Gloucestershire Hospitals
NHS Foundation Trust

Abatacept: Prescribing and Administering

1. Background:

Abatacept is a fusion protein that consists of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTL1-4) linked to a modified Fc portion of human immunoglobulin G1 (IgG1). It is from a group of drugs called cytokine inhibitors. Cytokines are small protein molecules, which occur in the body and are involved in inflammatory conditions. Abatacept modulates the T lymphocyte response, reducing inflammation through effects on cytokines such as TNF alpha, interferon and interleukin-2.

Abatacept is currently used at GHNHSFT within the NICE Technology Appraisal process to treat rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) after the failure of a TNF inhibitor and other disease modifying anti-rheumatic drugs (DMARDs).

For full guidance the NICE Technology Appraisals can be found at: www.nice.org.uk

Abatacept is available as an intravenous infusion and as a subcutaneous injection designed for the patient to self-administer at home, this will usually be supplied via Homecare. The decision as to which formulation the patient will receive will be decided by the rheumatology team on the basis of clinical need and suitability for each patient.

2. Contraindications:

- Hypersensitivity to the active substance or any excipients
- Severe or uncontrolled infections such as sepsis and opportunistic infections
- Use in combination with TNF inhibitor medicines
- Live vaccines must not be given concurrently or within 3 months of discontinuing abatacept

3. Prescribing Abatacept Infusions for Day Case Patients:

Abatacept must be prescribed on the “Gloucestershire Hospitals Day Case Prescription Chart”.

All details on the chart must be completed. This includes patients’ name, DOB, address and hospital number. An addressograph is sufficient.

The allergy section of the chart must be completed and patients’ weight must be documented on the chart.

Declaration
All abatacept prescription charts must have the declaration for treatment completed by the prescriber. He/She must indicate if treatment is in line with the appropriate NICE Technology Appraisal by adding the technology appraisal reference number and countersigning. If treatment is outside the NICE criteria but has been agreed by a Clinical Commissioning Group, the Individual Funding Request box must be ticked and the chart countersigned.

Dose of abatacept infusion is based on a dose of approximately 10mg/kg.

Dosing in RA:

Body Weight of the Patient	Dose	Number of vials*
Less than 60 kg	500 mg	2
60 kg to 100 kg	750 mg	3
More than 100 kg	1000 mg	4

* Each vial provides approximately 250mg abatacept for infusion

Dosing in JIA:

The recommended dose for patients 6-17 years of age with JIA who weigh less than 75kg is calculated based on the patient's body weight at each infusion. Paediatric patients weighing 75kg or more should receive dosing according to the table above.

Frequency of dosing:

- Patients not previously treated with abatacept require initial loading, where an infusion is given at weeks 0, 2 and 4 weeks
- Actual dose for administration is checked by nursing staff upon patient admission based on current weight. If the prescription requires amendment, the rheumatology consultant responsible for the patient should be contacted
- The Day Case Prescription charts are valid for 6 months only
- Pharmacy will be unable to dispense abatacept for charts which are out of date, incorrectly completed or where the declaration is incomplete

4. Prescribing Abatacept for Subcutaneous (SC) Injection via Homecare (only for Rheumatoid Arthritis):

- Abatacept subcutaneous injections may be initiated with or without in IV loading dose
- The subcutaneous product is administered weekly at a dose of 125mg
- If a single IV infusion is given to initiate treatment, the first 125mg SC injection should be administered within a day of the IV infusion, followed by the weekly 125mg dose
- Patients switching from abatacept intravenous therapy to subcutaneous administration should administer the first subcutaneous dose instead of the next scheduled intravenous dose
- The Pharmacy Homecare Office will provide the relevant Homecare registration and prescription forms for completion which should be returned to them for processing

5. Patient Preparation and Pre-Treatment Investigations:

- Prior to administration of the first dose, the following investigations must be performed:
  - Medical History, chest X ray and T spot test to exclude tuberculosis
  - Hepatitis B and C serology, HIV if appropriate
  - History to confirm previous exposure to Varicella Zoster or serology test
- For subsequent infusions bloods must be taken (for FBC, U&E's, LFT's and CRP) 2 weeks prior to date of infusion and will be checked by the infusion unit staff prior to the day of the infusion
- On admission carry out baseline observations Blood Pressure (BP), Pulse (P), Temperature, Urine Dip and Weight when patient arrives.
- Check blood results – (refer to blood monitoring below)
- Ensure no evidence of sepsis or clinically manifested infection.
- Check medication history to ensure no drug contraindications or changes to medication which the rheumatology team are unaware of

- Ensure no previous reactions, if this is the case, patient may require pre-treatment with paracetamol and/or antihistamine, contact rheumatology for advice. **Severe reactions are a contraindication to further treatment.**
- Cannulate patient.
- For patients receiving subcutaneous injections, bloods should be monitored at intervals of monthly unless stated otherwise and will be monitored by the rheumatology specialist nurses.

