ינואר 2022

<u>הנדון: עדכון עלונים של התכשיר PRADAXA</u>

PRADAXA 75
PRADAXA 110
PRADAXA 150

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת בורינגר אינגלהיים ישראל בע"מ מבקשת להודיעכם על עדכון בעלון לרופא.

ההתוויות הרשומות לתכשיר בישראל:

<u>Pradaxa 75 mg:</u>
Primary prevention of venous thromboembolic events in adult patients who have undergone elective total hip replacement surgery or total knee replacement surgery.
<u>Pradaxa 110 mg:</u>
Primary prevention of venous thromboembolic events in adult patients who have undergone elective total hip replacement surgery or total knee replacement surgery.
Prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation.
Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.
<u>Pradaxa 150 mg:</u>
Prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation.
Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

השינויים המשמעותיים ביותר בעלונים סומנו מטה.

<u>מקרא:</u>
<u>הוספת מידע חדש</u>- <u>טקסט כחול עם קו תחתון</u>
<u>הסרה</u>- טקסט אדום עם קו חוצה
<u>החמרה</u>- טקסט כחול על רקע צהוב

לכלל השינויים יש לעיין בעלון לרופא המאושר.

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות.
כמו כן, ניתן לקבלם על-ידי פנייה לבעל הרישום:
בורינגר אינגלהיים ישראל בע"מ, רח' מדינת היהודים 89 הרצליה פיתוח, ובטלפון 09-9730500.

ב ב ר כ ה,

מירי חזן
רוקחת ממונה
בורינגר אינגלהיים ישראל

עדכונים בעלון לרופא:

4.4 Special warnings and precautions for use (Applies to all dosages)

Haemorrhagic risk

For adult patients in situations of life-threatening or uncontrolled bleeding, when rapid reversal of the anticoagulation effect of dabigatran is required, the specific reversal agent (~~Praxbind~~ idarucizumab) is available ~~(see section 4.9).~~ Haemodialysis can remove dabigatran. For adult patients, fresh whole blood or fresh frozen plasma, coagulation factor concentration (activated or non-activated), recombinant factor VIIa or platelet concentrates are other possible options (see also section 4.9).

Discontinuation of ~~Pradaxa~~ dabigatran etexilate

[…]

When severe bleedings occur, treatment must be discontinued, the source of bleeding investigated and use of the specific reversal agent ~~Praxbind~~ (idarucizumab) may be considered ~~(see section 4.9 Management bleeding complications)~~ in adult patients. Haemodialysis can remove dabigatran.

Postoperative phase (Pradaxa 75&110mg)

[…]

Patients at risk for bleeding or patients at risk of overexposure, notably patients with ~~moderate~~ reduced renal ~~impairment (CrCL 30-50 mL/min)~~ function (see also table 2), should be treated with caution (see sections 4.4 and 5.1).

(Pradaxa 150 mg)

Patients at risk for bleeding or patients at risk of overexposure, notably patients with ~~moderate~~ reduecd renal function ~~impairment (CrCL 30-50 mL/min)~~ (see also table 3) should be treated with caution (see sections 4.4 and 5.1).

4.5 Interaction with other medicinal products and other forms of interaction (Pradaxa 75mg)

Interactions with anticoagulants and antiplatelet aggregation medicinal products

NSAIDs given for short-term analgesia have been shown not to be associated with increased bleeding risk when given in conjunction with dabigatran etexilate. With chronic use in a phase III clinical trial comparing dabigatran to warfarin for stroke prevention in atrial fibrillation patients (RE-LY)

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4.8 Undesirable effects (Applies to all dosages)

[…]

Tabulated list of adverse reactions (Pradaxa 150 mg)

Table 8: Adverse reactions

Gastrointestinal ulcer including oesophageal ulcer – uncommon

Description of selected adverse reactions (Applies to all dosages)

Bleeding reactions

[…]

Known bleeding complications such as compartment syndrome and acute renal failure due to hypoperfusion and anticoagulant-related nephropathy in patients with predisposing risk factors have been reported for ~~Pradaxa~~ dabigatran etexilate.

[…]

~~Paediatric population (DVT/PE)~~ (Pradxa 110 mg & 150mg)

~~In the clinical study 1160.88 in total, 9 adolescent patients (age 12 to < 18 years) with diagnosis of primary VTE received an initial oral dose of dabigatran etexilate of 1.71 (± 10 %) mg/kg bodyweight. Based on dabigatran concentrations as determined by the diluted thrombin time test and clinical assessment, the dose was adjusted to the target dose of 2.14 (± 10%) mg/kg bodyweight of dabigatran etexilate. On treatment 2 (22.1 %) patients experienced mild related adverse events (gastrooesophageal reflux / abdominal pain; abdominal discomfort) and 1 (11.1 %) patient experienced a not related serious adverse event (recurrent VTE of the leg) in the post treatment period > 3 days after stop of dabigatran etexilate.~~

5. PHARMACOLOGICAL PROPERTIES (Pradxa-110mg &150mg)

5.1 Pharmacodynamic properties

~~Paediatric population~~

~~The pharmacokinetics and pharmacodynamics of dabigatran etexilate administered twice daily for three consecutive days (total 6 doses) at the end of standard anticoagulant therapy were assessed in an open-label safety and tolerability study in 9 stable adolescents (12 to < 18 years). All patients received an initial oral dose of 1.71 (± 10%) mg/kg of dabigatran etexilate (80 % of the adult dose of 150 mg/70 kg adjusted~~

~~for the patient's weight). Based on dabigatran concentrations and clinical assessment, the dose was subsequently modified to a target dose of 2.14 (± 10 %) mg/kg of dabigatran etexilate (100 % of the adult dose adjusted for the patient's weight). In this small number of adolescents, dabigatran etexilate capsules were apparently tolerated with only three mild and transient gastrointestinal adverse events reported by two patients. According to the relatively low exposure, coagulation at 72 hrs (presumed dabigatran trough level at steady state or close to steady state conditions) was only slightly prolonged with aPTT at maximum 1.60 fold, ECT 1.86 fold, and Hemoclot® TT (Anti-FIIa) 1.36 fold, respectively. Dabigatran plasma concentrations observed at 72 hrs were relatively low, between 32.9 ng/mL and 97.2 ng/mL at final doses between 100 mg and 150 mg (gMean dose normalized total dabigatran plasma concentration of 0.493 ng/mL/mg).~~

5.3 Preclinical safety data (Applies to all dosages)

In a juvenile toxicity study conducted in Han Wistar rats, mortality was associated with bleeding events at similar exposures, at which bleeding was seen in adult animals. In both adult and juvenile rats, mortality is considered to be related to the exaggerated pharmacological activity of dabigatran in association with the exertion of mechanical forces during dosing and handling. Data of the juvenile toxicity study did neither indicate an increased sensitivity in toxicity, nor any toxicity specific to juvenile animals.

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