



Summary of Investigation Results

Dopamine receptor agonists

August 22, 2019

Non-proprietary name

- a. Ropinirole hydrochloride
- b. Pramipexole hydrochloride hydrate
- c. Talipexole hydrochloride
- d. Rotigotine
- e. Cabergoline
- f. Bromocriptine mesilate
- g. Pergolide mesilate
- h. Apomorphine hydrochloride hydrate

Branded name (Marketing authorization holder)

See the attachment

Indications

See the attachment

Summary of revisions

1. Precaution for drug withdrawal syndrome should be added in the Important Precautions section.
2. "Drug withdrawal syndrome" should be added in the Other Adverse Reactions section.

Investigation results and background of the revision

Cases of drug withdrawal syndrome have been reported in Japan and overseas.

Considering the expected mechanism where dopamine receptor agonists induce drug withdrawal syndrome, MHLW/PMDA concluded that a precaution regarding drug withdrawal



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syndrome for the entire dopamine receptor agonist class was appropriate and 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.

Number of cases and patient mortalities reported in Japan during the previous 3 fiscal years

No cases involving drug withdrawal syndrome have been reported to date.



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Attachment

	Non-proprietary name	Brand name (Marketing authorization holder)	Indications
a	Ropinirole hydrochloride	ReQuip Tablets 0.25 mg, 1 mg, 2 mg, CR Tablets 2 mg, 8 mg (Glaxo Smith Kline K.K.), and the others	Parkinson's disease
b	Pramipexole hydrochloride hydrate	BI•Sifrol Tablets 0.125 mg, 0.5 mg (Boehringer Ingelheim Japan, Inc.), and the others	1. Parkinson's disease 2. Moderate to severe idiopathic restless legs syndrome
		Mirapex-LA Tablets 0.375 mg, 1.5 mg (Boehringer Ingelheim Japan, Inc.), and the others	Parkinson's disease
c	Talipexole hydrochloride	Domin Tablets 0.4 (Boehringer Ingelheim Japan, Inc.)	Parkinson's disease
d	Rotigotine	Neupro patch 2.25 mg, 4.5 mg, 9 mg, 13.5 mg, 18 mg (Otsuka Pharmaceutical Co., Ltd.)	Neupro patch 2.25 mg, 4.5 mg: • Parkinson's disease • Moderate to severe idiopathic restless legs syndrome Neupro patch 9 mg, 13.5 mg, 18 mg: • Parkinson's disease
e	Cabergoline	Cabaser Tablets 0.25 mg, 1.0 mg (Pfizer Japan Inc.), and the others	Parkinson's disease Galactorrhea Hyperprolactinemic ovulation disorder Hyperprolactinemic pituitary adenoma (limited to cases not requiring surgical procedure) Postpartum lactation suppression



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f	Bromocriptine mesilate	Parlodel Tablets 2.5 mg (Sun Pharma Japan Limited), and the others	Acromegaly Pituitary gigantism Galactorrhea Postpartum lactation suppression Hyperprolactinemic ovulation disorder Hyperprolactinemic pituitary adenoma (limited to cases not requiring surgical procedure) Parkinson's syndrome
g	Pergolide mesilate	Permax 50 µg, 250 µg (Kyowa Kirin Co., Ltd.), and the others	Parkinson's disease
h	Apomorphine hydrochloride hydrate	Apokyn subcutaneous injection 30 mg (Kyowa Kirin Co., Ltd.)	Improvement of wearing-off symptom in Parkinson's disease (cases that did not adequately respond to frequently administered levodopa-containing drugs or antiparkinsonian drugs at increased doses)