אפריל 2018

<u>רופא/ה, רוקח/ת נכבד/ה,</u>

חברת קמהדע מבקשת להודיע על עידכון מידע כמפורט להלן, עבור התכשיר:

IXIARO ; איקסיארו

Suspension for injection IM

מרכיבים פעילים בהתאם לרישיון:
JAPANESE ENCEPHALITIS PURIFIED INACTIVATED VACCINE 6 AU / 0.5 ML

התוויה:

Ixiaro is indicated for active immunization against Japanese encephalitis in adults, adolescents, children and infants aged 2 months and older.

Ixiaro should be considered for use in individuals at risk of exposure through travel or in the course of their occupation.

מהות השינויים:
1. העלון לרופא עודכן בסעיפים הבאים (מפורטים להלן רק תתי הסעיפים שבהם נעשו השינויים העיקריים; החמרות הודגשו בצהוב):

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

<u>Posology</u>

Adults

The primary vaccination series consists of two separate doses of 0.5 ml each, according to the following conventional schedule:
First dose at Day 0.
Second dose: 28 days after first dose.
Rapid schedule Adults 18-65 years of age:
Persons aged 18-65 years can be vaccinated in a rapid schedule as follows:
First dose at Day 0.
Second dose: 7 days after first dose.
With both schedules, primary immunisation should be completed at least one week prior to potential exposure to Japanese encephalitis virus (JEV) (see section 4.4).
It is recommended that vaccines who received the first dose of IXIARO complete the primary 2-dose vaccination course with IXIARO.
If the primary immunization of two injections is not completed, full protection against the disease might not be achieved. There is data that a second injection given up to 11 months after the first dose results in high seroconversion rates (see section 5.1).
Booster Dose *(Adults)*
A booster dose (third dose) should be given within the second year (i.e. 12 - 24 months) after primary immunization, prior to potential re-exposure to JEV.
Persons at continuous risk for acquiring Japanese encephalitis (laboratory personnel or persons residing in endemic areas) should receive a booster dose at month 12 after primary immunization (see section 5.1). Data on the need for further booster doses are not available.
As with many vaccines, the immune response in older persons (≥ 65 years of age) to IXIARO is lower than in younger adults. Duration of protection is uncertain in older persons, therefore the physician should take this into account when considering a booster dose (third dose) before any further exposure to JE virus.

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4.8 UNDESIRABLE EFFECTS

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Adult and older adults (≥65 years) population

Blood and lymphatic system disorders
Uncommon: lymphadenopathy
Rare: thrombocytopenia

Nervous system disorders
Very common: headache
Uncommon: migraine, dizziness
Rare: paraesthesia, neuritis, dysgeusia, syncope*

Ear and labyrinth disorders
Uncommon: vertigo

Eye disorders
Rare: eyelid oedema

Cardiac disorders
Rare: palpitations, tachycardia

Respiratory, thoracic and mediastinal disorders
Rare: dyspnoea

Gastrointestinal disorders
Common: nausea
Uncommon: vomiting, diarrhoea, abdominal pain

Skin and subcutaneous tissue disorders
Uncommon: rash, pruritus, hyperhidrosis
Rare: urticaria, erythema

Musculoskeletal and connective tissue disorders
Very common: myalgia
Uncommon: musculoskeletal stiffness, arthralgia
Rare: pain in extremity

General disorders and administration site conditions
Very common: injection site pain, injection site tenderness, fatigue
Common: influenza-like illness, pyrexia, other injection site reactions e.g. redness, hardening, swelling, itching
Uncommon: chills, malaise, asthenia
Rare: oedema peripheral

Investigations
Uncommon: hepatic enzymes increased

*reported also from post-marketing experience

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5.1 PHARMACODYNAMIC PROPERTIES

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Immunogenicity in older adults (≥65 years)

The immunogenicity of IXIARO was evaluated in an open-label, uncontrolled trial in 200 healthy older adults aged 65 to 83 years, including subjects with stable underlying conditions like hypercholesterolemia, hypertension, cardiovascular disease or non insulin-dependent diabetes mellitus. JEV neutralizing antibodies were determined 42 days after the second dose of the primary series (Day 70). Older adults have a lower immune response to vaccination compared to younger adults or children, in terms of seroconversion rates (percentage of subjects with $PRNT_{50}$ titer ≥1:10) and geometric mean titers (Table 9).

Table 9: Seroconversion rates and geometric mean titer of JEV neutralizing antibody at Day 70 in the Intent-to-treat Population, for the entire study population and stratified by age

Seroconversion rates and geometric mean titer for JEV neutralizing antibody at Day 70				
	n / N	SCR	GMT	95% CI
Total Study Population	128/197	65%	37	29.2, 47.8
Age group 65 - <75 years	113/173	65.3%	37.2	28.6, 48.3
Age group ≥75 years	15/23	65.2%	42.2	19.2, 92.7

העלון לרופא המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות: https://www.old.health.gov.il/units/pharmacy/trufot/index.asp, וניתן לקבלו מודפס ע"י פניה לבעל הרישום, חברת קמהדע בע"מ (טל' 08-9406472).

בברכה,
פנינה נודל,
רוקחת ממונה