5484

PACKAGE LEAFLET: INFORMATION FOR THE USER

Intratect® 50 g/l solution for infusion

Human normal immunoglobulin (IVIg)

Biotest

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Intratect is and what it is used for

Intratect is an extract of human blood which contains antibodies (the body's own defensive substances) to diseases, available in the form of an infusion solution. The solution is ready for infusion into a vein (a "drip").

Intratect contains human normal immunoglobulin (antibodies) from blood donated by a broad spectrum of the population and is likely to contain antibodies to most common infectious diseases. Adequate doses of Intratect can restore normal values when blood levels of Immunoglobulin G are low.

Intratect is used in adults, and children and adolescents (0-18 years) who do not have sufficient antibodies (replacement therapy) in cases of:
- Patients born with lack of antibodies (primary immunodeficiency syndromes)
- Hypogammaglobulinemia and repeated bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed
- Hypogammaglobulinaemia and repeated 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

Intratect is also used in adults, and children and adolescents (0-18 years) to treat inflammatory disorders (immunomodulation) such as:
- Primary immune thrombocytopenia (ITP, where a patient has reduced blood platelets) when the patient will have surgery in the near future or is at risk of bleeding
- Guillain-Barré syndrome (a disease that damages nerves and may lead to generalised palsy)
- Kawasaki disease (a disease in children which causes inflammations of several organs of the body and where the arteries in the heart become enlarged)

2. What you need to know before you use Intratect

Do not use Intratect
- If you are allergic to human immunoglobulin or any of the other ingredients of this medicine (listed in section 6). An allergic reaction may include rash, itching, difficulty breathing or swelling of the face, lips, throat or tongue.
- If you have an immunoglobulin A deficiency, especially if you have antibodies against immunoglobulin A in your blood.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Intratect if you
- suffer from a condition with low antibody levels in your blood (hypo- or agammaglobulinemia)
- have not received this medicine before or if there has been a long interval (e.g. several weeks) since you last received it (you will need to be closely monitored during your infusion and for an hour after your infusion has stopped)
- have been given Intratect recently (you will need to be observed during the infusion and for at least 20 minutes after your infusion)
- have had a reaction to other antibodies (in rare cases you may be at risk of allergic reactions)
- have or have had a kidney disorder
- have received medicines that may harm your kidneys (if your kidney function worsens, you may need to stop treatment with Intratect)

Your doctor will take special care if you are overweight, elderly, diabetic, or if you suffer from high blood pressure, low blood volume (hypovolaemia), if your blood is thicker than normal (high blood viscosity), if you have been bed-ridden or immobile for some time (immobilisation) or if you have problems with your blood vessels (vascular diseases) or other risks for thrombotic events (blood clots).

Please note - reactions

You will be carefully observed during the infusion period with Intratect to make sure that you do not suffer a reaction. Your doctor will make sure that the rate at which Intratect is infused is suitable for you.

If you notice any of the following signs of a reaction, i.e. sudden wheeziness, difficulty in breathing, fast pulse, swelling of the eyelids, face, lips, throat or tongue, rash or itching (especially affecting your whole body) during the infusion of Intratect, tell your doctor immediately. The rate of infusion can be slowed or the infusion can be stopped altogether.

Information on transmission of infectious agents

Intratect is made from human plasma (the liquid part of blood). When medicines are made from human blood or plasma, it is important to prevent infections being passed on to patients. Blood donors are tested for viruses and infections. Manufacturers of these products also process the blood or plasma to inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are given, the possibility of passing on infection cannot be totally excluded.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus.

The measures taken may be of limited value against non-enveloped viruses such as hepatitis A virus and parvovirus B19.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

Other medicines and Intratect

Tell your doctor if you are using, have recently used or might use any other medicines.

Intratect can reduce the effectiveness of some vaccines such as:
- measles
- rubella
- mumps
- chicken pox

You may have to wait up to 3 months before you can have some vaccines and up to a year before you can have a measles vaccine.

Effects on blood tests

Intratect can affect blood tests. If you have a blood test after receiving Intratect, please inform the person taking your blood or your doctor that you have received Intratect.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby,ask your doctor for advice before taking this medicine.
Your doctor will decide if Intratect may be used during pregnancy and breast-feeding.

