DocuSign Envelope ID: EBF929F0-96CF-4C3A-B40B-FCD3D7FE6F55

MSD (Pty) Ltd
(Reg. No. 1996/003791/07)
117 - 16th Road
Private Bag 3
Halfway House, 1685
South Africa
Tel: +27(0)11-655-3000
Fax: +27(0)11-655-3180

MSD
INVENTING FOR LIFE

IMPORTANT MEDICINE SAFETY INFORMATION

25 May 2021

Dear Healthcare Professional

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

MSD (Pty) Ltd, as directed by the South African Health Products Regulatory (SAHPRA) would like to inform healthcare professionals about the risk of dopamine dysregulation syndrome (DDS) associated with the use of dopamine containing medicines in the treatment of Parkinson's Disease. The Professional Information (PI) and Patient Leaflet (PIL) for carbidopa and levodopa (SINEMET and SINEMET CR™) will be amended to reflect this safety issue.

Summary

DDS is an addictive disorder that may occur with chronic use of all dopaminergic medicines. The most common symptom of DDS is compulsive dopaminergic drug cravings and misuse at doses above those needed to control motor symptoms, even in cases where symptoms of parkinsonism are absent. These excessive doses may, in some cases result in severe dyskinesias. Patients suffering from DDS, without the medication, may feel depressed or fatigued but become euphoric or grandiose when on the medication.

Background on the safety concern

This safety concern originated from a review of published literature conducted by the Pharmacovigilance Risk Assessment Committee (PRAC) in 2017, with a subsequent recommendation to update the labelling for dopaminergic medicines to include information about the risk of DDS. Following PRAC's recommendation, a review on all dopaminergic medicines was conducted and documented evidence that DDS may occur with chronic use of all dopaminergic medicines was found.

DocuSign Envelope ID: EBF929F0-96CF-4C3A-B40B-FCD3D7FE6F55

Advice to Healthcare professionals

- DDS is an addictive disorder which consist of a series of complications such as compulsive use of dopaminergic medications, aggressive or hypomanic behaviours during excessive use. Withdrawal states are characterised by dysphoria and anxiety, caused by long-term dopaminergic treatment in patients with Parkinson's disease.
- The risk of DDS may occur in patients on chronic treatment with dopaminergic medicines used for Parkinson's disease.
- Patients and caregivers should be warned of the symptoms of DDS prior to initiation of carbidopa and levodopa therapy,
- Caregivers or family members should be advised to tell their doctor if they notice addiction-like symptoms.

Healthcare professionals are urged to report any adverse drug reactions (ADRS), or product quality issues to SAHPRA Pharmacovigilance unit 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 DR reporting, please call the National Adverse Events Monitoring Centre (NADEMC) on (021) 447 1618.

Company	Name of product	Active Ingredient(s)	Registration Number	Contact details
MSD (Pty) Ltd	SINEMET 25/ 100 mg	carbidopa and levodopa 25 mg/100 mg	P/5.4.1/141	Tel: 011 655 3042 Fax: 011 655 3127 Nicky Holl: Pharmacovigilance Country Lead Email: pharmacovigilance.zaf@merck.com
	SINEMET 25/ 250 mg	carbidopa and levodopa 25 mg/ 250 mg	F/5.4.1/56	
	SINEMET CR	carbidopa and levodopa 50 mg/200 mg	Y/5.4.1/279	

References

1) Pressman P et al., Very Well Health. Dopamine Dysregulation Syndrome. A Rare Complication of Parkinson's Disease Medications https://www.verywellhealth.com/dopamine-dysregulation-syndrome-2488783 (Updated on 15 January 2020, Accessed on 19 June 2020).

DocuSign Envelope ID: EBF929F0-96CF-4C3A-B40B-FCD3D7FE6F55

2) Kummer A et al, Arq. Neuro-Psiquiatr. vol.64 no.4 Dec. 2006:1019-1022. Dopamine Dysregulation Syndrome in Parkinson's Disease. https://www.scielo.br/scielo.php?pid=S0004-282X2006000600026&script=sci_arttext (Accessed 19 June 2020)

3) Warren et al., 2017 J Neurol Neurosurg Psychiatry; 88(12): 1060-1064

https://pubmed.ncbi.nlm.nih.gov/29018160/ (Accessed 04 August 2020)

Yours faithfully,

Dushenthree Kettledas
Responsible Pharmacist
MSD (Pty) Ltd