Health Technology Briefing
February 2022

Abatacept for treating idiopathic inflammatory myopathies

Company/Developer	Bristol-Myers Squibb Pharmaceuticals

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 17286	NICE ID: 10095	UKPS ID: 646818

Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

Summary

Abatacept is currently in clinical development for the treatment of adult patients with Idiopathic inflammatory myopathies (IIM). 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. The severity and symptoms of IIMs vary from person to person. Patients may experience trips and falls and be very tired after walking or standing. Damage to muscle and joints in IIM, can lead to disability and other complications including breathing and swallowing difficulties, cardiovascular disease, and infections. Many patients have symptoms despite using current standard treatments, hence the need for more effective and less-toxic therapies.

Abatacept 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 in the disease activity in IIMs. Abatacept is administered subcutaneously and can be self-injected by competent patients or their carers following their initial dose, allowing for home administration, thereby reducing patient day case attendances. Abatacept is designed to be used in addition to a patient's standard treatment for IIM. If licensed, abatacept would provide an additional treatment option for adult patients with IIMs.

Proposed Indication

Adults with active idiopathic inflammatory myopathies (IIM).[1]

Technology

Description

Abatacept (Orencia) is a fusion protein that consists of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to a modified Fc portion of human immunoglobulin G1 (IgG1). Abatacept selectively modulates a key costimulatory signal required for full activation of T lymphocytes expressing CD28. Full activation of T lymphocytes requires two signals provided by antigen presenting cells: recognition of a specific antigen by a T cell receptor (signal 1) and a second, costimulatory signal. A major costimulatory pathway involves the binding of CD80 and CD86 molecules on the surface of antigen presenting cells to the CD28 receptor on T lymphocytes (signal 2). Abatacept selectively inhibits this costimulatory pathway by specifically binding to CD80 and CD86.[2]

Abatacept is in clinical development for the treatment of patients with IIM. In the phase III clinical trial (NCT02971683), abatacept is administered as a subcutaneous weekly injection in addition to the subject's current standard treatment for 24 weeks followed by a 28 week open-label period of abatacept treatment plus the subject's current standard treatment.[1]

Key Innovation

Historically, IIMs have been difficult to treat as standard treatment with glucocorticoids and synthetic immunosuppressants are associated with side effects and many patients have an incomplete response and may acquire disability despite ongoing treatment. Increasing evidence suggest biological therapies, such as abatacept, hold the potential to improve outcomes in IIM.[3,4]

Abatacept can be administered as a potential alternative to intravenous immunoglobulin (IVIg) for patients who are not well controlled on standard therapies. IVIg is an expensive blood product, requiring regular hospital admission for intravenous infusion and may be subject to supply shortages. The subcutaneous and self-injected administration of abatacept additionally allows for home administration, thereby reducing patient day case attendances. Abatacept also provides additional benefits in terms of quality of life and muscle strength when compared to standard treatment. If licensed, abatacept would provide an additional treatment option for adult patients with IIMs.[5]

Regulatory & Development Status

Abatacept is licensed in EU/UK for use in rheumatoid arthritis, polyarticular juvenile idiopathic arthritis and psoriatic arthritis.[6,2]

Abatacept is in phase II/III clinical development for a large number of indications, including:[7]

- Prevention of graft versus host disease (GVHD)
- Interstitial Lung Disease (ILD)
- Type 1 diabetes mellitus
- Systemic Lupus Erythematosus (SLE)
- Uveitis

Patient Group

Disease Area and Clinical Need

IIM are a heterogeneous group of diseases that are characterised by inflammation of muscle tissue (myositis) which can lead to profound weakness, fatigue and disability.[8] There are different types of IIM, and they include: polymyositis, which affects many different muscles, particularly the shoulders, hips and thigh muscles. It is more common in women and tends to affect people aged 30 to 60. Dermatomyositis is a type of myositis which affects several muscles and causes a rash. It is more common in women and can also affect children (juvenile dermatomyositis). Another type of myositis is inclusion body myositis (IBM), which causes weakness in the thigh muscles, forearm muscles and the muscles below the knee. It may also cause problems with swallowing (dysphagia). IBM is more common in men and tends to affect people over 50.[9] 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. In the long-term, people with IIM are at increased risk for stroke, heart attack and osteoporosis.[5]

The incidence of IIMs varies depending on the population and ethnicity. The estimated incidence in England ranges from 1.16 to 19 per one million-person years. There are approximately 500 new adult cases of IIMs with muscle and skin involvement per year in England and Wales.[5] In England, in 2021-21, there were 394 finished consultant episodes (FCE) and 340 admissions for other myopathies (ICD-10 code G72.4) which resulted in 246 day cases and 734 FCE bed days.[10] The 5-year survival rates for IIM patients range from 63% to 95%.[3]

