Medicines & Healthcare products Regulatory Agency

MEDICINES NOTIFICATION

CLASS 4 MEDICINES DEFECT INFORMATION

Caution in Use
Distribute to Pharmacy/Wholesaler Level

Date: 01 October 2024 EL (24)A/45 DMRC Ref: 32407021

Dear Healthcare Professional,

Sandoz Limited

Rosuvastatin 20mg Tablets PL 04416/1425

SNOMED Code: 35036111000001106

Batch Number	Expiry Date	Pack Size	First Distributed
NL8148	Sep 2025	28	18/01/2024
NW1590	Apr-2026	28	Not yet distributed
NW1591	Apr 2026	28	Not yet distributed

Active Pharmaceutical Ingredient: rosuvastatin calcium

Rosuvastatin 40mg Tablets PL 04416/1426

SNOMED Code: 35036311000001108

Batch Number	Expiry Date	Pack Size	First Distributed
NJ2462	Aug 2025	28	15/11/2023
NU8004	Feb 2026	28	13/06/2024
NX2653	Apr 2026	28	16/08/2024
NU8003	Mar 2026	28	Not yet distributed

Active Pharmaceutical Ingredient: rosuvastatin calcium

Brief description of the problem
Sandoz Ltd. has informed the MHRA that there is missing safety information in the Patient Information Leaflet (PIL) and Summary of Product Characteristics (SmPC) for Rosuvastatin 20mg and 40mg Tablets. The summary of the missing safety information is tabulated in Annex 1.

Advice for healthcare professionals
There is no risk to product quality or impact to safety of the medicines listed in this notification because of this missing information, full details in Annex – Table 1.

- The information missing in **Sections 4.1 and 4.2** of the SmPC pertains to the use of rosuvastatin in children aged 6 years with Homozygous familial hypercholesterolaemia, which is an approved condition. The reference SmPC has updates to include additional details about this approved use.
- The updated text in the lactation section now includes information that rosuvastatin is found in breast milk and may be harmful to infants. This aligns with the current Sandoz SmPC, which already advise against using rosuvastatin during pregnancy and lactation in **Sections 4.6 and 4.3.** The information on fertility was already present but has now been separated into its own heading to comply with changes in the SmPC template.
- The updated text regarding fusidic acid clarifies that there have been no studies conducted on the interaction between rosuvastatin and fusidic acid. However, the interaction was already described in the Sandoz SmPC in **Section 4.5 "**Interaction with other medicinal products and other forms of interaction".
- The updated information in the reference SmPC from clinical trials shows that roxadustat, teriflunomide, capmatinib, fostamatinib, febuxostat, and tafamidis can increase rosuvastatin area under the curve (AUC) levels by 1.9 to 2.9 times. However, the current Sandoz SmPC already states in **Section 5.2 and 4.5** that the "elimination half-life of rosuvastatin does not increase with higher doses, and caution should be taken if the rosuvastatin dose exceeds 20 mg."
- The PIL is missing information related to telling your doctor if you are taking any of the following medication: roxadustat, teriflunomide, capmatinib, fostamatinib, febuxostat, and tafamidis.

Considering the above omissions, the majority of the safety information is already covered in other sections of the Sandoz SmPC and PIL.

Healthcare professionals are advised to review the content of this notification, as it provides information that is missing from the current SmPC and PIL on the existing clinical concepts (as detailed above) and take this into account when prescribing.

If the medicines listed in this notification are supplied or dispensed, ensure that patients are aware of the information missing from the PIL on interaction with other medicines (see table 2 of Annex 1). Advise patients that if they are taking any of the medications listed in table 2 of Annex 1 they should discuss this with their prescribing healthcare professional before they start taking the medication.

Due to supply considerations, batches listed as not yet distributed will not be repackaged with the updated PIL prior to distribution. The specified 'Not yet distributed' batches are scheduled to be distributed shortly to avoid any supply considerations. Sandoz Ltd. has confirmed that all future batches (not listed in this notification) of the product will contain the updated PIL.

Advice for patients

Patients do not need to take any action. The information in Annex – Table 2 is missing from the Patient Information Leaflet. The missing information, summarised in this notification, does not change or affect the quality of the product. Therefore, you can safely continue your treatment. However, should you experience any adverse effects/side effects with the prescribed medication please contact your healthcare professional.

Patients who experience adverse reactions or have any questions about their medication should seek medical attention. Any suspected adverse reactions should also be reported via the MHRA Yellow Card scheme.

