Thymoglobulin®

Contraindications

– Active, acute or chronic infections, which would contraindicate any additional immunosuppression.
– Hypersensitivity to rabbit proteins or any of the recipients.

Special warnings and special precautions for use

THYMOGLOBULINE® should be administered under strict medical supervision in a hospital setting and patients must be carefully monitored during the infusion.

Additional information

Clinical side effects

Rapid infusion rates have been associated with case reports consistent with CRS. In rare cases, a serious CRS can be fatal.

Malignancy

The use of immunosuppressive agents, including THYMOGLOBULINE®, may increase the incidence of malignancies, in particular lymphoma or post-transplant lymphoproliferative disease (PTLD).

Hypersensitivity

The dose adjustment of THYMOGLOBULINE® differs from that of other anti-thymocyte immunoglobulins because the protein composition and concentrations vary depending on the source of anti-thymocyte immunoglobulin used. Therefore, the doctors must ensure that the dose prescribed is suitable for the anti-thymocyte immunoglobulin administered.

Thrombocytopenia and/or leucopenia (in particular lymphocytopenia and neutropenia) have been identified; these conditions are reversible after dose adjustments. When thrombocytopenia and/or leucopenia are not part of the underlying condition or are not associated with the condition for which THYMOGLOBULINE® is being administered, the following dose reductions are suggested:

– a reduction in dose must be envisaged if the platelet count is between 30,000 and 75,000 cells/mm³ or if the number of white blood cell count is between 2,000 and 3,000 cells/mm³;
– stopping THYMOGLOBULINE® treatment must be considered if persistent and severe thrombocytopenia (< 50,000 cells/mm³) or development of leucopenia (< 2,000 cells/mm³).

Method of administration

Rabbit anti-human thymocyte immunoglobulin is usually administered in the context of a therapeutic regimen combining several immunosuppressive agents.

Administer the doses of intravenous corticosteroids and anthracyclines required prior to infusion of rabbit anti-human thymocyte immunoglobulin.

Preparation of the solution for infusion

The reconstituted solution is clear or slightly opalescent.

Infuse into a large vein. Adjust the infusion rate so that the total duration of infusion is at least 4 hours.
In vitro baseline value) as early as 1 day post-treatment initiation. The lymphopenia
Infections, reactivation of infection and sepsis have been reported after
T-cells and stimulates their proliferation (in the same manner for the CD4+ and
THYMOGLOBULINE ® may be explained by the following mechanisms:
• Lymphocyte depletion probably constitutes the primary mechanism of the
THYMOGLOBULINE ® does not activate
and CD57).
• Rabbits are almost unaffected. Most of the subsets have recovered more
than 50% of their initial value before the end of the second month. CD4-cell
depletion is very long-lasting and persists at 6 months with, as a result, an
inversion of the CD4/CD8 ratio.
• Pharmacokinetic properties
Following the first infusion of 1.25 mg/kg of THYMOGLOBULINE ® (in cases of
kidney-transplant), serum rabbit IgG levels of between 10 and 40 g/ml are
obtained. The serum levels decline steadily until the following infusion with an
estimated elimination half-life of 2-3 days. The trough rabbit IgG levels increase
progressively to reach 20 to 170 g/ml at the end of an 11-day course of
treatment. A gradual decline is subsequently observed following discontinuation
of treatment with rabbit anti-human thymocyte immunoglobulin. However, rabbit
IgG remains detectable in 40% of patients at 2 months.
• Significant immunization against rabbit IgG is observed in about 40% of
patients. In most cases, immunization develops within the first 15 days of
therapy. Patients presenting with immunization show a faster decline in
trough rabbit IgG levels.
• Preclinical safety data
Non-clinical data reveal from toxicity studies with single and repeated
administrations did not reveal the specific toxicity of THYMOGLOBULINE ® .
No mutagenicity reproduction or genotoxicity studies have been conducted with
THYMOGLOBULINE ® .
• PHARMACEUTICAL PARTICULARS
- List of excipients
- - Gibvin
- - sodium chloride
- - Mannitol.
- Incompatibilities
According to a single compatibility study the association of THYMOGLOBULINE ® ,
heparin, and hydrocortisone in a dextrose infusion solution caused precipitates,
and is not recommended. In the absence of other compatibility studies, this
medicinal product must not be mixed with other medicinal products with the
exception of those mentioned in the special precautions for disposal and handling.
• Shelf life
5 years.
After reconstitution, immediate use is recommended from a microbiological point of
view. However, chemical and physical stability during use has been
demonstrated all 2 to 8°C, for 24 hours.
• Special precautions for storage
Store in a refrigerator between +2°C and +8°C.
During transport, shipment at standard storage conditions (2°C-8°C) is
recommended. However, short temperature excursions up to 25°C during
transport will not alter the product quality.
• Nature and contents of outer packaging
Powder in a vial (type 1 glass) with a stopper (chlorobutyl) in one box.
• Instructions for use and handling
Reconstitute the powder using 5 ml of sterile water for injections to obtain a
solution containing 5 mg protein per ml.
The reconstitution must be carried out in accordance with good practices
regulations, particularly in terms of asepsis.
• The solution is clear or slightly opalescent. Reconstituted product should be
impacted visually for particulate matter and discoloration. Should some
particulate matter remain, continue to gently rotate the vial until no particulate
matter remains. If particulate matter persists, discard the vial. Immediate use of
reconstituted product is recommended. Each vial is for single use only.
• On the daily dose, the reconstitution of several vials of
THYMOGLOBULINE ® (powder might be needed. Determine the number of vials
to be used and round up to the nearest vial. To avoid inadvertent administration
of particulate matter from reconstitution, it is recommended to use a 0.22 μm-micron
filter before the administration of THYMOGLOBULINE ® . The daily dose is
diluted in an infusion solution (9mg/ml sodium chloride (0%) solution for
injection or 5% dextrose) as to obtain a total infusion volume of 50 to 500 ml
(usually 50 ml/iv).
• The product should be administered on the same day.
Any unused product or waste material must be disposed of in accordance with
local regulations.