PRAC starts safety review of pseudoephedrine-containing products

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Information on Pseudoephedrine

- Pseudoephedrine is taken by mouth and is used alone or in combination with other medicines to treat nasal congestion (a blocked nose), headache, fever and pain resulting from a cold, flu or allergic rhinitis (inflammation of the nasal passages). It works by stimulating nerve endings to release the chemical noradrenaline, which causes the blood vessels to constrict (narrow). This reduces the amount of fluid released from the vessels, resulting in less swelling and less mucus production in the nose.
- Pseudoephedrine-containing medicines are authorised in various EU Member States alone, or in combination with other medicines. Within the EU, pseudoephedrine-containing medicines are available under various trade names, including Actifed, Aerinaze, Aspirin Complex, Clarinase, Humex rhume, and Nurofen Cold and Flu.

In Malta the following products are authorised through various licensing procedures.

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
Ibuprofen 200mg, Pseudoephedrine hydrochloride 30mg	Nurofen Cold & Flu	Film-coated tablet	OTC	MA1447/00104	Reckitt Benckiser Ireland Ltd
Ibuprofen 200mg, Pseudoephedrine hydrochloride 30mg	Advil Cold & Flu	Film-coated tablet	OTC	MA460/01001	GlaxoSmithKline Consumer Healthcare (Ireland) Limited
Paracetamol 500mg, Pseudoephedrine hydrochloride 30mg	Panadol Cold & Flu	Film-coated tablet	OTC	MA1177/00701	GlaxoSmithKline Consumer Healthcare Hellas Single Member Societe Anonyme
Paracetamol 500mg, Pseudoephedrine hydrochloride 30mg	Panadol Cold & Flu	Film-coated tablet	OTC	PI908/10501A	NeoFarma Pharmaceuticals Limited
Paracetamol 500mg, Pseudoephedrine hydrochloride 15mg, Chlorphenamine maleate 1mg	SNIP	Tablet	OTC	MA032/06402	Medochemie Limited
Diphenhydramine hydrochloride 12.5mg, Paracetamol 500mg, Pseudoephedrine hydrochloride 22.5mg	Benylin Four Flu	Film-coated tablet	OTC	MA1315/00204	Johnson & Johnson (Ireland) Limited

Paracetamol 500mg, Pseudoephedrine hydrochloride 30mg, Dextromethorphan hydrobromide 15mg, Ascorbic acid 60mg	Parcoten Cold & Flu	Film-coated tablet	OTC	AA115/01703	Delorbis Pharmaceuticals Limited
Paracetamol 500mg, Pseudoephedrine hydrochloride 30mg	Panadol Cold and Flu	Film-coated tablet	OTC	PI521/08202B	Medicem Limited
Paracetamol 325mg, Pseudoephedrine hydrochloride 30mg, Dextromethorphan hydrobromide 15mg,	Daleron COLD3	Film-coated tablet	OTC	MA982/02701	TAD Pharma GmbH
Pseudoephedrine hydrochloride 60mg	Sudafed	Film-coated tablet	OTC	AA908/09901	NeoFarma Pharmaceuticals Limited
Pseudoephedrine hydrochloride 60mg	Sudafed	Film-coated tablet	OTC	AA288/00802	V.J. SALOMONE PHARMA LIMITED
Cetirizine dihydrochloride 5mg, Pseudoephedrine hydrochloride 120mg	Cirrus	Prolonged-release tablet	OTC	MA030/00801	UCB Pharma SA
Dextromethorphan hydrobromide 10mg/5ml, Triprolidine hydrochloride 1.25mg/5ml, Pseudoephedrine hydrochloride 30mg/5ml	Actifed DM Cough Linctus	Oral solution	POM	MA192/02001	Glaxo SmithKline Ireland Limited
Triprolidine hydrochloride 1.25mg/5ml, Guaifenesin 100mg/5ml, Pseudoephedrine hydrochloride 30mg/5ml	Actifed Expectorant	Oral solution	POM	MA192/02003	Glaxo SmithKline Ireland Limited
Loratadine 5mg, Pseudoephedrine sulfate 120mg	Clarinase Repetabs	Prolonged-release tablet	OTC	MA897/00201	Bayer SA-NV
Triprolidine hydrochloride 1.25mg, Pseudoephedrine hydrochloride 30mg	Medofed	Oral solution	POM	MA032/03101	Medochemie Limited
Dextromethorphan hydrobromide 10mg/5ml, Triprolidine hydrochloride 1.25mg/5ml, Pseudoephedrine hydrochloride 30mg/5ml	Actifed DM Cough Linctus	Oral solution	OTC	MA192/02002	Glaxo SmithKline Ireland Limited
Triprolidine hydrochloride 1.25mg/5ml, Guaifenesin 100mg/5ml, Pseudoephedrine hydrochloride 30mg/5ml	Actifed Expectorant	Oral solution	OTC	MA192/02004	Glaxo SmithKline Ireland Limited
Triprolidine hydrochloride 1.25mg, Pseudoephedrine hydrochloride 30mg	Medofed	Oral solution	OTC	MA032/03104	Medochemie Limited
Cetirizine dihydrochloride 5mg, Pseudoephedrine hydrochloride 120mg	Cirrus	Prolonged-release tablet	POM	PI908/17202A	NeoFarma Pharmaceuticals Limited
Pseudoephedrine hydrochloride 30mg/5ml, Triprolidine hydrochloride 1.25mg/5ml	ACTIFED	Syrup	POM	PI274/01301A	Alfred Gera & Sons Limited

