Belimumab IV - Systemic Lupus Erythematosus (SLE) - Full Clinical Guideline

Reference no.: CG-RHEUM/2018/009

Purpose
To ensure that patients are receiving Belimumab (Benlysta) in a safe and effective manner.

Belimumab is a monoclonal antibody which inhibits the activity of B lymphocyte stimulator (BLyS).

Indications for Treatment
Belimumab in combination with other non-biologic immunosuppressant treatment and corticosteroids is indicated for the treatment of adult patients with severe active SLE who have had an inadequate response or intolerance to other disease modifying drugs and corticosteroids. Patients must have a positive dsDNA antibody and low complement.

Belimumab will be given as add on therapy to patients on a stable dose of immunosuppressant treatment plus corticosteroids.

Prior to treatment

- Counselling of the patient regarding possible side effects of Belimumab therapy and provision of information sheet to take place before first treatment.
- Patients should have a BILAG and SELENASLEDAI documented. A SELENASLEDAI score >10 indicates active disease eligible for treatment.
- Patients should have positive dsDNA antibodies and a low complement level

Contraindications

- Active severe infection
- Women who are breast feeding or pregnant (discontinue for 12 months in males and females before conception)
- History of hypersensitivity to the drug or any other components of the infusion
- Hepatitis B C or HIV disease
- Patients with severe active lupus nephritis or CNS lupus
- Hypogammaglobulinaemia
- Organ or bone marrow transplant
- Little data for treating patients over 65 years

Treatment Schedule

Initiation of therapy should be by Consultant Rheumatologist only.

Belimumabimab is administered as an intravenous infusions of 10mg/ kg body weight at week 0, week 2 and week 4 and at 4 weekly intervals thereafter. Patients should also be pre-treated 1 hour before with paracetamol 1g orally and chlorpheniramine (piriton) 4mg orally.

Belimumab should only be administered in an environment with immediately available full resuscitation facilities. A bed is required for all infusions. A doctor should be readily available in case of reaction.

Prior to initiating therapy please check the following has been done:

- BILAG and SELENASLEDAI score
- Full blood count, ESR
- Initial profile and Liver function tests
- CRP
- urinalysis
- Chest x-ray within the past 6 months and TB screening as per guidelines
- Baseline immunoglobulins
- Hepatitis screen
- Pneumovax status (need to have at least 4 weeks before treatment if not had)

Preparation

Reconstituted and diluted solution has a shelf life of 8 hours at 2-8°C or room temperature. The infusion may therefore be completed within 8 hours of reconstitution. Belimumab is normally prepared in a 250ml bag of normal saline (fluid will have been withdrawn such that the volume to be infused is 250mls).

A Peripheral Catheter needs to be inserted on the day of the infusion. A 500ml bag of normal saline should be hanging by the patient's bed in case of hypotension.

Do not give other IV fluids or drugs through the same line. A filter is not required.

Before each administration

Measure and record: weight,
pulse,
blood pressure
temperature,
urinalysis

Collect*:* Full blood count, ESR
IP and LFT CRP

NB. If these have not been done within a week of the infusion these should be done as urgent samples and the results checked prior to prescribing treatment.

Paracetamol, chlorpheniramine 10 mg IV and Adrenaline 0.5ml 1 in 1000 IM should be readily available (as per anaphylaxis protocol).

During infusion
NB This infusion must be given via a Volumetric Infusion pump (i.e. Baxter Colleague) and an infusion Pump Checklist completed. The infusion is given over 1 hour. The infusion rate may be slowed or interrupted if the patient develops an infusion reaction. It must be discontinued if the patient develops severe anaphylaxis.

A doctor should be readily available for the entire infusion

Check BP, pulse and temperature every 30 minutes during the infusion and 1 hourly for four hours post infusion 1 and 2 and for 2 hours post subsequent infusions.
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If **minor infusions reactions** occur slow the infusion, stop if necessary and restart at a slower rate.
If **severe reactions** occur **(bronchospasm, severe breathlessness, hypoxia).** Treat with Adrenaline, chlorpheniramine and intravenous steroids in accordance with the current anaphylaxis guidelines (see copy in day case office)

Side Effects
Infusion reactions occur in 0.9% of patients following the first infusion and are more common after the first two infusions. Infusion reactions may include pruritis, fever, urticaria/rash, chills, pyrexia, rigors, sneezing, angioneurotic oedema, throat irritation, cough and brochospasm, with or without hypotension or hypertension. Infusion reactions can occur for up to several hours after the infusion has been administered. Patients should be advised that hypersensitivity can occur on the day of, or day after the infusion, they should be told of the signs and symptoms to watch for and to seek medical help if they occur.

Patients are at increased risk of infection (approx 1% per patient per year) particularly upper respiratory tract infections, bronchitis, gastroenteritis and urinary tract infections.

Other side effects include nausea or diarrhoea, arthralgia/musculoskeletal pain, fever, migraines or rashes.

Rare (<1/1000) side effects include delayed hypersensitivity

There have also been reports of progressive focal leukoencephalopathy in patients treated with Belimumab. Patients should be monitored for new neurological symptoms

It is unknown if there is a long term increased risk of some malignancies.

After infusion
Giving set is disconnected after a saline flush, but the cannula is left in situ until after observation period is complete.
Patient can go home 4hour after infusion 1 and 2 and 2hours after subsequent infusions if they are well and observations have been satisfactory.

Inform patient of date of next infusion.
Monitoring of blood tests continues as for methotrexate.
It is for the physician to report severe adverse reactions to the manufacturers

Subsequent Assessment of Disease
Blood tests (FBC, ESR, U+E, LFT) should be performed before each infusion and results checked.

Health and Safety
Belimumab is not cytotoxic and requires no special precautions or procedures in case of spillage

Withdrawal from Treatment
Failure to respond at 6 months (improvement of SELENASLEDAI score of <4) will lead to withdrawal of treatment

References

1. Benlysta summary of product characteristics September 2016
2. NICE TAG 397 June 2016

Documentation Controls

Development of Guideline:	Rheumatology department
Consultation with:	
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