse events reported at the end of week 2 and at the third month, respectively. Another 4 cases (13.8%) could not complete the study; 3 cases were lost for follow-up and one needed to have an operation for another disease. Therefore, 23 patients completed the study. The main study results were analyzed according to the Full Analysis Set of 29 patients in which the results after 6-month treatment were compared with the findings at inclusion.

During the first 3-month of treatment, the doses of L-dopa were kept constant in all patients. For piribedil, the doses were titrated upward to 150 mg/day at D28. However, 5 out of 28 patients (17.9%) still received piribedil at the dose of 100 mg/day due to satisfactory efficacy at this dose. At the end of study period (M6), 7 out of 23 patients (30.4%) received only 100 mg/day of piribedil.

**Efficacy of piribedil**

UPDRS part III score during 6-month treatment with piribedil gradually decreased with time (Fig. 1). UPDRS part III score improved by 64.3%, decreasing from 19.8 ± 11.4 to 6.6 ± 4.7 (Table 2) with the mean score decrease of 13.3 ± 10.3. These results have been confirmed by the Per Protocol Analysis in which UPDRS part III score improved by 67.5%, decreasing from 19.8 ± 11.4 to 6.2 ± 4.8 with the mean score reduction of 14.5 ± 10.9 (data not shown). The responder rates (percentage of patients demonstrating improvement >30% on UPDRS III score) were 82.8% at the end of three months and 93.1% at the end of six months (Fig. 3).

The total score on UPDRS part II after 6 month treatment decreased by 49.1% from 7.2 ± 5.4 to 2.7 ± 2.1 with the mean score variation of 4.7 (Table 2 and Fig. 2). Hoehn and Yahr stage of all patients were significantly improved. At inclusion 58.6% of patients had Hoehn and Yahr stage I or II handicap for a disease duration of 18.3 ± 8.2 months with the mean score of 2.0 ± 0.6. After 6-month treatment with piribedil, this percentage increased to 87.0% with the mean score reduced to 1.6 ± 0.7 (Tables 2 and 3).

Schwab and England Activities of Daily Living score significantly improved in all patients.

**Table 2.** Efficacy of piribedil in Parkinson’s disease patients after 6-month treatment (Full analysis set; N=29)

<table>
<thead>
<tr>
<th>Parkinson’s disease</th>
<th>Score</th>
<th>Δ% (D00-M6)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS III</td>
<td>19.8 ± 11.4</td>
<td>6.6 ± 4.7</td>
<td>64.3</td>
</tr>
<tr>
<td>UPDRS II</td>
<td>7.2 ± 5.4</td>
<td>2.7 ± 2.1</td>
<td>49.1</td>
</tr>
<tr>
<td>Hoehn and Yahr</td>
<td>2.0 ± 0.6</td>
<td>1.6 ± 0.7</td>
<td>20.7</td>
</tr>
<tr>
<td>Schwab and England</td>
<td>84.3 ± 13.7</td>
<td>93.5 ± 5.7</td>
<td>8.7</td>
</tr>
</tbody>
</table>

* Comparing mean score at M6 with baseline values

Δ% = Percentage difference from baseline, ND = Not determined
According to the protocol, it was possible to adjust the dose of L-dopa after 3-month. However, in the present study, no patient required L-dopa dose adjustment until the end of the 6-month period.

**Acceptability and safety of piribedil**

Six patients dropped out from the study. Two (6.9%) due to adverse effects; 3 due to loss of follow-up and 1 needed to have an operation for another disease. Side effects leading to withdrawal were myalgia and headache in one case, and nausea, vomiting and hallucination in the other case. During the 6-month treatment, 13 patients reported multiple tolerable side effects. Most of them were nausea and vomiting (8 cases), dizziness (4 cases), hallucination, dryness of mouth and vertigo (2 cases each). Even though domperidone had been authorized in the protocol as concomitant treatment to avoid potential gastrointestinal adverse events related to piribedil, only 3 out of 8 patients with nausea and vomiting received domperidone. Peak dose dyskinesia was observed once in one patient at D14.

There were no statistical significant differences for BMI, blood pressure and heart rate throughout the study period, except for heart rate on supine position (Table 5 and Fig. 4). No abnormalities in hematologic, hepatic, or renal function were observed throughout the study period.

**Discussion**

L-dopa has been the gold standard in the treatment of Parkinson’s disease for many years. However, L-dopa can lose clinical efficacy with time, frequently leading to motor fluctuations. The motor symptoms initially controlled return, and the autonomy the patient had regained is gradually lost again, necessitating L-dopa dose increase. But dose increase usually results in motor complications, mainly dyski-
nesias. Moreover, the psychological well-being of the patient can be dramatically affected. Therefore, the rational option, in order to reduce the risk of L-dopa related motor complications, is to first start treatment with a dopamine agonist and defer the initiation of L-dopa in the treatment of Parkinson’s disease (4).

