Summary of Investigation Results
Preparations containing levodopa

January 21, 2020

Non-proprietary name
a. Levodopa
b. Levodopa/carbidopa hydrate
c. Levodopa/carbidopa hydrate/entacapone
d. Levodopa/benserazide hydrochloride

Branded name (Marketing authorization holder)
See Attachment

Indications
See Attachment

Summary of revisions
Language concerning dopamine dysregulation syndrome should be added to the Important Precautions section.

Investigation results and background of the revision
Cases of dopamine dysregulation syndrome have been reported in patients treated with levodopa in Japan. MHLW/PMDA concluded that revision of the package insert was necessary based on the results of their investigation of the currently available evidence and in consultation with expert advisors as well as taking into account the language in the European package inserts.
Number of cases and patient mortalities reported in Japan during the previous 3 fiscal years

Cases involving dopamine dysregulation syndrome

a. No cases have been reported to date.

b. A total of 2 cases have been reported to date (A causal relationship between the drug and event could not be ruled out for either of these cases.)

   No patient mortalities have been reported to date.

c. 1 case has been reported to date (A causal relationship between the drug and event could not be established for this case.)

   No patient mortalities have been reported to date.

d. No cases have been reported to date.
### Attachment

<table>
<thead>
<tr>
<th>Non-proprietary name</th>
<th>Branded name (Marketing authorization holder)</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. <strong>Levodopa</strong></td>
<td>Dopaston Capsules 250 mg, Dopaston Powder 98.5%, Dopaston for Intravenous Use 25 mg, 50 mg (Ohara Pharmaceutical Co., Ltd.), Dopasol Tablets 200 mg (Alfresa Pharma Corporation)</td>
<td>Dopaston Capsules 250 mg, Dopaston Powder 98.5%, Dopaston for Intravenous Use 25 mg, 50 mg: Parkinson’s disease and Parkinson’s syndrome Dopasol Tablets 200 mg: Treatment and prophylaxis of the following symptoms associated with Parkinson’s disease/Parkinson’s syndrome Akinesia, muscle rigidity, tremor, impaired activities of daily living, mask-like faces, gait disturbance, language disorder, abnormal posture, pulsion, oily face, dysgraphia, psychiatric symptom, and ptyalism</td>
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<tr>
<td>b. <strong>Levodopa/carbidopa hydrate</strong></td>
<td>Neodopaston Combination Tablets L100, L250 (Daiichi Sankyo Co., Ltd.), Menesit Tablets 100, 250 (MSD K.K.), and the others</td>
<td>Parkinson’s disease and Parkinson’s syndrome</td>
</tr>
<tr>
<td>b. <strong>Levodopa/carbidopa hydrate</strong></td>
<td>Duodopa enteral combination solution (AbbVie GK)</td>
<td>Improvement of circadian change (wearing-off phenomenon) of symptoms of Parkinson’s disease in which sufficient effect cannot be</td>
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<td>Non-proprietary name</td>
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<td>Indications</td>
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<td>c. Levodopa/carbidopa hydrate /entacapone</td>
<td>Stalevo Combination Tablets L50, L100 (Novartis Pharma K.K.)</td>
<td>Parkinson's disease (when circadian rhythm of symptoms [wearing-off] is observed in administration of levodopa/carbidopa)</td>
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<td>d. Levodopa/benserazide hydrochloride</td>
<td>Neodopasol Combination Tablets (Alfresa Pharma Corporation), EC-Dopar Tablets (Kyowa Kirin Co., Ltd.), Madopar Combination Tablet (Taiyo Pharma Co., Ltd.)</td>
<td>Parkinson's disease and Parkinson's syndrome</td>
</tr>
</tbody>
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