Clinical Commissioning Policy
Abatacept for refractory idiopathic inflammatory myopathies (adults and children aged 2 years and over) [211002P] (URN:1925)

Publication date: November 2021 **Version number:** 1.0

Commissioning position

Summary

Abatacept is recommended to be available as a treatment option through routine commissioning for refractory idiopathic inflammatory myopathies within the criteria set out in this document. The policy is restricted to patients aged 2 years and over as per the drug's licence in other indications.

Executive summary

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

Plain language summary

About idiopathic inflammatory myopathies

Idiopathic inflammatory myopathies (IIM) are chronic inflammatory conditions characterised by muscle inflammation. This leads to weakness which has significant impact on patients' mobility and quality of life. IIMs are said to be 'heterogenous'; which means that the severity and symptoms of the disease vary from person to person. Features may include damage to skin, joints, lungs, heart, stomach and gut. IIMs affect both children and adults. Children most commonly experience both skin and muscle features, such as muscle weakness and skin ulcers. In children the condition is called juvenile idiopathic inflammatory myopathy (juvenile IIM) or juvenile dermatomyositis. Skin involvement in children can be severe, leading to painful ulceration. In the long-term, people with IIM are at increased risk for stroke, heart attack and osteoporosis.

The cause of IIMs is not fully understood, but they are thought to be 'autoimmune' diseases. In autoimmune disease, the body's immune system incorrectly attacks and damages its own cells.

About current treatment

IIMs are currently treated using a range of medicines which aim to reduce or alter the activity of the immune system - 'immuno-suppressant' or 'immune modulatory' medicines. People may require combinations of these treatments, and some will need to go to hospital for treatments given intravenously, such as intravenous immunoglobulin (IVIg), rituximab or

cyclophosphamide. Patients are also given physiotherapy aimed at improving muscle strength and function.

About abatacept

Abatacept belongs to a group of medicines called biological therapies. It is a protein which interrupts the interaction between T cells, a type of white blood cell involved in inflammation, and the other immune cells which activate these T cells. This results in decreased T cell activation, and therefore decreased inflammation, a key process of the disease activity in IIMs.

What we have decided

NHS England has carefully reviewed the evidence to treat refractory idiopathic inflammatory myopathies (adults and children aged 2 years and over) with abatacept. We have concluded that there is enough evidence to make the treatment available at this time. Additional benefit was found for abatacept compared to standard treatment for two critical outcomes (quality of life and muscle strength, both included in the total improvement score) and one important outcome (disease activity).

Links and updates to other policies

This document should be used in conjunction with Rituximab for the treatment of dermatomyositis and polymyositis (adults) 2016.

Committee discussion

Clinical Panel noted that as a 3rd line therapy, Abatacept is likely to be an effective alternative to IVIg. For 2020/21, the MDSAS database (which monitors the use of immunoglobulin in the NHS) registered a total of 177,841g of immunoglobulin was administered to 365 patients with a diagnosis of 'inflammatory myopathies'. Abatacept is likely to be used in a significant proportion of this group (estimated at approximately 50-75%) and thus help preserve limited supplies of IVIg for those patients where IVIg is the only treatment option.

See the committee papers (link) for full details of the evidence.

The condition

IIMs are a group of chronic inflammatory conditions characterised by muscle inflammation, leading to weakness which has a significant impact on patients' mobility and quality of life, and can affect patients of all ages. This policy for IIMs include dermatomyositis, polymyositis and juvenile dermatomyositis and excludes inclusion body myositis. The following conditions are also included in the broader remit of the policy, but there is a limited evidence base; statin-induced immune-mediated necrotising myopathy due to anti-HMG-CoA reductase antibodies and dermatomyositis associated with cancer are included in the remit of this policy.

IIMs are said to be heterogenous; which means that the severity and symptoms of the disease vary from person to person. Other features include damage to skin, joints, lungs, heart, stomach and gut. IIMs affect both children and adults. Skin involvement in children can be severe, leading to painful ulceration. In the long-term, people with IIM are at increased risk for stroke, heart attack and osteoporosis.

Refractory idiopathic inflammatory myopathy is defined as the intolerance to or an inadequate response to glucocorticoids and at least two other conventional immunosuppressive or immunomodulatory agents (1st line treatment), and rituximab second line (which can be given to patients with myositis-specific or myositis-associated antibodies).