Another option is to add a dopamine agonist, such as piribedil instead of increasing the dose of L-dopa in insufficiently controlled patients, which provides a marked supplementary improvement. The present results confirmed that piribedil in early combination with L-dopa is effective in Thai Parkinson’s disease patients. The treatment significantly improved motor functions as shown by the reduced scores on the UPDRS part III scale (64.3% improvement; Table 2). Most of the patients responded to the treatment (93.1%), demonstrating more than 30% improvement in UPDRS part III score. The responder rate was already 83% after three month (Fig. 3, 4). The present results are in agreement with those of Kwiecinski et al (15), in which after six months treatment with piribedil in early combination with L-dopa, UPDRS III score decreased by 9.1 ± 8.7 in the Full Analysis Set of 271 patients with the response rate of 61% (15). However, the presented response rate was higher (93.1% versus 61%). This difference in response rate was also found compared with the results of Ziegler et al (16) in which the response rate in 115 patients was 61.8% after six months treatment with piribedil in combination with L-dopa. This may be due to the fact that the mean duration of disease in the present study was 18.3 ± 8.2 months (Table 1), whereas the duration in the mentioned studies was longer. These results suggest that early combination of piribedil with L-dopa improves treatment efficacy and quality of life in patients with Parkinson’s disease.

Combination of piribedil with L-dopa at an early stage of Parkinson’s disease could enable a reduction in L-dopa dose and, therefore, preventing long-term complications of L-dopa therapy. At advanced stages of Parkinson’s disease, this combination therapy could provide an increase in treatment efficacy whilst avoiding motor fluctuations or dyskinesias related to high doses of L-dopa. In the present study, even though the protocol allowed for L-dopa dose adjustment after 3 months no patient required an increase of L-dopa dose. At the end of the study period some patients (30.4%) received piribedil at the dose of 100 mg/day instead of 150 mg/day. It is possible that these patients would have benefited from an increase of piribedil dose and reduction of L-dopa dose in order to reduce long-term side effects of L-dopa.

Tolerance of piribedil was found to be satisfactory. Only 6.9% of patients withdrew from the study because of side effects. They tended to occur with the initiation of treatment and to abate as tolerance develops over several days to weeks (17). In the presented study, the most frequently reported side effect was nausea and vomiting (27.6%). In order to prevent this effect, concomitant domperidone therapy should be prescribed. Some patients also reported dizziness, though there was no indication of a hypotensive effect. Only one patient reported peak dose dyskinesis after 2 weeks of treatment, which did not reoccur even though the patient continued the treatment until the end of the six-month study period.

**Conclusion**

The present study shows that 6 months of treatment with piribedil 50 mg in retard form significantly improves motor score in patients insufficiently controlled by L-dopa. The recommended piribedil dose of 150 mg/day gave an excellent response rate in 93%
of patients. Piribedil was effective and well tolerated during a 6-month treatment in early Parkinson’s disease patients insufficiently controlled by L-dopa.

Acknowledgement

The authors wish to thank Servier (Thailand) Ltd. for their financial support.

References

การศึกษาประสิทธิภาพและความปลอดภัยของยาพีริบิดิลในการใช้ร่วมกับเลโวโดปาในระยะต้นของโรคพาร์กินสัน: การศึกษาแบบเปิดในเวลา 6 เดือน

จิตถนอม สุวรรณเตมีย์, สามารถ นิธินันทน์, สุวัฒน์ ศรีสุวรรณานุก, สมศักดิ์ พทิพย์ธีรธรรม, อภิชาติ พิศาลพงศ์, สิวาพร จันทร์กระจ่าง, อุดม บัณฑกุล

ภูมิหลัง: พีริบิดิลเป็นยากระตุ้นตัวรับโดปามีนชนิด non-ergotที่ออกฤทธิ์เฉพาะต่อตัวรับD2/D3และมีผลกระตุ้นα2-adrenoceptorsแต่ไม่มีคุณสมบัติในการกระตุ้นตัวรับ5-HT2A/2Cหากจากศึกษาต่างๆพบว่าพีริบิดิลมีประสิทธิภายนอกการกระตุ้นยาพีริบิดิลเพื่อใช้ร่วมกับยาเลโวโดปามีประโยชน์ในการรักษา

