מרץ 2020

רופא/ה, רוקח/ת נכבד/ה,

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

שם התכשיר:	**Optivate 1000 IU אופטיוואט**	**Optivate 500 IU אופטיוואט**
מרכיבים פעילים:	Factor VIII 1000 IU/vial von Willebrand factor 2600 IU/vial	Factor VIII 500 IU/vial von Willebrand factor 1300 IU/vial
צורת מינון, צורת מתן:	Powder for Solution for Injection, IV	
התויה:	Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).	

מהות השינוי: עידכון עלון לרופא. הודעה זו כוללת החמרות (בצהוב). בעלון שינויים נוספים שאינם החמרה.

4.4 Special warnings and special precautions for use

…

Inhibitors

The formation of neutralising antibodies (inhibitors) to factor VIII is a known complication in the management of individuals with haemophilia A. These inhibitors are usually IgG immunoglobulins directed against the factor VIII procoagulant activity, which are quantified in Bethesda Units (BU) per mL of plasma using the modified assay. The risk of developing inhibitors is correlated to the severity of the disease as well as the exposure to factor VIII, this risk being highest within the first 20 exposure days. Rarely, inhibitors may develop after the first 100 exposure days.

Cases of recurrent inhibitor (low titre) have been observed after switching from one FVIII product to another in previously treated patients with more than 100 exposure days who have a previous history of inhibitor development. Therefore, it is recommended to monitor patients carefully for inhibitor occurrence following any product switch.

The clinical relevance of inhibitor development will depend on the titre of the inhibitor, with low titre inhibitors which are transiently present or remain consistently low titre posing less of a risk of insufficient clinical response than high titre inhibitors.

In general, all patients treated with human coagulation factor VIII should be carefully monitored for the development of inhibitors by appropriate clinical observations and laboratory tests.

See also section 4.8 Undesirable effects.

Head Office 2 Holtzman St., Science Park, P.O. Box 4081, Rehovot, 7670402, Israel | Tel. +972-8-9406472 | Fax. +972-89406473

Plant Kibbutz Beit Kama, M.P Negev 8532500, Israel | Tel. +972-8-9913111 | Fax. +972-8-9912083

If the expected factor VIII activity plasma levels are not attained, or if bleeding is not controlled with an appropriate dose, testing for factor VIII inhibitor presence should be performed. In patients with high levels of inhibitor, factor VIII therapy may not be effective and other therapeutic options should be considered. Management of such patients should be directed by physicians with experience in the care of haemophilia and factor VIII inhibitors.

Cardiovascular events

In patients with existing cardiovascular risk factors, substitution therapy with FVIII may increase the cardiovascular risk.

Catheter-related complications

If a central venous access device (CVAD) is required, risk of CVAD-related complications including local infections, bacteraemia and catheter site thrombosis should be considered.

Prevention of infection transmission

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia).

Appropriate vaccination (hepatitis A and B) should be considered for patients in regular/repeated receipt of human plasma derived factor VIII products.

4.8 Undesirable effects

…

MedDRA Standard System Organ Class	**Adverse Reactions**	**Frequency**
… Blood and Lymphatic System Disorders	FVIII inhibition	Uncommon (PTPs)* Very common (PUPs)*

Head Office 2 Holtzman St., Science Park, P.O. Box 4081, Rehovot, 7670402, Israel | Tel. +972-8-9406472 | Fax. +972-89406473

Plant Kibbutz Beit Kama, M.P Negev 8532500, Israel | Tel. +972-8-9913111 | Fax. +972-8-9912083

* Frequency is based on studies with all FVIII products which included patients with severe haemophilia A. PTPs = previously-treated patients, PUPs = previously-untreated patients.

6.3 Shelf life

Product sealed in vial- the expiry date of the product is indicated on the packaging materials.
Reconstituted product – 1 hour.

6.4 Special precautions for storage

Store at 2°C -25°C.
Do not freeze.
Keep the vial in the outer carton to protect from light.
Following reconstitution, use as soon as possible and certainly within 1 hour.

העלון לרופא המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס ע"י פניה לבעל הרישום, חברת קמהדע בע"מ (טל' 08-9406472).

להלן הקישור למאגר התרופות:

https://data.health.gov.il/drugs/index.html#/byDrug

בברכה,

צוות רישום קמהדע בע"מ

Head Office 2 Holtzman St., Science Park, P.O. Box 4081, Rehovot, 7670402, Israel | Tel. +972-8-9406472 | Fax. +972-89406473

Plant Kibbutz Beit Kama, M.P Negev 8532500, Israel | Tel. +972-8-9913111 | Fax. +972-8-9912083