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Pseudoephedrine: Risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)

Dear Healthcare Professional,

This Direct Healthcare Professional Communication has been submitted to you on behalf of Alfred Gera & Sons Limited, Bayer SA-NV, Delorbis Pharmaceuticals Limited, GlaxoSmithKline (Ireland) Limited, Haleon Hellas Single Member Societe Anonyme, under the distinctive title of Haleon Hellas, Johnson & Johnson (Ireland) Limited, JV Healthcare Limited, Medicem Limited, Medochemie Limited, Neofarma Pharmaceuticals Limited, NM Pharma Limited, Reckitt Benckiser Ireland Ltd., Rowa Pharmaceuticals Limited, TAD Pharma GmbH, UCB Pharma SA, V.J. Salomone Pharma Limited. in agreement with the European Medicines Agency and the Malta Medicines Authority would like to inform you of the following:
Risks of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)

Summary

- **Few cases of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) have been reported with the use of pseudoephedrine-containing medicines.**
- **Pseudoephedrine-containing medicines are contraindicated in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease or renal failure, as these conditions increase the risks of PRES or RCVS.**
- **Symptoms of PRES and RCVS include sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances.**
- **Patients should be advised to immediately stop using these medicines and seek medical assistance if signs or symptoms of PRES or RCVS develop.**

Background on the safety concern

Pseudoephedrine is authorised alone or in combination with other substances, for short-term symptomatic relief of nasal or sinus congestion caused by the common cold or allergic rhinitis, or vasomotor rhinitis, or aerotitis.

Cases of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS), which are serious conditions affecting the cerebral blood vessels, have been reported in patients taking pseudoephedrine-containing medicines. Most reported cases resolved following discontinuation and appropriate treatment. No fatal cases of PRES or RCVS have been reported.

Following an EU-wide review of reported cases and other available data to evaluate the risks of PRES and RCVS with pseudoephedrine-containing medicines, it has been concluded that pseudoephedrine is associated with risks of PRES and RCVS and that the product information should be updated to include information on these adverse reactions and measures to reduce the risks.

The newly identified risks of PRES or RCVS should be considered in the context of the overall safety profile of pseudoephedrine, which also includes other cardiovascular and cerebrovascular ischaemic events.

Overview of PRES and RCVS

PRES can manifest with a wide variety of acute or subacute neurological symptoms, including headache, mental status alteration, seizures, visual disturbances and/or focal neurologic deficits. An acute or sub-acute onset of the symptoms (hours to days) is typical. PRES is usually reversible; symptoms cease within several days or weeks with the reduction of blood pressure and withdrawal of causative drugs.

RCVS usually manifests with thunderclap headache (severe pain peaking in seconds), typically bilateral, with posterior onset followed by diffuse pain frequently accompanied by nausea, vomiting, photophobia and phonophobia. Transient focal deficits can be present in some patients. Ischaemic and haemorrhagic stroke are the major complications of the syndrome.

Call for reporting

Healthcare providers and patients are encouraged to report adverse reactions in accordance with the national spontaneous reporting system for Adverse Drug Reactions (ADRs). Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Malta Medicines Authority Post-licensing, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, or sent by email to: postlicensing.medicinesauthority@gov.mt. Please report the product name and relevant details.

Adverse events should also be reported:

Company contact point

Company	Product Name	Email	Phone
Alfred Gera & Sons Ltd.	Actifed 30mg/1.25mg per 5ml Syrup	pv@alfredgera.com	+356 79221091
Bayer SA-NV Belgium	Clarinase Repetabs 5mg/120mg prolonged-release tablets	pv@alfredgera.com	+356 79221091
Delorbis Pharmaceuticals Ltd.	Parcoten Cold & Flu 500 mg/30 mg/15 mg/60 mg Film-coated tablets	delorbis@delorbispharma.eu	+357 22 845000
GlaxoSmithKline (Ireland) Limited	Actifed Expectorant Oral Solution	mt.safety@gsk.com	+356 80065004
Haleon Hellas Single Member Societe Anonyme	Panadol Cold & Flu 500mg / 30mg film-coated Tablets	pv.cee@haleon.com	+356 79221091
Haleon Ireland Limited	Advil Cold & Flu Coated Tablets Ibuprofen 200 mg Pseudoephedrine Hydrochloride 30 mg	pv.cee@haleon.com	+356 79221091
JV Healthcare Limited	ACTIFED 30mg/1.25mg per 5ml Syrup	info@jvpharma.eu	+356 21437551

Johnson & Johnson (Ireland) Ltd.	Benylin Four Flu Film-Coated Tablets Paracetamol 500mg	regvjsp@vjsalomone.com	+356 21220174 +356 99644126
Medicem Limited	ACTIFED 30mg/1.25mg per 5ml Syrup	medicemmalta@gmail.com	+356 21653767 +356 99319002
Medochemie Ltd.	Medofed Compound Oral Solution	pharmacovigilance@medochemie.com alex.fenech@europharma.com.mt	+356 23859239
Medochemie Ltd.	Medofed 30 mg/1.25 mg per 5 ml, oral solution	pharmacovigilance@medochemie.com alex.fenech@europharma.com.mt	+356 23859239
Medochemie Ltd.	SNIP 325mg/15mg/1mg tablets	pharmacovigilance@medochemie.com alex.fenech@europharma.com.mt	+356 23859239
NM Pharma Ltd.	Prosinus 500 mg/30 mg film-coated tablets	pv@nmpharma.com.mt	+356 27559990
Neofarma Pharmaceuticals Ltd.	Panadol Cold and Flu 500mg / 30mg film-coated Tablets	info@neofarma.com.mt	+356 20109494 +356 99109494
Neofarma Pharmaceuticals Ltd.	Sudafed Decongestant Tablets	info@neofarma.com.mt	+356 20109494 +356 99109494
Neofarma Pharmaceuticals Ltd.	Cirrus 5 mg/120 mg Prolonged Release Tablets	info@neofarma.com.mt	+356 20109494 +356 99109494
Neofarma Pharmaceuticals Ltd.	ACTIFED 30mg/1.25mg per 5ml Syrup	info@neofarma.com.mt	+356 20109494 +356 99109494
Neofarma Pharmaceuticals Ltd.	Clarityne-D 5mg/120mg Prolonged-Release Tablets	info@neofarma.com.mt	+356 20109494 +356 99109494
Reckitt Benckiser Ireland Ltd.	Nurofen Cold & Flu Film-Coated Tablets Ibuprofen 200mg Pseudophedrine hydrochloride 30mg	pv@charlesdegiorgio.com dmifsud@charlesdegiorgio.com	+356 25600801
Rowa Pharmaceuticals Limited	Brupro Cold & Flu 200 mg/30 mg film-coated tablets	pv@rowa-pharma.ie	+356 23385313 +356 79829369
TAD Pharma GmbH	Daleron COLD3 325 mg/30 mg/15 mg film-coated tablets	drug-Safety@tad.de	+49 4721606 0

UCB Pharma SA	Cirrus 5 mg/120 mg Prolonged Release Tablets	sales@pharmasud.com	+356 21376436
VJ Salomone Pharma Ltd, Malta	Non-Drowsy Sudafed Decongestant 60mg film-coated Tablets	regvjsp@vjsalomone.com	+356 21220174 +356 99644126

Yours faithfully,

Post-Licensing Directorate
Medicines Authority

Disclaimer
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The MMA receives the relevant contact details from both the Medical Council and the Pharmacy Council. Should you wish to amend your details including address, you are asked to contact the Medical Council or Pharmacy Council directly, as may apply.