วัตถุประสงค์: เพื่อประเมินประสิทธิภาพและความปลอดภัยของการใช้พีริบิดิลเมื่อใช้ร่วมกับยาเลโวโดปาระบบการเคลื่อนไหว (motor symptoms)ของโรคพาร์กินสัน

วิธีการศึกษา: เป็นการศึกษาแบบเปิดระยะเวลา 6 เดือน ในผู้ป่วยโรคพาร์กินสันที่เป็นคนไทยและไม่สามารถควบคุมอาการได้ด้วยการใช้ยาเลโวโดปา (< 600 มก./วัน) โดยผู้ป่วยจะได้รับยาพีริบิดิลชนิดออกฤทธิ์ในขนาด 50 มก. คอย ๆ ปรับขนาดยาขึ้นจนถึง 150 มก./วัน (50 มก.วันละ 3 ครั้ง) ภายในเวลา 5 สัปดาห์และให้ยาในขนาดดังกล่าวต่อไปจนครบ 6 เดือน การใช้ยาจะเป็นแบบเติมยาหรือยาได้รับยาได้รับอยู่แล้ว โดยให้คุณสมบัติของยา เลโวโดปามาในขนาด 3 เดือนตามปริมาณยา

ปัจจัยหลักในการประเมินประสิทธิภาพของยาได้แก่การเปลี่ยนแปลงระดับคะแนนของ UPDRS part IIIหลังโดยการวัด 6 เดือนเพื่อเทียบกับก่อนได้รับยาโดยการใช้วิธีวิเคราะห์แบบFull Analysis Set ความเบี่ยงเบนของคะแนนและสัดส่วนของผู้ป่วยที่ตอบสนองต่อการใช้ยาที่มีค่าคะแนน UPDRS part III ลดลงจากก่อนได้รับยาตามที่ 30% ปัจจัยรองได้แก่การเปลี่ยนแปลงของคะแนนของยาได้รับยาในเรื่อง 3เดือนสุดท้ายของการศึกษา ค่าคะแนนที่เปลี่ยนไปของ UPDRS part II, Hoehn and Yahr stage, และ Schwab and England Activity ในเรื่องความปลอดภัยของการใช้ยาผู้ป่วยจะประเมินโดยการตรวจจดอาการ ซึ่งนำหน้าวิดีแอนเดอร์สิตและข้อต่อเกิดขึ้นทั้งไข้ ลดลงจาน รายงานอาการข้างเคียงจากการรักษา

ผลการศึกษา: มีผู้ป่วยจำนวน 29 คน (55.2% เป็นเพศชาย) อายุเฉลี่ย 64.0±7.2 ปี และคาดเฉลี่ยของระยะเวลาในการเริ่มใช้ยาพาร์กินสันในขณะเริ่มการศึกษา 18.3±8.2 เดือน คาดเฉลี่ยของคะแนน UPDRS part III 19.8±11.4หลังการรักษาคุณภาพพิริบิดิลรวมกับยาได้รับยาเป็นเวลา 6เดือน ระดับคะแนนต่ำสุดลดลงอย่างมีนัยสำคัญทางสถิติโดยมีระดับคะแนนลดลงเป็น 6.6±4.7 (P<0.0001) จากคะแนนกลาง 13.3±10.3 และมีผู้ป่วยที่ตอบสนองต่อการรักษาจำนวน 27 คน (93.1%) คาดความคิดเห็น UPDRS part III ลดลงอย่างมีนัยสำคัญทางสถิติ 7.2±5.4 กลับการรักษาเป็น 2.7±2.1 เมื่อสูงสุดการรักษา (P=0.0001) Hoehn and Yahr stage และ Schwab and England Activity มีการเปลี่ยนแปลงในทางที่ดีขึ้นอย่างมีนัยสำคัญ รายงานจากการข้างเคียงจากการใช้ยาหลายกลุ่มเกิดขึ้นระบบทางเดินอาหาร ความดันโลหิตและอัตราการเต้นของหัวใจเปลี่ยนแปลงอย่างไม่มีนัยสำคัญทางสถิติ ในระหว่างการศึกษาพบอาการ Peak dose Dyskinesia ในผู้ป่วย 1ราย และมีผู้ป่วยเพียง 2ราย (6.9%) ที่ถอนตัวจากการศึกษาเนื่องจากอาการข้างเคียง

สรุป: พีริบิดิลมีประสิทธิภาพและความปลอดภัยในการรักษาอาการทางการเคลื่อนไหว ในระยะต้นการรักษาผู้ป่วยพาร์กินสันระยะแรกซึ่งไม่สามารถควบคุมอาการโดยดีอย่างเวลายังไม่ได้รับยา