הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך: 18/02/2013
שם תכשיר באנגלית ומספר הרישום: Octagam_
שם בעל הרישום: ג'נמדיקס_

טקסט חדש	טקסט נוכחי	ההחמרות המבוקשות - הפרק בעלון
Filtration of OCTAGAM is not required.		CLINICAL PARTICULARS ***Method of administration***
~~The product should be brought to room or body temperature before use.~~ ~~The solution should be clear or slightly opalescent.~~ ~~Do not use solutions that are cloudy or have deposits.~~ ~~Certain severe adverse drug reactions may be related to the rate of infusion. The recommended infusion rate given under "3.2 Method of administration" must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.~~ ~~Certain adverse reactions may occur more frequently:~~ • ~~in case of high rate of infusion~~ • ~~in patients with hypo- or agammaglobulinaemia, with or without IgA deficiency~~ • ~~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~~ *4.4.1* ~~*True*~~***Sensitivity*** Severe hypersensitivity reactions ~~are rare. They can~~ may occur (See 4.3).~~in very seldom cases of IgA deficiency with anti-IgA antibodies.~~ ~~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.~~ ~~Potential complications can often be avoided by ensuring:~~ • ~~that patients are not sensitive to human normal immunoglobulin by initially injecting the product slowly (1 ml/kg/hour);~~	The product should be brought to room or body temperature before use. The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits. Certain severe adverse drug reactions may be related to the rate of infusion. The recommended infusion rate given under "3.2 Method of administration" must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period. Certain adverse reactions may occur more frequently: • in case of high rate of infusion • in patients with hypo- or agammaglobulinaemia, with or without IgA deficiency • 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 True hypersensitivity reactions are rare. They can occur in very seldom cases of IgA deficiency with anti-IgA antibodies. 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. Potential complications can often be	CLINICAL PARTICULARS **Special warnings and precautions for use**

~~• that patients are carefully monitored for any symptoms throughout the infusion period; in particular, patients naive to human normal immunoglobulin, patients switched from an alternative IVIg product to OCTAGAM or when there has been a long interval since the previous infusion should be monitored 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.~~ ~~There is clinical evidence of an association between IVIg administration and thromboembolic events such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses which is assumed to be related to a relative increase in blood viscosity through the high influx of immunoglobulin in at-risk patients. Caution should be exercised in prescribing and infusing IVIg in obese patients and in patients with pre-existing risk factors for thrombotic events (such as advanced age, hypertension, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilisation, severely hypovolemic patients, patients with diseases which increase blood viscosity).~~ ~~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.~~ ~~In case of renal impairment, IVIg discontinuation should be considered. While these reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IVIg products, 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 sucrose may be considered.~~ ~~In patients at risk for acute renal failure or thromboembolic adverse reactions, IVIg products should be administered at the minimum rate of infusion and dose practicable.~~ In case of hypersensitivity, OCTAGAM infusion should be immediately discontinued and appropriate treatment instituted. Epinephrine should be immediately available for treatment of acute severe hypersensitivity reaction. IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactoid reactions when administered OCTAGAM.	avoided by ensuring: • that patients are not sensitive to human normal immunoglobulin by initially injecting the product slowly (1 ml/kg/hour); • that patients are carefully monitored for any symptoms throughout the infusion period; in particular, patients naive to human normal immunoglobulin, patients switched from an alternative IVIg product to OCTAGAM or when there has been a long interval since the previous infusion should be monitored 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. There is clinical evidence of an association between IVIg administration and thromboembolic events such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses which is assumed to be related to a relative increase in blood viscosity through the high influx of immunoglobulin in at-risk patients. Caution should be exercised in prescribing and infusing IVIg in obese patients and in patients with pre-existing risk factors for thrombotic events (such as advanced age, hypertension, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilisation, severely hypovolemic patients, patients with diseases which increase blood viscosity). 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. In case of renal impairment, IVIg discontinuation should be considered. While these reports of renal dysfunction and acute renal failure have been	

~~OCTAGAM contains maltose, a disaccharide sugar, which is derived from corn. Anaphylactoid / anaphylactic reactions have been reported in association with infusion of other maltose / corn starch related products. Patients known to have corn allergies should either avoid using Octagam or be closely observed for signs and symptoms of acute hypersensitivity reactions.1~~ Patients known to have corn allergies should avoid using OCTAGAM. ***4.4.2 ~~In all~~Renal Failure*** Assure that patients~~, IVIg administration requires:~~ ~~adequate hydration~~ are not volume depleted prior to the initiation of the infusion of ~~IVIg~~OCTAGAM. Periodic monitoring of renal function tests and urine output is particularly important in patients judged to have a potential increased risk of developing acute renal failure. Renal function, including a measurement of blood urea nitrogen (BUN)/serum creatinine, should be assessed prior to the initial infusion of OCTAGAM and again at appropriate intervals thereafter. If renal function deteriorates, discontinuation of the product should be considered. For patients judged to be at risk for developing renal dysfunction and/or at risk of developing thrombotic events, it may be prudent to reduce the amount of product infused per unit time by infusing OCTAGAM at a maximum rate less than 0.07 ml/kg (3.3 mg/kg)/minute (200 mg/kg/hour). ***4.4.3 Blood Glucose Monitoring*** Blood Glucose Testing: some types of blood glucose testing systems (for example, those based on the glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase methods) falsely interpret the maltose contained in OCTAGAM as glucose. This has resulted in falsely elevated glucose readings and, consequently, in the inappropriate administration of insulin, resulting in life-threatening hypoglycemia. Also, cases of true hypoglycemia may go untreated if the hypoglycemic state is masked by falsely elevated glucose readings. Accordingly, when administering OCTAGAM, the measurement of blood glucose must be done with a glucose-specific method. The product information of the blood glucose testing system, including that of the test strips, should be carefully reviewed to determine if the system is appropriate for use with maltose-containing parenteral products. If any uncertainty exists, contact the manufacturer of the testing system to determine if the system is appropriate for use with maltose-containing parenteral products.	associated with the use of many of the licensed IVIg products, 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 sucrose may be considered. In patients at risk for acute renal failure or thromboembolic adverse reactions, IVIg products should be administered at the minimum rate of infusion and dose practicable. OCTAGAM contains maltose, a disaccharide sugar, which is derived from corn. Anaphylactoid / anaphylactic reactions have been reported in association with infusion of other maltose / corn starch related products. Patients known to have corn allergies should either avoid using OCTAGAM OR BE CLOSELY OBSERVED FOR SIGNS AND SYMPTOMS OF ACUTE HYPERSENSITIVITY REACTIONS.[1] In all patients, IVIg administration requires: adequate hydration prior to the infusion of IVIg • monitoring of urine output • monitoring of serum creatinine levels • avoidance of concomitant use of loop diuretics In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. The treatment required depends on the nature and severity of the side effect. In case of shock, standard medical treatment for shock should be implemented. 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	