Recommended Treatment Options

Exercise and physiotherapy are used to treat IIMs. Speech and language therapy may be recommended if severe myopathy affects swallowing and/or communication.[9]

Treatments used for IIM include:[9]

- Steroids
- Disease-modifying anti-rheumatic drug (DMARD) such as azathioprine, methotrexate, cyclophosphamide or mycophenolate
- Biologic therapies, such as rituximab
- Immunoglobulin therapy, used rarely

Clinical Trial Information

Trial	NCT02971683. 2016-002269-77. **IM101-611; A Phase 3, Randomized, Double-Blind Clinical Trial to Evaluate the Efficacy and Safety of Abatacept SC With Standard Treatment Compared to Standard Treatment Alone in Improving Disease Activity in Adults With Active Idiopathic Inflammatory Myopathy (IIM)** **Phase III** - ongoing **Locations:** 5 EU countries, USA and other countries **Primary completion date** - July 2020
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N=149; Subjects with a diagnosis of IIM; aged 18 years and older.
Intervention(s)	Abatacept (SC) weekly + Standard treatment

Comparator(s)	Matched placebo
Outcome(s)	**Primary outcome measure:** • Number of Participants Achieving International Myositis Assessment and Clinical Studies Definition of Improvement (IMACS DOI) at Week 24 without rescue [Time Frame: From first dose to 24 weeks after first dose. (Approximately 169 days)] See trial record for full list of other outcomes.
Results (efficacy)	See trial record.
Results (safety)	See trial record.

Estimated Cost

Abatacept is already marketed in the UK; the cost for 125mg/1ml pre-filled disposable injection is £1209.60.[11]

Relevant Guidance

NICE Guidance

No relevant NICE guidance identified.

NHS England (Policy/Commissioning) Guidance

- NHS England and NHS Improvement: Equality and Health Inequalities Impact Assessment (EHIA): Abatacept for refractory idiopathic inflammatory myopathies. (URN: 1925). Dec 2021
- NHS England. Clinical Commissioning Policy. Abatacept for refractory idiopathic inflammatory myopathies (adults and children aged 2 years and over). [211002P] (URN:1925). Nov 2021
- NHS England. Clinical priorities advisory group: Abatacept for refractory idiopathic inflammatory myopathies. (URN: 1925). Oct 2021.
- NHS England. Evidence Review: Abatacept for refractory idiopathic inflammatory myopathies. (URN: 1925). June 2020

Other Guidance

Additional Information

References

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3 Gazeley DJ, Cronin ME. Diagnosis and treatment of the idiopathic inflammatory myopathies. *Ther Adv Musculoskelet Dis* 2011;3(6):315-24. Available from: https://doi.org/10.1177/1759720X11415306.

4 Khoo T, Limaye V. Biologic therapy in the idiopathic inflammatory myopathies. *Rheumatol Int* 2020;40:191–205. Available from: https://doi.org/10.1007/s00296-019-04467-6.

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6 European Medicines Agency. *Orencia. EPAR. Medicine overview*. Available from: https://www.ema.europa.eu/en/documents/overview/orencia-epar-medicine-overview_en.pdf [Accessed 22nd Dec 2021].

7 Clinicaltrials.gov. *Abatacept clinical trials search* Available from: https://clinicaltrials.gov/ct2/results?term=abatacept&Search=Apply&recrs=b&recrs=a&recrs=f&recrs=d&recrs=g&recrs=e&recrs=m&age_v=&gndr=&type=&rslt=&phase=1&phase=2 [Accessed 14th January 2021].

8 Speciality Pharmacy Service. *New medicines update: Orencia: Idiopathic inflammatory myopathies (IIM) in adults* 2022. Available from: https://www.sps.nhs.uk/medicines/abatacept/ [Accessed 14th January 2022].

9 National Health Service. *Condition overview: Myositis (polymyositis and dermatomyositis)*. Available from: https://www.nhs.uk/conditions/myositis/ [Accessed 22nd Dec 2021].

10 NHSDigital. *Hospital Episode Statistics (HES)*. 2021. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2020-21 [Accessed 22nd Dec 2021].

11 National Institute for Clinical Excellence. *BNF: Abatacept*. 2022. Available from: https://bnf.nice.org.uk/medicinal-forms/abatacept.html [Accessed 14th January 2022].

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