Patients fall into 3 disease activity categories: those with stable chronic disease, those with an acute flare of chronic disease, and those with new onset rapidly deteriorating disease. Rapidly deteriorating disease refers to patients with major organ involvement including severe lung/respiratory muscle/skin/cardiac involvement and/or dysphagia.

Current treatments

Current treatment for IIMs involves a stepwise approach:

1st line treatment: Begins with glucocorticoids and physiotherapy, progressing to glucocorticoids in combination with immunosuppressive agents.

2nd line treatment: Rituximab can then be given for patients with autoantibodies relevant to myositis (myositis-specific antibodies and myositis-associated antibodies).

3rd line treatment: If a patient does not respond to the above treatments or does not have autoantibodies relevant to myositis, the next available option is IVIg, which is given in hospital as an infusion over a 2-5-day admission.

4th line treatment: If treatment steps 1-3 fail to resolve symptoms, patients can be treated with intravenous cyclophosphamide, though this has a range of potential severe side effects. Treatment with cyclophosphamide is limited to the patients with the most severe refractory disease e.g., those with profound proximal muscle weakness, inability to swallow and/or interstitial lung disease.

The new treatment

Abatacept belongs to a group of medicines called biological therapies. It is a protein which interrupts the interaction between T cells, a type of white blood cell involved in inflammation, and other immune cells which activate these T cells. This results in decreased T cell activation, and therefore decreased inflammation, a key process of the disease activity in IIMs. Abatacept is licensed for treating rheumatoid arthritis, juvenile idiopathic arthritis and psoriatic arthritis. It is currently unlicensed for use in IIMs. It is administered subcutaneously and can be self-injected by competent patients or their carers following their initial dose, with some patients requiring initial intravenous loading dose(s). Abatacept has a known safety profile from its use in other conditions. Abatacept is associated with fewer hospitalised infections compared to rituximab in rheumatoid arthritis (Yun et al. 2016).

The primary purpose of the treatment with abatacept in IIM would be improved mobility, function and quality of life. This policy introduces abatacept as a potential alternative therapy to IVIg. IVIg is an expensive blood product, requiring regular hospital admission for intravenous infusion and may be subject to supply shortages. Introducing abatacept as an optional alternative treatment for some patients will therefore help to protect IVIg supply for other groups of patients whose need for replacement therapy is greatest. If abatacept is offered as an additional line of treatment before IVIg, IVIg use is relegated lower down the pathway. The subcutaneous administration of abatacept additionally allows for home administration, thereby reducing patient day case attendances.

Epidemiology and needs assessment

IIMs are rare diseases, usually characterised by a short and relatively severe onset and with chronic disease progression. The incidence of IIMs varies depending on the population and ethnicity. The estimated incidence ranges from 1.16 to 19 per one million-person years (Meyer et al., 2015, Parker et al., 2018). The overall IIMs prevalence ranges from 2.4 to 33.8 per 100 000 inhabitants (Meyer et al., 2015). According to the NHS England Specialised Commissioning Service Specification for Specialised Rheumatology Services, 2013/14, there are approximately 500 new adult cases of IIMs with muscle and skin involvement per year in England and Wales, while the incidence of new juvenile IIM cases is estimated at 20 to 30 new cases per year, according to the UK national registry data (Martin et al., 2011).

Evidence summary

NHS England has concluded that there is sufficient evidence to support a proposition for the routine commissioning of this treatment for the indication. The evidence review which inform this commissioning position can be accessed here: (add in links)

Implementation

Eligibility criteria

Potential patients should be discussed and ratified at the (virtual) regional multi-disciplinary team (MDT) meeting. The patient group is defined as confirmed adult/childhood idiopathic inflammatory myopathy fulfilling clinical International Myositis Classification Criteria Project (IMCCP) criteria. Patients should have refractory disease, defined as continued active disease despite treatment with corticosteroids, two disease-modifying anti-rheumatic drugs (DMARDs) and rituximab (if indicated) or who have had an adverse event with rituximab and/or secondary nonresponse to rituximab.

Active disease is defined as a score on the Manual Muscle Testing 8 (MMT-8) of:

- <125 (out of 150) in conjunction with 2 other abnormal Core Set Measures (CSM).

OR

- >125 (out of 150) in conjunction with 3 other abnormal CSM (Rider et al., 2018).

