אפריל 2020

רופא/ה נכבד/ה
רוקח/ת נכבד/ה שלום רב,

Forxiga 5 mg film-coated tablets : פרסום עדכון בעלוני התכשיר
Forxiga 10 mg film-coated tablets

הרכב:

Forxiga 5 mg film-coated tablets :
Each tablet contains dapagliflozin propanediol monohydrate equivalent to 5 mg dapagliflozin.

Forxiga 10 mg film-coated tablets:
Each tablet contains dapagliflozin propanediol monohydrate equivalent to 10 mg dapagliflozin.

התוויה:

Forxiga is indicated in adults aged 18 years and older for the treatment of insufficiency controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance.
- in addition to other medicinal products for the treatment of type 2 diabetes.

For study results with respect to combination of therapies, effects on glycaemic control and cardiovascular events, and the populations studied, see sections 4.4, 4.5 and 5.1.

חברת אסטרהזניקה ישראל מבקשת להודיע על עדכון עלון בהתאם להוראות משרד הבריאות בתאריך **אפריל 2020**

העדכון המהותי בעלון לרופא הוא:

4.2 Posology and method of administration

Prior to initiation of Forxiga

Assess renal function prior to initiation of FORXIGA therapy and periodically thereafter *[see Warnings and Precautions]*.
In patients with volume depletion, correct this condition prior to initiation of FORXIGA *[see Warnings and Precautions]*.

Special populations
Renal impairment

~~*The efficacy of dapagliflozin is dependent on renal function, and efficacy is reduced in patients who have moderate renal impairment and likely absent in patients with severe renal impairment. Forxiga is not recommended for use in patients with moderate to severe renal impairment (patients with creatinine clearance [CrCl] < 60 ml/min or estimated glomerular filtration rate [eGFR] < 60 ml/min/1.73 m2, see sections 4.4, 4.8, 5.1 and 5.2).*~~

~~*No dosage adjustment is indicated in patients with mild renal impairment.*~~

No dose adjustment is needed in patients with an eGFR greater than or equal to 45 mL/min/1.73 m^2.
Use of FORXIGA is not recommended when the eGFR is less than 45 mL/min/1.73 m^2.
FORXIGA is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m^2 *[see Contraindications (4.3)]*.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

FORXIGA is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m2

4.4 Special warnings and precautions for use

~~Renal impairment~~
~~The efficacy of dapagliflozin is dependent on renal function, and efficacy is reduced in patients who have moderate renal impairment and likely absent in patients with severe renal impairment (see section 4.2). In subjects with moderate renal impairment (patients with CrCl < 60 ml/min or eGFR < 60 ml/min/1.73 m2), a higher proportion of subjects treated with dapagliflozin had adverse reactions of increase in creatinine, phosphorus, parathyroid hormone (PTH) and hypotension, compared with placebo. Forxiga is not recommended for use in patients with moderate to severe renal impairment (patients with CrCl < 60 ml/min or eGFR < 60 ml/min/1.73 m^2). Forxiga has not been studied in severe renal impairment (CrCl < 30 ml/min or eGFR < 30 ml/min/1.73 m^2) or end-stage renal disease (ESRD).~~

~~Monitoring of renal function is recommended as follows:~~
~~• Prior to initiation of dapagliflozin and at least yearly, thereafter (see sections 4.2, 4.8, 5.1 and 5.2)~~
~~• Prior to initiation of concomitant medicinal products that may reduce renal function and periodically~~
~~thereafter~~
~~• For renal function approaching moderate renal impairment, at least 2 to 4 times per year. If renal function~~
~~falls below CrCl < 60 ml/min or eGFR < 60 ml/min/1.73 m^2, dapagliflozin treatment should be discontinued.~~

5. Pharmacological properties

5.1 Pharmacodynamic properties

~~Renal impairment~~
Glycaemic control in patients with ~~Moderate renal impairment~~ CKD 3A ~~(eGFR ≥ 30~~ 45 to < 60 ml/min/1.73 m2)
~~The efficacy of dapagliflozin was also assessed separately in a dedicated study of diabetic subjects with moderate renal impairment (252 subjects with mean eGFR 45 ml/min/1.73 m2). The mean change from baseline in HbA1c at 24 weeks was -0.44% and -0.33%, for dapagliflozin 10 mg and placebo, respectively.~~
The efficacy of dapagliflozin was assessed in a dedicated study in diabetic patients with an eGFR ≥ 45 to < 60 mL/min/1.73 m2 who had inadequate glycaemic control on usual care. Treatment with dapagliflozin resulted in reductions in HbA1c and body weight compared with placebo
(Table 9).

Table 9. Results at Week 24 of a placebo-controlled study of dapagliflozin in diabetic patients with an eGFR > 45 to < 60 mL/min/1.73 m^2

	Dapagliflozin[a] 10 mg	Placebo[a]
N[b]	159	161
HbA1c (%)		
Baseline (mean)	8.35	8.03
Change from baseline[b]	-0.37	-0.03
Difference from placebo[b] (95% CI)	-0.34* (-0.53, -0.15)	
Body weight (kg)		
Baseline (mean)	92.51	88.30
Percent change from baseline[c]	-3.42	-2.02
Difference in percent change from placebo[c] (95% CI)	-1.43* (-2.15, -0.69)	

[a] Metformin or metformin hydrochloride were part of the usual care in 69.4% and 64.0% of the patients for the dapagliflozin and placebo groups, respectively.
[b] Least squares mean adjusted for baseline value
[c] Derived from least squares mean adjusted for baseline value
* p<0.001

העדכון המהותי בעלון לצרכן הוא:

2. <u>לפני שימוש בתרופה</u>

לפני הטיפול בפורסיגה ספר לרופא, לרוקח או לאחות אם:

- הנך סובל לעיתים קרובות מזיהומים בדרכי השתן

מקרא לעדכונים המסומנים

הוספת טקסט מהותי מסומנת בצבע. מחיקת טקסט מסומנת בקו חוצה

העלונים מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בכבוד רב,
קארין קנבל דובסון

רוקחת ממונה
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