Driving and using machines

The ability to drive and operate machines may be impaired by some adverse reactions associated with Intratect. Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines

3. How to use Intratect

Intratect is intended for intravenous administration (infusion into a vein). It is given to you by a doctor or nurse. The dose will depend on your condition and your body weight. Your doctor will know the right amount to give you.

At the beginning of your infusion you will receive Intratect at a slow rate. Your doctor may then gradually increase the infusion rate.
The infusion rate and its frequency are dependent on the reason you are being given Intratect.

Use in children and adolescents

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.

For replacement therapy in patients with a weak immune system (immunodeficiency) and for patients with congenital AIDS, the infusion is given every 3 to 4 weeks.

To treat inflammatory disorders (immunomodulation) the infusion may be given as followed:

Primary immune thrombocytopenia: for the treatment of an acute episode an infusion is given on day 1, this dose may be repeated once in 3 days. Alternatively a lower dosage may be given daily for 2 to 5 days.

The following information is intended for healthcare professionals only:

Method of administration

Intratect is intended for intravenous infusion. During the infusion, an initial rate of no more than 1.4 ml/kg/h for 30 minutes must not be exceeded. If well tolerated, the rate of administration may gradually be increased to a maximum of 1.9 ml/kg/h for the remainder of the infusion.

Special Precautions

Certain severe adverse drug reactions may be related to the rate of infusion. The recommended infusion rate given under "Method of administration" must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.
Any infusion-related adverse events should be treated by lowering the infusion rate or by stopping the infusion.

In all patients, intravenous immunoglobulin administration requires:
adequate hydration prior to the initiation of the infusion of intravenous immunoglobulin
monitoring of urine output
monitoring of serum creatinine levels
avoidance of concomitant use of loop diuretics

It is strongly recommended that every time Intratect is administered to a patient, the name and batch number of the product is recorded.

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

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Instructions for handling and disposal

Do not use Intratect after the expiry date which is stated on the label and outer carton.

The product must be brought to room or body temperature before use.

The solution should be clear or slightly opalescent and colourless or pale yellow. Solutions that are cloudy or have deposits should not be used.

The product once opened should be used immediately.

Any unused product or waste material should be disposed of in accordance with local requirements.

Dosage

The dose and dosage regimen is dependant on the indication. In replacement therapy the dose may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. 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 - 6 g/l. Three to six months are required after the initiation of therapy for equilibration to occur.
The recommended starting dose is 8 - 16 ml (0.4 - 0.8 g)/kg body weight (b.w.) given once, followed by at least 4 ml (0.2 g)/kg b.w. every three to four weeks.
The dose required to achieve a trough level of 5-6 g/l is of the order of 4 - 16 ml (0.2 - 0.8 g)/kg b.w./month. The dosage interval when steady state has been reached varies from 3 - 4 weeks.
Trough levels should be measured in order to adjust the dose and dosage interval.

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:

The recommended dose is 4 - 8 ml (0.2 - 0.4 g)/kg b.w. every three to four weeks.

Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation

The recommended dose is 4-8 ml (0.2-0.4 g)/kg every three to four weeks. The trough levels should be maintained above 5 g/l.

Primary immune thrombocytopenia:

There are two alternative treatment schedules:
16 - 20 ml (0.8 - 1 g)/kg b.w. on day one, this dose may be repeated once within 3 days,
8 ml (0.4 g)/kg b.w. given daily for two to five days.
The treatment can be repeated if relapse occurs.

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The following information is intended for healthcare professionals only:

Guillain Barré syndrome:

8 ml (0.4 g)/kg b.w./day over 5 days.

Kawasaki disease:

32 - 40 ml (1.6 - 2.0 g)/kg b.w. should be administered in divided doses over two to five days or 40 ml (2.0 g)/kg b.w. as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid.

The dosage recommendations are summarised in the following table:

Indications	Dose	Frequency of infusions
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
Replacement therapy in secondary immunodeficiency	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
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

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.

Guillain Barré syndrome: the infusion is given for 5 days.

Kawasaki disease: the infusion should be administered over 2 to 5 days or as a single dose.

For hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation to treat infection and prevent rejection, the infusion is given every 3 to 4 weeks. Where there is lack of antibody production, the infusion is given every month until there are normal levels of antibodies.