The other CSM needed consists of 2 or 3 of the following 6 measures:

1) Patient's global assessment of disease activity by visual analogue scale (VAS) with a minimum score of 2.0 cm out of 10.0 cm (Isenberg et al, 2004).
2) Physician's global assessment of disease activity by VAS with a minimum score of 2.0 cm out of 10.0 cm (Isenberg et al, 2004).
3) Health Assessment Questionnaire (HAQ) disability index with a minimum value of 0.25.
4) Elevated level of at least 1 (locally measured) muscle enzyme (creatine kinase, aldolase, lactate dehydrogenase, alanine aminotransferase, or aspartate amino-transferase AST) to a minimum of 1.3 times the upper limit of normal, with the most abnormal muscle enzyme value selected as the target enzyme to be followed.
5) Global extra-muscular disease activity score with a minimum value of 1.0cm (based on composite assessment of disease activity on the constitutional, cutaneous, skeletal, gastrointestinal, pulmonary, and cardiac scales of the Myositis Disease Activity Assessment Tool (MDAAT) over the past 4 weeks on the 0-10cm VAS scale).
6) Active interstitial lung disease defined as a decrease of 10% in forced vital capacity (FVC) and/or 15% of the diffusion capacity of the lung for carbon monoxide (DLCOcor) value.

Skin involvement should be assessed at baseline using the validated score Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) (Anyanwu et al., 2015).

Starting criteria

Patients with refractory IIM are a complex heterogeneous group of patients with multisystem clinical manifestations. Treatment with abatacept may be considered in:

- Patients with chronic, stable disease
- Chronic disease with acute flare
- New onset rapidly deteriorating disease
- Any patients transitioning from IVIg (see appendix 1)

Rapidly deteriorating disease refers to patients with major organ involvement including severe lung/respiratory muscle/skin/cardiac involvement and/or dysphagia.

Considering this, patients with refractory disease (see eligibility criteria for definition) will have all treatment decisions including the order of treatment discussed on a case-by-case basis with an expert MDT. Treatment may be given sequentially or concurrently depending on clinical status. In light of the COVID-19 pandemic then the regional MDT may decide it is appropriate to start patients on abatacept instead of rituximab.

In patients with rapidly deteriorating disease, commencing IVIg according to the IVIg Commissioning Guidelines may be indicated prior to and/or at the same time as commencing immunosuppressive therapy including abatacept for patients. Following commencement of abatacept, IVIg will be continued as bridging therapy with the aim of weaning IVIg down over time leaving abatacept as maintenance therapy.

Dosing in adults: abatacept can be administered as weekly subcutaneous injection (125 mg). In patients between the ages of 2 and 6 only subcutaneous administration of abatacept is recommended (50, 87.5 and 125 mg solutions) by the weight-based regimen as per SmPC table. Intravenous administration is not recommended for children under the age of 6 years (Electronic Medicines Compendium, Summaries of Product Characteristics). For patients six years of age and above both intravenous and subcutaneous abatacept can be used. IV loading can be used at initiation.

Stopping criteria

Treatment should stop if patients do not meet the criteria for minimal improvement from baseline, as per 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for response in both juvenile and adult DM (Rider et al., 2017). Assessment should be carried out after initial 6 months of therapy and 6-monthly thereafter to ensure a sustained response. After 3 years of treatment with abatacept patients will continue on some conventional oral DMARDs and these will be weaned over time.

		Worsening to 5% improvement	**> 5% to 15%**	**> 15% to 25%**	**> 25% to 40%**	**> 40%**
1	**Physician global activity**	0	7.5	15	17.5	20
2	**Parent global activity**	0	2.5	5	7.5	10
3	**Childhood Health Assessment Questionnaire**	0	5	7.5	7.5	10
4	**Enzyme (most abnormal) or Physical Summary Score of the Child Health Questionnaire-Parent Form 50**	0	2.5	5	7.5	7.5
5	**Extra-muscular activity or Disease Activity Score**	0	2.5	5	7.5	7.5
		Worsening to 2% improvement	**> 2% to 10%**	**> 10% to 20%**	**> 20% to 30%**	**> 30%**
6	**Manual muscle testing or Childhood Myositis Assessment Scale**	0	10	20	27.5	32.5

The scores are added up across all 6 categories and the total is the improvement score:

- For juvenile IIM, total improvement scores of ≥ 30, ≥ 45, and ≥ 70 represent minimal, moderate, and major improvement, respectively.

- For adult IIM, total improvement scores of ≥ 20, ≥ 40, and ≥ 60 were used to represent minimal, moderate, and major improvement, respectively.

