IMPORTANT MEDICINE SAFETY INFORMATION

15 October 2020

Dear Healthcare Professional

Re: DOPAMINERGIC MEDICINES USED IN THE TREATMENT OF PARKINSON'S DISEASE: RISK OF DOPAMINE DYSREGULATION SYNDROME

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), the companies listed below would like to inform you of the risk of a dopamine dysregulation syndrome (DDS) that may develop in patients with Parkinson's disease treated with dopaminergic medicines.

The Professional Information (PI) and Patient Information Leaflet (PIL) of dopaminergic containing medicines will be updated accordingly.

Summary

DDS is defined as the compulsive misuse of dopaminergic medicinal products and may result in craving for higher doses of dopaminergic medicines used for the treatment of Parkinson's disease, that are in excess of the doses needed to control movement symptoms adequately. In some cases, this may result in severe dyskinesia. DDS has been observed in some patients with Parkinson's disease during treatment with apomorphine, bromocriptine, cabergoline, levodopa/carbidopa, levodopa/benserazide, pramipexole, ropinirole and rotigoline.

Background on the safety concern

This safety concern is based on the European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee's (PRAC) recommendation from 2017, regarding the risk of DDS associated with carbidopa/ levodopa. Following PRAC's recommendations, a review on all dopaminergic medicines was conducted and documented evidence that DDS may occur with chronic use of all dopaminergic medicines was found.

Advice to healthcare professionals

Before the start of treatment with dopaminergic medicines for Parkinson's disease, patients and caregivers must be warned about the potential risk of developing DDS.

It is necessary to advise patients, if taking dopaminergic medicinal products to tell their doctor if the family / caregiver notice any addiction like symptoms.

Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality issues to SAHPRA via the eReporting link available on the SAHPRA website (www.sahpra.org.za). Alternatively, please complete the ADR reporting form accessible via the SAHPRA website at https://www.sahpra.org.za/documents/12e54dcaADRForms.pdf and email it to adr@sahpra.org.za or fax to (021) 448 6181. For more information on ADR reporting, please call the National Adverse Events Monitoring Centre (NADEMC) on (021) 447 1618.

For further information, kindly contact the respective companies below:

Company	Product Name	Active Ingredient(s)	Registration Number	Contact Details
Roche Products (Pty) Ltd	Madopar (tablets)	Levodopa/ benserazide 200/50	P/5.4.1/150	**Tel:** +27 11 502 5000 **Fax:** +27 11 268 5748 **Email:** global.irt_sahubtcs@roche.com
	Madopar HBS (capsule)	Levodopa/ benserazide 100/25	31/5.4.1/0194	
Ascendis Pharma (Pty) Ltd	Pramex 0,125	Pramipexole dihydrochloride	43/5.4.1/0624	**Tel:** +27 11 036 9651/9661 **Fax:** +27 866772110 **Email:** aysha.gani@ascendishealth.com dawn.keswa@ascendishealth.com
	Pramex 0,25	Pramipexole dihydrochloride	43/5.4.1/0623	
	Pramex 0,5	Pramipexole dihydrochloride	43/5.4.1/0622	
	Pramex 1,0	Pramipexole dihydrochloride	43/5.4.1/0625	
	Pramex 1,5	Pramipexole dihydrochloride	43/5.4.1/0626	
Ingelheim Pharmaceuticals (Pty) Ltd	Pexola 0,125 mg tablets	Pramipexole dihydrochloride monohydrate	32/5.4.1/0298	**Tel:** +27 11 348 2400 **Fax:** +27 86 407 1026 **Email:** PV_local_South_Africa@boehringer-ingelheim.com
	Pexola 0,25 mg tablets	Pramipexole dihydrochloride monohydrate	32/5.4.1/0299	
	Pexola 1,0 mg tablets	Pramipexole dihydrochloride monohydrate	32/5.4.1/0300	
	Pexola ER 0,375 mg extended release tablets	Pramipexole dihydrochloride monohydrate	43/5.4.1/1062	

	Pexola ER 0,75 mg extended release tablets	Pramipexole dihydrochloride monohydrate	43/5.4.1/1063	
	Pexola ER 1,5 mg extended release tablets	Pramipexole dihydrochloride monohydrate	43/5.4.1/1064	
	Pexola ER 3,0 mg tablets	Pramipexole dihydrochloride monohydrate	43/5.4.1/1065	
	Pexola ER 4,5 mg extended release tablets	Pramipexole dihydrochloride monohydrate	43/5.4.1/1066	
Teva	Teva Carbilevo 25/100	Carbidopa / Levodopa	32/5.4.1/0081	**Tel:** +27 11 055 0200 **Fax**: + 27 11 388 2688 **Email:** safety.south-africa@ teva.co.il
	Teva Carbilevo 25/250	Carbidopa / Levodopa	32/5.4.1/0024	
SUN Pharmaceuticals S.A. (Pty) Ltd	LECARDOP 25/ 100	Levodopa 100 mg Carbidopa 25 mg	45/5.4.1/0765	**Tel**: +27 12 643 2083 **Fax** : +27 12 643 2001/3 **Email**: Reshma.joshi@sunpharma.com Barryjames.lewis@ sunpharma.com
	LECARDOP 25/ 250	Levodopa 250 mg Carbidopa 25 mg	45/5.4.1/0764	
Aspen Pharmacare	Aspen Bromocriptine 2.5 mg tablets	Bromocriptine Mesylate equivalent to Bromocriptine	30/21.12/0459	**Tel:** +27 800 118 088 **Fax:** +27 11 239 6303

				Email: drugsafety@aspenpharma.com
	Pexasp 1 mg tablets	Pramipexole dihydrochloride monohydrate	42/5.4.1/1024	
	Pexasp 0,125 mg tablets	Pramipexole dihydrochloride monohydrate	42/5.4.1/1023	
	Pexasp 0,25 mg tablets	Pramipexole dihydrochloride monohydrate	42/5.4.1/1022	
	Carbilev 25/250 tablets	Levodopa/ Carbidopa	30/5.4.1/0269	
	Carbilev 25/100 tablets	Levodopa/ Carbidopa	30/5.4.1/0271	
GSK South Africa	Requip XL 2mg	Ropinirole hydrochloride	41/5.4.1/0604	**Tel:** +27 11 745 6000 **Email** Mu.Zinchub@gsk.com
	Requip XL 4 mg	Ropinirole hydrochloride	41/5.4.1/0606	
	Requip XL 8 mg	Ropinirole hydrochloride	41/5.4.1/0607	

References

1. Cartoon J, Ramalingam J. Dopamine dysregulation syndrome in non-Parkinson's disease patients: a systematic review. Australas Psychiatry. 2019; 27(5): 456-461.
2. Evans AH,. Lees, JA. Dopamine dysregulation syndrome in Parkinson's disease. Curr Opin Neurol. 2004; 17:393–398.

Yours sincerely,

Roche Products (Pty) Ltd

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