Medicines & Healthcare products Regulatory Agency

Further Information
For medical information queries, please contact: sandozgb@EU.propharmagroup.com, Telephone: +44 1276 698 101.

For stock control queries, please contact: sales.sandoz-gb@sandoz.com , Telephone: +44 1276 698607.

Recipients of this Medicines Notification should bring it to the attention of relevant contacts by copy of this notice. NHS regional teams are asked to forward this to community pharmacists and dispensing general practitioners for information.

Yours faithfully

Defective Medicines Report Centre
10 South Colonnade
Canary Wharf
London
E14 4PU
Telephone +44 (0)20 3080 6574
DMRC@mhra.gov.uk

Annex 1

Table 1 - Summary of updated missing safety information from SmPC

<table>
<tr><th colspan="3">Summary of updated missing safety information from SmPC</th></tr>
<tr><th>Affected section of SmPC</th><th>Superseded Sandoz text</th><th>New, updated text in reference SmPC</th></tr>
<tr><td>4.1 Therapeutic indications: Treatment of hypercholesterolaemia</td><td>Homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments (e.g.LDL apheresis) or if such treatments are not appropriate.</td><td>Addition of “Adults, adolescents and children aged 6 years or older with” homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate.</td></tr>
<tr><td>4.2 Posology and method of administration: Treatment of hypercholesterolaemia</td><td>Experience in children with homozygous familial hypercholesterolaemia is limited to a small number of children aged between 8 and 17 years.</td><td>Heading of “Heterozygous familial hypercholesterolaemia” and detailed information on dosing In children 6 to 17 years of age with homozygous familial hypercholesterolaemia added.</td></tr>
<tr><td>4.5 Interaction with other medicinal products and other forms of interaction: <u>Effect of co-administered medicinal products on rosuvastatin</u></td><td>Current text under Table 1 (Effect of co-administered medicinal products on rosuvastatin exposure [AUC] from published clinical trials) in Interactions requiring rosuvastatin dose adjustments, does not have information on the change in AUC levels of rosuvastatin when interacting with Roxadustat, Teriflunomide, Capmatinib, Fostamatinib, Febuxostat and Tafamidis.</td><td>
<table>
<tr><th>Interacting drug dose regimen</th><th>Rosuvastatin dose regimen</th><th>Change in rosuvastatin AUC*</th></tr>
<tr><td>Roxadustat 200 mg QOD</td><td>10 mg, single dose</td><td>2.9-fold ↑</td></tr>
<tr><td>Teriflunomide</td><td>Not available</td><td>2.5-fold ↑</td></tr>
<tr><td>Capmatinib 400mg BID</td><td>10 mg, single dose</td><td>2.1-fold ↑</td></tr>
<tr><td>Fostamatinib 100 mg twice daily</td><td>20 mg, single dose</td><td>2.0-fold ↑</td></tr>
<tr><td>Febuxostat 120 mg OD</td><td>10 mg, single dose</td><td>1.9-fold ↑</td></tr>
<tr><td>Tafamidis 61 mg BID on Days 1 & 2, followed by OD on Days 3 to 9</td><td>10 mg, single</td><td>dose 2.0-fold ↑</td></tr>
</table>
Additional text for Fusidic Acid is added as follows “Interaction studies with rosuvastatin and fusidic acid have not been conducted.”</td></tr>
<tr><td>4.6: Fertility, pregnancy and lactation</td><td>Fertility, pregnancy and lactation
Since cholesterol and other products of cholesterol biosynthesis</td><td>Information on Lactation added that “Limited data from published reports</td></tr>
</table>

	are essential for the development of the foetus, the potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. Animal studies provide limited evidence of reproductive toxicity (see section 5.3). If a patient becomes pregnant during use of this product, treatment should be discontinued immediately. Rosuvastatin is excreted in the milk of rats. There are no data with respect to excretion in milk in humans.	indicate that Rosuvastatin is present in human milk" and that "there is a potential risk for adverse reactions in the infant". Additionally; "Fertility: There are no known effects on fertility after use of rosuvastatin" is added.

Table 2 - Summary of updated missing safety information from the PIL

Affected section of Reference PIL	New, updated text in Reference PIL
What Rosuvastatin is and what it is used for	used in adults, adolescents and children 6 years or older to treat high cholesterol
Other medicines and Rosuvastatin	Tell your doctor if you are taking any of the following: • capmatinib (used to treat cancer), • fostamatinib (used to treat low platelet counts), • febuxostat (used to treat and prevent high blood levels of uric acid), • teriflunomide (used to treat multiple sclerosis),