KAMADA
High Quality Pharmaceuticals

תאריך: 02.2023

רופא/ה, רוקח/ת נכבד/ה,

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

אינטראטקט 100 גרם / ליטר ; Intratect 100 g/l

מרכיבים פעילים וכמותם: Human Normal Immunoglobulin 100 mg/ml

צורת מינון ודרך מתן: Solution for Infusion, IV

התווית התכשיר ע"פ הרישיון העדכני: ראו סעיף 4.1 למטה.

<u>מהות השינוי:</u>

שינוי התוויה ומשטר מינון, כדלהלן (ראו סעיפים 4.1 ו- 4.2 למטה ובעלון):

1. **עדכון נוסח התוויה עבור Replacement therapy.**
2. **תוספת התוויות עבור Immunomodulation.**
3. **עדכון פרק משטר המינון, כולל תוספת משטר מינון בהתאם לתוספת ההתוויה הנ"ל.**

להלן השינויים בעלון (מידע חדש באפור; מחיקות בקו חוצה):

4.1 Therapeutic indications

<u>Replacement therapy in adults, and children and adolescents (0-18 years) in:</u>

- Primary immunodeficiency syndromes (PID) with impaired antibody production.
- Secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either **proven specific antibody failure (PSAF)*** or serum IgG level of <4 g/l.
- ~~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.~~
- ~~Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation (HSCT).~~
- ~~Congenital AIDS with recurrent bacterial infections.~~

* PSAF= failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines

<u>Immunomodulation in adults, and children and adolescents (0-18 years) in:</u>

- 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 (in conjunction with acetylsalicylic acid; see section 4.2)
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
- Multifocal motor neuropathy (MMN)

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

4.2 Posology and method of administration

Posology

The dose and dose regimen is dependent on the indication.

~~In replacement therapy t~~The dose may need to be individualised for each patient dependent on the ~~pharmacokinetic and~~ clinical response. Dose based on bodyweight may require adjustment in underweight or overweight patients.

The following dose regimens are given as a guideline.

Replacement therapy in primary immunodeficiency syndromes

The dose regimen should achieve a trough level of IgG (measured before the next infusion) of at least ~~5 to~~ 6 g/l or within the normal reference range for the population age. Three to six months are required after the initiation of therapy for equilibration (steady- state IgG levels) to occur. The recommended starting dose is ~~4-8 ml (~~0.4-0.8 g~~)~~/kg given once, followed by at least ~~2 ml (~~0.2 g~~)~~/kg given every three to four weeks.

The dose required to achieve a trough level of IgG of ~~5-~~6 g/l is of the order of ~~2-8 ml (~~0.2-0.8 g~~)~~/kg/month. The dosage interval when steady state has been reached varies from 3-4 weeks.

IgG trough levels should be measured and assessed in conjunction with the incidence of infection. To reduce the rate of bacterial infections ~~infection~~, it may be necessary to increase the dosage and aim for higher trough levels.

~~*Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibioties 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.*~~

~~The recommended dose is 2-4 ml (0.2-0.4 g)/kg every three to four weeks.~~

~~*Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation*~~

Secondary immunodeficiencies (as defined in section 4.1)

The recommended dose is 0.2-0.4 g/kg every three to four weeks. ~~The trough levels should be maintained above 5 g/l.~~IgG trough levels should be measured and assessed in conjunction with the incidence of infection. Dose should be adjusted as necessary to achieve optimal protection against infections, an increase may be necessary in patients with persisting infection; a dose decrease can be considered when the patient remains infection free.

Primary immune thrombocytopenia

There are two alternative treatment schedules:

- ~~8-10 ml (~~0.8-1 g~~)~~/kg given on day one, this dose may be repeated once within 3 days
- ~~4 ml (~~0.4 g~~)~~/kg given daily for two to five days.

The treatment can be repeated if relapse occurs.