Pseudoephedrine hydrochloride 30mg/5ml, Triprolidine hydrochloride 1.25mg/5ml	ACTIFED	Syrup	POM	AA521/09201	Medicem Limited
Pseudoephedrine hydrochloride 30mg/5ml, Triprolidine hydrochloride 1.25mg/5ml	ACTIFED	Syrup	OTC	AA908/26001	NeoFarma Pharmaceuticals Limited
Triprolidine hydrochloride 1.25mg/5ml, Guaifenesin 100mg/5ml, Dextromethorphan hydrobromide 15mg/5ml, Pseudoephedrine hydrochloride 20mg/5ml	Medofed Compound	Oral solution	POM	AA032/03105	Medochemie Limited
Loratadine 5mg, Pseudoephedrine sulfate 120mg	Clarityne-D	Prolonged-release tablet	OTC	PI908/00601A	NeoFarma Pharmaceuticals Limited

Information from the EMA about the safety concern

- The review of medicines containing pseudoephedrine has been initiated at the request of the French medicines agency (ANSM) under Article 31 of Directive 2001/83/EC.
- The EMA Pharmacovigilance Risk Assessment Committee (PRAC), which is responsible for the evaluation of safety issues for human medicines, has started a review of medicines containing pseudoephedrine. This came following concerns about the risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS), conditions affecting blood vessels in the brain. PRES and RCVS can involve reduced blood supply (ischaemia) to the brain and may cause major and life-threatening complications in some cases. Common symptoms associated with PRES and RCVS include headache, nausea and seizures.
- The review follows new data from a small number of cases of PRES and RCVS in people using pseudoephedrine-containing medicines which were reported in pharmacovigilance databases and the medical literature. These medicines have a known risk of cardiovascular and cerebrovascular ischaemic events (side effects involving ischaemia in the heart and brain), including stroke and heart attack. Restrictions and warnings are already included in the medicines' product information to reduce these risks. Considering the seriousness of PRES and RCVS, the overall safety profile of pseudoephedrine and the indications for which the medicines are approved, the PRAC will review available evidence and decide whether the marketing authorisations for pseudoephedrine-containing medicines should be maintained, varied, suspended or withdrawn across the EU.
- PRAC will make a set of recommendations which will then be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt an opinion. A European Commission decision on this opinion will be issued in due course and will be the final stage of the review procedure. The adoption by the European Commission of a legally binding decision will be applicable in all EU Member States.

For more information please see the European Medicines Agency's press release.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on pseudoephedrine-containing medicines. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate
Malta Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Malta Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Malta Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Malta Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

Feedback:

We thank you for your interest and look forward to hearing your opinion.

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Pharmacovigilance Section

Post-Licensing Directorate

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