4.4.4 Hyperproteinemia ~~• monitoring of urine output~~ ~~• monitoring of serum creatinine levels~~ ~~• avoidance of concomitant use of loop diuretics~~ ~~In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. The treatment required depends on the nature and severity of the side effect.~~ ~~In case of shock, standard medical treatment for shock should be implemented.~~ ~~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 HIV, HBV and HCV.~~ ~~The measures taken may be of limited value against non-enveloped viruses such as HAV and parvovirus B19.~~ ~~There is a reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to the viral safety.~~ ~~It is strongly recommended that every time that Octagam is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.~~ Hyperproteinemia, increased serum viscosity and hyponatremia may occur in patients receiving IVIg therapy. The hyponatremia is likely to be a pseudohyponatremia as demonstrated by a decreased calculated serum osmolality or elevated osmolar gap. Distinguishing true hyponatremia from pseudohyponatremia is clinically critical, as treatment aimed at decreasing serum free water in patients with pseudohyponatremia may lead to volume depletion, a further increase in serum viscosity and a disposition to thromboembolic events.	unknown or emerging viruses and other pathogens. The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV. The measures taken may be of limited value against non-enveloped viruses such as HAV and parvovirus B19. There is a reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to the viral safety. It is strongly recommended that every time that Octagam is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.	

4.4.5 Thrombotic events Thrombotic events have been reported in association with IVIg therapy. Patients at risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization and/or known or suspected hyperviscosity. The potential risks and benefits of IVIg should be weighed against those of alternative therapies for all patients for whom IVIg administration is being considered. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia / markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. ***4.4.6 Aseptic meningitis syndrome*** Aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with IVIg treatment. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae. The syndrome usually begins within several hours to two days following IVIg treatment and rapid infusion. It is characterized by symptoms and signs including severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, nausea and vomiting. Cerebrospinal fluid (CSF) studies are frequently positive with pleocytosis up to several thousand cells per cu mm, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dl. Patients exhibiting such symptoms and signs should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. It appears that patients with a history of migraine may be more susceptible. ***4.4.7 Hemolysis*** IVIg products can contain blood group antibodies which may act as hemolysins and induce in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, hemolysis. Hemolytic anemia can develop subsequent to IVIg therapy due to enhanced RBC sequestration (See 4.8). IVIg recipients should be monitored for clinical signs and symptoms of hemolysis. If signs and/or symptoms of hemolysis are present after IVIg infusion, appropriate confirmatory laboratory testing should be done.		

4.4.8 Transfusion-Related Acute Lung Injury (TRALI) There have been reports of noncardiogenic pulmonary edema [Transfusion-Related Acute Lung Injury (TRALI)] in patients administered IVIg. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever and typically occurs within 1-6 hours after transfusion. Patients with TRALI may be managed using oxygen therapy with adequate ventilatory support. IVIg recipients should be monitored for pulmonary adverse reactions. If TRALI is suspected, appropriate tests should be performed for the presence of anti-neutrophil antibodies in both the product and patient serum. ***4.4.9 General*** Because this product is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent. All infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Octapharma. The physician should discuss the risks and benefits of this product with the patient, before prescribing or administering it to the patient. ***4.4.10 Laboratory Tests*** If signs and/or symptoms of hemolysis are present after IVIg infusion, appropriate confirmatory laboratory testing should be done. If TRALI is suspected, appropriate tests should be performed for the presence of anti-neutrophil antibodies in both the product and patient serum. Because of the potentially increased risk of thrombosis, baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies.		
In general, various minor allergic and hypersensitivity type of reactions and headache, chills, back pain, chest pain, fever, vomiting, cutaneous reactions, ~~fatigue,hot flushes~~arthralgia, and nausea may occasionally occur. Reactions to intravenous immunoglobulins tend to be related to the dose and the rate of infusion. …	In general, various minor allergic and hypersensitivity type of reactions and headache, chills, back pain, chest pain, fever, cutaneous reactions, fatigue, hot flushes and nausea may occasionally occur. Reactions to intravenous immunoglobulins tend to be related to the dose and the rate of infusion. …	Undesirable effects

Very rarely Octagam may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.	rarely Octagam may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.	