6. Preparation of Infusion:

Reconstitution

- Determine the dose and number of vials of abatacept required (refer to section 3)
- Remove flip-top from the vial and wipe the top with a 70% alcohol swab
- Under aseptic conditions, reconstitute each vial with 10 mL of water for injections, using the **silicone-free disposable syringe provided with each vial** and an 18-21 gauge needle
- Insert the syringe needle into the vial through the centre of the rubber stopper and direct the stream of water for injections to the glass wall of the vial
- Do not use the vial if the vacuum is not present
- Remove the syringe and needle after 10 mL of water for injections have been injected into the vial
- To minimise foam formation in solutions of abatacept, the vial should be rotated with gentle swirling until the contents are completely dissolved. **Do not shake**. Avoid prolonged or vigorous agitation.
- Upon complete dissolution of the powder, the vial should be vented with a needle to dissipate any foam that may be present
- After reconstitution the solution should be clear and colourless to pale yellow. Do not use if opaque particles, discolouration, or other foreign particles are present

Dilution

- Immediately after reconstitution, the concentrate must be further diluted to 100 mL with sodium chloride 9 mg/mL (0.9%) solution for injection
- From a 100 mL infusion bag or bottle, withdraw a volume of sodium chloride 9 mg/mL (0.9%) solution for injection equal to the volume of the reconstituted vials
- Slowly add the reconstituted abatacept solution from each vial to the infusion bag or bottle using the same **silicone-free disposable syringe provided with each vial**.
- Gently mix. The final concentration of abatacept in the bag or bottle will depend upon the amount of active substance added, but will be no more than 10 mg/ml
- Any unused portion in the vials must be immediately discarded in accordance with local requirements
- Check the infusion with another trained member of staff and label the bag using a white sticker.

7. Administration of Infusion:

- Use an infusion set with an in-line, sterile, non-pyrogenic, low protein-binding filter (pore size 1.2 micrometer or less) obtained from stores.
- Administer the abatacept infusion intravenously over a period of 30 minutes.
- It is recommended that the administration of the solution for infusion is started as soon as possible and within 24 hours of preparation if stored refrigerated at 2°C to 8°C
- Do not infuse abatacept in the same intravenous line as any other agents

8. Monitoring of Infusion:

- Abatacept has rarely been associated with acute infusion-related reactions, including anaphylactic shock and delayed hypersensitivity reactions.
- Acute infusion reactions including anaphylactic reactions may develop within seconds or within a few hours following infusion
- As this is rare, pre-treatment to prevent an infusion reaction is not required
- Check observations on initiation of infusion and on completion after 30 minutes if any concerns
- If acute reactions occur, the infusion must be stopped immediately

9. Treatment of Infusion Reaction:

- An infusion reaction is any reaction occurring during or within 1-2 hours of an infusion. This can be classified into mild, moderate and severe.
- ***Mild*** reactions include: Mild fever, chills, nausea, headache, pruritus, dizziness and cough
- ***Moderate*** reactions include: Chest pain, shortness of breath, hypo/hypertension, palpitations, urticarial, elevated temperature
- ***Severe*** reaction include significant hypo/hypertension, stridor, chest discomfort or shortness of breath, bronchospasm, angioedema of upper airway, elevated temperature
- If a patient has any reaction:
    - STOP infusion immediately
    - Obtain medical assistance
    - If a severe reaction or anaphylaxis is suspected treat as per anaphylaxis protocol
    - Contact the consultant rheumatologist responsible for the patient's care
- The decision to retreat a patient with abatacept who has had a reaction to it will be made by the consultant rheumatologist responsible for that patient's care. **A severe or anaphylactic reaction is a contraindication to on-going treatment**

References:

1. Summary of Product Characteristics for *Orencia 250mg powder for concentrate for solution for infusion*® Last updated on the Electronic Medicines Compendium 07/08/2017. Accessed via the Electronic Medicines Compendium http://emc.medicines.org.uk on *19/12/2017*
2. Summary of Product Characteristics for *Orencia 125mg solution for injection in pre-filled pen*® Last updated on the Electronic Medicines Compendium 30/07/2017. Accessed via the Electronic Medicines Compendium http://emc.medicines.org.uk on *19/12/2017*
3. National Institute for Health and Care Excellence (NICE) www.nice.org.uk NICE TA195 – Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor
4. National Institute for Health and Care Excellence (NICE) www.nice.org.uk NICE TA373 – Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis

Appendix

ABATACEPT BLOOD MONITORING GUIDANCE

SEEK ADVICE FROM THE RHEUMATOLOGY TEAM IF:-

- Neutrophils < 1.8 x 109
- Platelets <140 x 109
- ALT or alk phos more than 2 times upper limit of normal.

NORMAL BLOOD RANGES

Liver function tests:

ALT (alanine aminotransferase) and AST
Men: ALT < 50
Women: ALT < 35

Alkaline phosphatase (alk phos)
Men and women (30-130) Seek advice if alkaline phosphatase >160