Guillain Barré syndrome

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

~~4 ml (~~0.4 g~~)~~/kg/day over 5 days (possible repeat of dosing in case of relapse).

Kawasaki disease

~~16-20 ml (1.6-~~2.0 g~~)~~/kg should be administered ~~in divided doses over two to five days or 20 ml (2.0 g)/kg~~ as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid.

Chronic inflammatory demyelinating polyneuropathy (CIDP)

Starting dose: 2 g/kg divided over 2 -5 consecutive days

Maintenance doses: 1 g/kg over 1-2 consecutive days every 3 weeks.

The treatment effect should be evaluated after each cycle; if no treatment effect is seen after 6 months, the treatment should be discontinued.

If the treatment is effective long term treatment should be subject to the physicians discretion based upon the patient response and maintenance response. The dosing and intervals may have to be adapted according to the individual course of the disease.

Multifocal Motor Neuropathy (MMN)

Starting dose: 2 g/kg given over 2-5 consecutive days.

Maintenance dose: 1 g/kg every 2 to 4 weeks or 2 g/kg every 4 to 8 weeks.

The treatment effect should be evaluated after each cycle; if no treatment effect is seen after 6 months, the treatment should be discontinued.

If the treatment is effective long term treatment should be subject to the physicians discretion based upon the patient response and maintenance response. The dosing and intervals may have to be adapted according to the individual course of the disease.

The dosage recommendations are summarised in the following table:

Indication	Dose	Frequency of~~infusions~~ injections
Replacement therapy ~~in primary immunodeficiency~~	~~starting dose: 0.4-0.8 g/kg~~	
	~~thereafter: 0.2-0.8 g/kg~~	~~every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l~~
Primary immunodeficiency syndromes	starting dose: 0.4-0.8 g/kg Maintenance dose: 0.2-0.8 g/kg	every 3-4 weeks
~~Replacement therapy in s~~Secondary immunodeficiencies (as defined in section 4.1)	0.2-0.4 g/kg	every 3-4 weeks ~~to obtain IgG trough level of at least 5-6 g/l~~
~~Congenital AIDS~~	~~0.2-0.4 g/kg~~	~~every 3-4 weeks~~
~~Hypogammaglobulinaemia (< 4 g/l) in patients after allogeneic haematopoietic stem cell transplantation~~	~~0.2-0.4 g/kg~~	~~every 3-4 weeks to obtain IgG trough level above 5 g/l~~

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

Immunomodulation:		
Primary immune thrombocytopenia	0.8-1 g/kg or 0.4 g/kg/d	on day 1, possibly repeated once within 3 days for 2-5 days
Guillain Barré syndrome	0.4 g/kg/d	for 5 days
Kawasaki disease	~~1.6-2 g/kg~~ ~~Or~~ 2 g/kg	~~in divided doses over 2-5 days in association with acetylsalicylic acid~~ in one dose in association with acetylsalicylic acid
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	Starting dose: 2 g/kg Maintenance dose: 1 g/kg	in divided doses over 2-5 days every 3 weeks over 1-2 days
Multifocal Motor Neuropathy (MMN)	Starting dose: 2 g/kg Maintenance dose: 1 g/kg or 2 g/kg	over 2-5 consecutive days every 2-4 weeks or every 4-8 weeks over 2-5 days

Paediatric population

The posology in children and adolescents (0-18 years) is not different to that of adults as the posology for each indication is given by body weight and adjusted to the clinical outcome of the above-mentioned conditions.

Hepatic impairment

No evidence is available to require a dose adjustment.

Renal impairment

No dose adjustment unless clinically warranted, see section 4.4.

Elderly

No dose adjustment unless clinically warranted, see section 4.4.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים ע"י פניה לבעל הרישום, חברת קמהדע בע"מ (טל' 08-9406472).
להלן הקישור למאגר התרופות: https://israeldrugs.health.gov.il/#!/byDrug

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