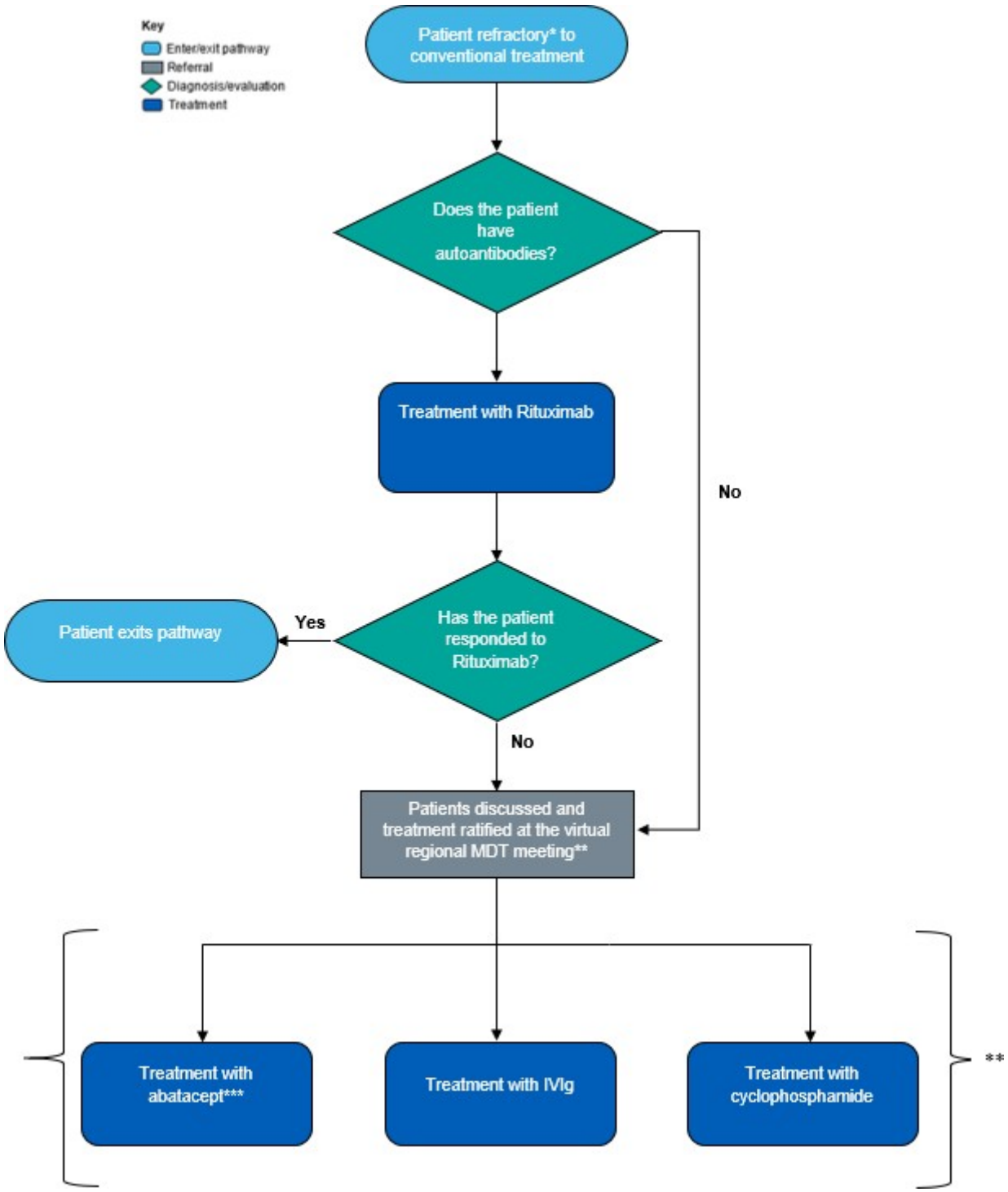
Online tools to calculate the improvement score for each age group can be found here:
https://www.niehs.nih.gov/research/resources/imacs/response_criteria/adult.html
https://www.niehs.nih.gov/research/resources/imacs/response_criteria/pediatric.html

If the CDASI is used to monitor skin involvement, treatment should be stopped if there is failure to achieve a 40% improvement from baseline scores after 6 months, and 6-monthly thereafter to ensure a sustained response (Ahmed et al. 2020).

Monitoring

Patients will initially be assessed at 3 months and then every 6 months thereafter for the duration of treatment with abatacept (as per rheumatoid arthritis treatment guidelines).

