Notification: KRKA, D.D., NOVO MESTO, Reformulation of Telmisartan/Hydrochlorothiazide Krka 40 mg/12.5 mg tablets (PLGB 01656/0343), Telmisartan/Hydrochlorothiazide Krka 80 mg/12.5 mg tablets (PLGB 01656/0344), Telmisartan/Hydrochlorothiazide Krka 80 mg/25 mg tablets; PLGB 01656/0345
Active Ingredient: Telmisartan, Hydrochlorothiazide

Background

Krka, d.d., Novo mesto, submitted a variation concerning the reformulation of Telmisartan/Hydrochlorothiazide tablets (40 mg/12.5 mg, 80 mg/12.5 mg, and 80 mg/25 mg), involving a transition from a bilayer to a monolayer formulation.

The objective of this reformulation was to create a combination medicinal product in the form of a monolayer tablet, with telmisartan and hydrochlorothiazide as active ingredients in a single formulation.

This change was implemented to optimize the manufacturing process and is supported by the conducted bioequivalence study. Importantly, the reformulation was not driven by any pharmacovigilance or safety concerns.

It is important to note that:

- **The changes in description, appearance and excipients due to reformulation of the tablets DO NOT change how the medicine is used, its dose, or what it is used for.**
- **The changes do not affect the product's quality or effectiveness, so there are no safety concerns due to these changes.**
- **These changes have been reviewed and approved by the MHRA.**

Important changes include:

1. **New description and appearance of the tablets:**

The table below presents Side-by-Side Comparison of Previous and New Formulation (Appearance and Description per Strength).

Product	PREVIOUS	NEW
Telmisartan/ Hydrochlorothiazide Krka 40 mg/12.5 mg tablets	**Description** White to almost white or pinkish white on one side and pink marbled on the opposite side of two-layer, oval, biconvex tablet, tablet dimensions 15 mm x 7 mm. **Appearance** 	**Description** Light pink, mottled, oval, biconvex tablets, market with L1 on the side, length approximately 14 mm. **Appearance** 
Telmisartan/ Hydrochlorothiazide Krka 80 mg/12.5 mg tablets	**Description** White to almost white or pinkish white on one side and pink marbled on the opposite side of two-layer, oval, biconvex tablet, tablet dimensions 18 mm x 9 mm. **Appearance** 	**Description** Light orange, mottled, oval, biconvex tablets, market with L2 on the side, length approximately 17 mm. **Appearance** 
Telmisartan/ Hydrochlorothiazide Krka 80 mg/25 mg tablets	**Description** White to yellowish white on one side and yellow marbled on the opposite side of two-layer, oval, biconvex tablet, tablet dimensions 18 mm x 9 mm. **Appearance** 	**Description** Light brownish yellow, mottled, oval, biconvex tablets, market with L3 on the side, length approximately 17 mm. **Appearance** 

2. New excipients

Excipients selected for the pharmaceutical reformulation of the product are well-established and widely recognized for their use in manufacturing of solid dosage forms. The excipients were selected to achieve characteristic of tablets, meeting the specification of the finished product.

The table below presents Side-by-Side Comparison between Previous and New Formulation (Excipients per Strength).

Product	PREVIOUS	NEW
Telmisartan/ Hydrochlorothiazide Krka 40 mg/12.5 mg tablets	Hydroxypropylcellulose Lactose monohydrate Magnesium stearate Mannitol Meglumine Povidone (K30) Silica, colloidal anhydrous Sodium hydroxide (E524) Sodium stearyl fumarate Sorbitol (E420) Red ferric oxide (E172)	Povidone K30, Sodium hydroxide, Mannitol, Cellulose, microcrystalline, Meglumine, Croscarmellose sodium, Sodium stearyl fumarate, Silica, colloidal anhydrous Red iron oxide (E172)
Telmisartan/ Hydrochlorothiazide Krka 80 mg/12.5 mg tablets	Hydroxypropylcellulose Lactose monohydrate Magnesium stearate Mannitol Meglumine Povidone (K30) Silica, colloidal anhydrous Sodium hydroxide (E524) Sodium stearyl fumarate Sorbitol (E420) Red ferric oxide (E172)	Povidone K30, Sodium hydroxide, Mannitol, Cellulose, microcrystalline, Meglumine, Croscarmellose sodium, Sodium stearyl fumarate, Silica, colloidal anhydrous Red iron oxide (E172) Yellow iron oxide (E172)
Telmisartan/ Hydrochlorothiazide Krka 80 mg/25 mg tablets	Hydroxypropylcellulose Lactose monohydrate Magnesium stearate Mannitol Meglumine Povidone (K30) Silica, colloidal anhydrous Sodium hydroxide (E524) Sodium stearyl fumarate Sorbitol (E420) Yellow ferric oxide (E172)	Povidone K30, Sodium hydroxide, Mannitol, Cellulose, microcrystalline, Meglumine, Croscarmellose sodium, Sodium stearyl fumarate, Silica, colloidal anhydrous Yellow iron oxide (E172)

A clear and detailed description of the new monolayer tablet's appearance has been included in the updated SmPC and PIL. The updated versions are also available on the eMC and dm+d websites, enabling patients and healthcare professionals to refer to the SmPC and PIL to view the tablet's new characteristics (e.g., shape, colour, imprint) and confirm that they have received the correct product.

Additionally, any questions related to the reformulation from patients or healthcare professionals can be directed to the local responsible person, who will provide an adequate and timely response.

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