KAMADA
High Quality Pharmaceuticals

אוקטובר 2020

רופא/ה, רוקח/ת נכבד/ה,

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

GAMMAPLEX; גמאפלקס

Solution for infusion, IV

מרכיבים פעילים בהתאם לרישיון: IMMUNOGLOBULIN NORMAL HUMAN 5 G / 100 ML

המאושר להתויה:

Replacement therapy in adults, and children and adolescents in:
- Primary immunodeficiency syndromes with impaired antibody production
- Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed
- Hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation
- Congenital AIDS with recurrent bacterial infections

Immunomodulation in adults, and children and adolescents in:
- Primary immune thrombocytopenia (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count
- Guillain Barré syndrome
- Kawasaki disease

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 immunoglobulins) or to any of the excipients listed in section 6.1 (see section 4.4).
Hereditary fructose intolerance (see section 4.4).
Babies and young children (see section 4.4).
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 (see section 4.4).
Patients with selective IgA deficiency who developed antibodies to IgA, as administering an IgA-containing product can result in anaphylaxis. ~~Hypersensitivity to human immunoglobulins, especially in patients with antibodies against IgA.~~

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 (0.01 – 0.02 ml/kg/min)
- are carefully monitored for any symptoms throughout the infusion period. In particular, patients naïve to human normal immunoglobulin, patients switched from an alternative 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.
- Adverse reactions may occur more frequently:

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- in patients who receive human normal immunoglobulin for the first time or, in rare cases, when the human normal 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 reactions are rare. ~~They can occur in patients with 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.~~

Anaphylaxis can develop in patients:

- with undetectable IgA who have anti-IgA antibodies
- who had tolerated previous treatment with human normal immunoglobulin

In case of shock, standard medical treatment for shock 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, hypovolaemia, 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. In case of renal impairment, IVIg discontinuation should be considered.

While reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IVIg products containing various excipients such as sucrose, glucose and maltose, those containing sucrose as a stabiliser accounted for a disproportionate share of the total number. In patients at risk, the use of IVIg products that do not contain these excipients may be considered. Gammaplex does not contain sucrose, maltose or glucose.

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 mm^3, 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 IVIgs. 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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4.5 Interactions with other medicinal products and other forms of interaction

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Loop diuretics

Avoidance of concomitant use of loop diuretics.

4.8 Undesirable effects

Summary of the safety profile

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- (rarely) transient cutaneous reactions (including cutaneous lupus erythematosus - frequency unknown)
- cases of Transfusion Related Acute Lung Injury (TRALI)

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MedDRA System Organ Class (SOC)	Adverse reaction	Frequency per patient	Frequency per infusion
Respiratory, thoracic and mediastinal disorders	… Transfusion related acute lung injuries (TRALI)	Not Known	Not Known
Skin and subcutaneous tissue disorders	… Cutaneous lupus erythematosus	Not Known	Not Known

6.2 Incompatibilities

In the absence of compatibility studies, 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

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