Patient pathway



*Refractory disease is defined as continued active disease despite treatment with corticosteroids and two DMARDs. Rituximab is then given if the patient has autoantibodies.

** At every stage of subsequent treatment, the patient is discussed with the MDT to adapt their management plan accordingly. The order of treatment is determined by clinical need, response, evidence of rapidly progressing disease and prior trialled treatments. Treatments may be given sequentially or concurrently.

*** Abatacept can either be given prior to IVIg or cyclophosphamide, or concomitantly with IVIg in patients transitioning from IVIg; this is an MDT-dependent decision.

Governance arrangements

The Service Specification A13/S/a Specialised Rheumatology Services (Adult) describes the governance arrangements for this service for adults and the Service Specification E03/S/b Paediatric Medicine: Rheumatology describes the governance arrangements for this service for children.

Any provider organisation treating patients with this intervention will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process. Abatacept must only be used for treatment in specialised centres or in collaboration with specialised centres under the supervision of a multi-disciplinary team.

Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Mechanism for funding

Abatacept for the treatment of refractory idiopathic inflammatory myopathies within the criteria in this document will be commissioned and funded by NHS England and NHS Improvement Specialised Commissioning under existing arrangements for the provision of Specialised Rheumatology services. All associated activity should be recorded to the following lines:

- NCBPS26Z Rheumatology (Adults)
- NCBPS23W Children's Services – Rheumatology

Audit requirements

Patient data to be mandatorily collected as part of the Myositis Disease Activity Assessment Visual Analogue Scales (MYOACT) Registry or the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (JDCBSR) to monitor efficacy and safety according to agreed outcomes. Patients should be registered on the MYOACT registry or the JDCBSR Registry and outcome data collected as per the predefine case report form at baseline, 3 months, 6 months, 12 months and then annually. An annual audit should report on the following outcomes:

- Time to definition of improvement
- Time to clinical remission
- Duration of effect
- Timing of re-treatment
- Reduction/Discontinuation in steroids/immunosuppressants
- Frequency of re-treatment
- Serious adverse effects
- Health assessment questionnaires (HAQ or CHAQ)

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Definitions

Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)	A validated instrument to assess skin activity in patients with idiopathic inflammatory myopathy
Idiopathic inflammatory myopathy (IIM)	A group of conditions that are characterized by inflammation of skeletal muscles and sometimes a skin rash is present
Manual muscle testing (MMT)	A standardised set of assessments that measure muscle strength and function
Myositis Disease Activity Assessment Tool (MDAAT)	A combined tool that captures the physician's assessment of IIM disease activity of various organ systems
Rapidly deteriorating disease	Patients presenting with major organ involvement including severe lung/respiratory muscle/skin/cardiac involvement and/or dysphagia
Visual analogue scale (VAS)	A subjective rating scale

References

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Appendix 1

Care Pathway Design Principles

Below is an example care pathway for IVIG to abatacept switch which has been developed by the CRG for use by clinicians:

A. Identification process

1. Patient identified with diagnosis of inflammatory myopathy e.g. polymyositis or dermatomyositis and receiving maintenance IVIg

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2. Discuss patient at local MDT meeting to confirm clinically appropriate for patient to switch e.g. no history of chronic infection

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3. If suitable to switch, discuss with patient at next clinic visit or attendance on day case unit.
As per local departmental procedure, patient to be counselled and consent re abatacept and screening bloods to be performed e.g. hepatitis B and C and HIV status (NB patient may have passive acquisition of hep B antibodies from IVIg treatment- to discuss with local hepatology/virology team as appropriate).
Complete baseline Blueteq form

B. Switching process

Baseline (day1): *administer usual dose of IVIg.*
Administer first dose of weekly s/c abatacept as per departmental policy.
Perform outcome measures.

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Continue weekly injections of s/c abatacept.

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***At* 4 weeks** *give half normal dose of IVIG*

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***At* 8 weeks** *give half normal dose of IVIG*

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At* 12 weeks *perform outcome measures as per MYOACT registry

At* week 26*: perform outcome measures
if no positive response/benefit seen, stop abatacept and review treatment options including returning to previous maintenance IVIg regime at MDT meeting
If response, discuss at MDT meeting and complete 6 month Blueteq form. Continue weekly s/c abatacept.
At 12 months: perform outcome measures

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***At* 2 years:** *Review patient and assess response to determine if patient should continue with weekly s/c abatacept or discontinue because their disease is well controlled/in remission.*
Continue to perform regular outcome measures every 6-12 months.