KAMADA
High Quality Pharmaceuticals

דצמבר 2019

רופא/ה, רוקח/ת נכבד/ה,

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

Megalotect CP; מגלוטקט CP

Solution for Infusion, IV

מרכיבים פעילים:

IMMUNOGLOBULIN NORMAL HUMAN (at least) 96 %
HUMAN PLASMA PROTEIN 50 MG/ML
CYTOMEGALOVIRUS ANTIBODY 100 U/ML

המאושר להתויה:

Prophylaxis of clinical manifestations of cytomegalovirus infection in patients subjected to immunosuppressive therapy, particularly in transplant recipients.

מהות השינוי: עידכון עלון לרופא. בהודעה זו מצוינים השינויים המהווים החמרה (הודגשו בצהוב). בעלון שינויים נוספים שאינם החמרה.

4.3 Contraindications

- Hypersensitivity to the active substance (human cytomegalovirus immunoglobulin) or to any of the excipients listed in section 6.1.
  ~~Hypersensitivity to human immunoglobulins, especially in patients with antibodies against IgA.~~
- Patients with selective IgA deficiency who developed antibodies to IgA, as administering an IgA-containing product can result in anaphylaxis.

4.4 Special warnings and precautions for use

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Precautions for use

Potential complications can often be avoided by ensuring that patients:

- are not sensitive to human ~~normal~~ immunoglobulin by initially injecting the product slowly (0.08 ml/kg/~~BW~~body weight /hour),
- are carefully monitored for any symptoms throughout the infusion period. In particular, patients naive to human ~~normal~~ immunoglobulin, patients switched from an ~~alternative~~ intravenous human immunoglobulin (IVIg) product or when there has been a long interval since the previous infusion, should be monitored at the hospital during the first infusion and for the first hour after the first infusion, in order to detect potential adverse signs. All other patients should be observed for at least 20 minutes after administration.

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Infusion reaction

Certain adverse reactions (e.g. headache, flushing, chills, myalgia, wheezing, tachycardia, lower back pain, nausea, and hypotension) may be related to the rate of infusion. The recommended infusion rate given under section 4.2 must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.

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Adverse reactions may occur more frequently

- in patients who receive human immunoglobulin for the first time or, in rare cases, when the human immunoglobulin product is switched or when there has been a long interval since the previous infusion
- in patients with an untreated infection or underlying chronic inflammation

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Hypersensitivity

~~True hypersensitivity~~ Hypersensitivity reactions are rare. ~~They~~

Anaphylaxis can develop in patients-

- with undetectable IgA who have anti-IgA antibodies.

~~IVIg is not indicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern.~~

- ~~Rarely, human normal immunoglobulin can induce a fall in blood pressure with anaphylactic reaction, even in patients~~ who had tolerated previous treatment with human ~~normal~~ immunoglobulin.

In case of shock, standard medical treatment for shock therapy should be implemented.

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Acute renal failure

Cases of acute renal failure have been reported in patients receiving IVIg therapy. In most cases, risk factors have been identified, such as pre-existing renal insufficiency, diabetes mellitus, hypovolemia, overweight, concomitant nephrotoxic medicinal products, or age over 65.

Renal parameters should be assessed prior to infusion of IVIg, particularly in patients judged to have a potential increased risk for developing acute renal failure, and again at appropriate intervals. In patients at risk for acute renal failure, IVIg products should be administered at the minimum rate of infusion and dose practicable.

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Aseptic meningitis syndrome (AMS)

Aseptic meningitis syndrome has been reported to occur in association with IVIg treatment. The syndrome usually begins within several hours to 2 days following IVIg treatment. Cerebrospinal fluid studies are frequently positive with pleocytosis up to several thousand cells per mm3, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dl. AMS may occur more frequently in association with high-dose (2 g/kg) IVIg treatment.

Patients exhibiting such signs and symptoms should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis.

Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae.

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Neutropenia/Leukopenia

A transient decrease in neutrophil count and/or episodes of neutropenia, sometimes severe, have been reported after treatment with IVIg. This typically occurs within hours or days after IVIg administration and resolves spontaneously within 7 to 14 days.

Transfusion related acute lung injury (TRALI)

In patients receiving IVIg, there have been some reports of acute non-cardiogenic pulmonary oedema [Transfusion Related Acute Lung Injury (TRALI)]. TRALI is characterised by severe hypoxia, dyspnoea, tachypnoea, cyanosis, fever and hypotension. Symptoms of TRALI typically develop during or within 6 hours of a transfusion, often within 1-2 hours. Therefore, IVIg recipients must be monitored for and IVIg infusion must be immediately stopped in case of pulmonary adverse reactions. TRALI is a potentially life-threatening condition requiring immediate intensive-care-unit management.

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Interference with serological testing

After the administration of immunoglobulin the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing.

Passive transmission of antibodies to erythrocyte antigens, e.g. A, B, D may interfere with some serological tests for red cell ~~allo~~ antibodies for example the direct antiglobulin test (DAT, direct Coombs' test)~~, reticulocyte count and haptoglobin~~.

4.5 Interactions with other medicinal products and other forms of interaction

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Loop diuretic

Avoidance of concomitant use of loop diuretics

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions caused by human normal immunoglobulins (in decreasing frequency) encompass (see also section 4.4):

- chills, headache, dizziness, fever, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate low back pain.
- reversible haemolytic reactions; especially in those patients with blood groups A, B, and AB and (rarely) haemolytic anaemia requiring transfusion
- (rarely) a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.
- (rarely) transient cutaneous reactions (including cutaneous lupus erythematosus – frequency unknown)

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- (Very rarely): Thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism, deep vein thromboses.
- Cases of reversible aseptic meningitis
- Cases of increased serum creatinine level and/or occurrence of acute renal failure
- Cases of Transfusion Related Acute Lung Injury (TRALI)

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MedDRA System Organ Class	**Adverse reactions**
… Immune system disorders …	Anaphylactic shock, anaphylactic reaction, anaphylactoid reaction hypersensitivity
… General disorders and administration site conditions …	Chills, pyrexia, fatigue

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products, nor with any other IVIg products.

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

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