If you miss an infusion

Intratect will be given to you in hospital by a doctor or nurse so you are unlikely to miss an infusion. However, tell your doctor if you think you have missed an infusion.

If you receive more Intratect than you should

An overdose can lead to fluid overload and increased thickness of the blood, especially in elderly patients or patients with impaired heart or kidney function. If you think you have been given too much Intratect, tell your doctor, who will decide if the infusion should be stopped and an alternative treatment given.
If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side-effects, although not everybody gets them.

Frequencies outlined below have been generally calculated based on number of patients treated if not otherwise specified, e.g. by number of infusions.

If you notice any of the following effects, tell your doctor immediately:

- rash,
- itching,
- wheezing,
- difficulty in breathing,
- swelling of the eyelids, face, lips, throat or tongue,
- extremely low blood pressure with symptoms like dizziness, confusion, fainting, fast pulse

This can be an allergic or a serious allergic reaction (anaphylactic shock) or a hypersensitivity reaction.

The following side effects have been reported during clinical trials with Intratect:

Common: may occur with up to 1 in 10 infusions:

- headache
- fever

Uncommon: may occur with up to 1 in 100 infusions

- mildly increased breakdown of red blood cells in the blood vessels (haemolysis)
- disturbed sense of taste
- high blood pressure
- inflammation of a superficial vein
- feeling sick (nausea)
- vomiting
- abdominal pain
- rash with raised spots
- chills
- feeling hot
- increased body temperature
- positive blood test for antibodies against red blood cells

The following side effects have been reported spontaneously with Intratect:

Not known (frequency cannot be estimated from the available data)

- severe chest pain or chest pressure (angina pectoris)
- shivering or trembling (rigors)
- (anaphylactic) shock, allergic reaction
- difficulty in breathing (dyspnoe)
- low blood pressure
- back pain
- decrease in number of white blood cells (leukopenia)

Human immunoglobulin preparations in general may cause the following additional side effects:

uncommon (may affect up to 1 in 100 patients):

- headache, dizziness
- nausea, vomiting
- joint pain, moderate low back pain
- low blood pressure
- chills, fever
- allergic reactions

Rare (may affect up to 1 in 1,000 patients)

- a sudden fall in blood pressure in isolated cases an anaphylactic shock
- temporary skin reactions

Very rare (may affect up to 1 in 10,000 patients)

- thromboembolic reactions such as
  - heart attack (cardial infarction),
  - stroke,
  - blood clots in blood vessels in the lung (pulmonary embolism),
  - blood clots in a vein (deep vein thromboses)

Not known (frequency cannot be estimated from the available data)

- temporary acute inflammation of the protective membranes covering the brain and spinal cord (meningitis)
- results of blood tests which indicate that the renal function is impaired and/or sudden kidney failure
- decrease in the number of red blood cells due to a breakdown of these cells in the blood vessels ((reversible) haemolytic reactions)

If a side effect occurs, the infusion rate will be decreased or stopped.

Reporting of side effects

If you get any side effects talk to your doctor, pharmacist or nurse. This includes any side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Intratect

Keep this medicine out of the sight and reach of children.

Your pharmacist or doctor knows how to store Intratect.

Keep the vial in the outer carton in order to protect from light.

Do not store above 25°C. Do not freeze.

6. Contents of the pack and other information

What Intratect contains

The active substance of Intratect is human immunoglobulin for intravenous administration.

Intratect contains 50 g/l human plasma proteins of which at least 96% is immunoglobulin G (IgG). The IgG subclass distribution is approx. 57% IgG1, 37% IgG2, 3% IgG3 and 3% IgG4. The maximum immunoglobulin A (IgA) content is 900 micrograms/ml.

The other ingredients are: glycine and water for injections.

What Intratect looks like and the contents of the pack

Intratect is a solution for infusion. The solution is clear or faintly opalescent (milky colours like an opal) and colourless to pale yellow.

Pack containing 1 vial with 1 g in 20 ml of solution
Pack containing 1 vial with 2.5 g in 50 ml of solution
Pack containing 1 vial with 5 g in 100 ml of solution
Pack containing 1 vial with 10 g in 200 ml of solution

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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