Health Technology Briefing
July 2025

Ianalumab for Sjogren's syndrome

Company/Developer	Novartis Pharmaceuticals UK Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 26509	NICE ID: 10483	UKPS ID: 672357

Licensing and Market Availability Plans

In phase III clinical development.

Summary

Ianalumab is in development for the treatment of adult patients with active Sjögren's syndrome. Sjögren's syndrome is a complex autoimmune disease, in which the body's immune system attacks exocrine glands, such as the glands that produce saliva or tears. The severity and types of symptoms vary between individuals, but common symptoms include dry eyes and mouth, aching muscles, joint pain and extreme tiredness. Other symptoms include dry or itchy skin, persistent coughs, a quiet or hoarse voice and swelling of the glands of the cheeks, neck or under the jaw. These symptoms can have a noticeable negative impact on an individual's quality of life, for example a dry mouth can make eating certain foods difficult, and sustained periods of dry eyes may contribute to vision problems. Current treatments aim to relieve the symptoms of dryness that occur with Sjögren's syndrome.

Ianalumab is a monoclonal antibody (a type of protein) that binds to and blocks the BAFF receptor. This has two effects, firstly it can induce the destruction of B-cells which are part of the immune system attacking the body's glands in Sjögren's syndrome. Secondly, ianalumab interrupts BAFF-mediated signalling which promotes further B-cell growth, survival and multiplication. Both effects work together to reduce the number of active B-cells in the body, thereby reducing disease activity. Ianalumab is administered though injection under the skin. If licensed, ianalumab would provide a treatment option that targets for the first time the underlying cause of Sjögren's syndrome.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

For the treatment of patients with active Sjogren's syndrome.[1,2]

Technology

Description

Ianalumab (VAY736) is a monoclonal antibody that selectively binds to and inhibits the BAFF receptor.[3] Ianalumab's mechanism of action has two strands, firstly direct lysis of B-cells (i.e., the breakdown of a cell caused by damage to its plasma membrane) by antibody-dependent cellular cytotoxicity, as well as mechanical BAFF receptor inhibition that interrupts BAFF-mediated signalling for further B-cell maturation, survival and proliferation, thereby reducing the number of active B-cells.[3,4]

Ianalumab is currently in clinical development for the treatment of Sjogren's syndrome. In the phase III clinical trials (NEPTUNUS-1, NCT05350072; NEPTUNUS-2, NCT05349214) participants are administered subcutaneous (SC) ianalumab[1,2].

Key Innovation

Sjögren's syndrome is a complex autoimmune disease, that leads to the malfunction and subsequent destruction of exocrine glands. Currently approved treatments aim to relieve the symptoms of dryness derived from the malfunctioning glands, with treatment for serious organ involvement having been adapted from other rheumatic diseases with similar disease profiles.[3] There is evidence that B-cells are involved multiple pathways involved in the development of Sjögren's syndrome, however there are no technologies currently recommended by the National Institute for Health and Care Excellence (NICE) that target the underlying involvement in the disease.[5,6]

Ianalumab's mechanism of action reduces systemic B-cell activity through two processes and there is evidence that suggests ianalumab is capable of lowering disease activity and increase salivary flow.[3] As such, ianalumab may represent a novel approach to the treatment of dryness and organ disruption in Sjögren's syndrome patients by targeting the underlying B-cell involvement. If licensed, ianalumab may provide an additional treatment option for the treatment of Sjögren's syndrome in adults.

Regulatory & Development Status

Ianalumab does not currently have Marketing Authorisation in the EU/UK for any indication.

Ianalumab is also in phase II/III clinical development for:[7]

- Primary immune thrombocytopenia
- Lupus nephritis
- Systemic lupus erythematosus
- Diffuse cutaneous systemic sclerosis
- Warm autoimmune haemolytic anaemia
- Hidradentis suppurativa

Ianalumab has been awarded the US Food and Drug Administration (FDA) Fast Track designation for Sjogren's syndrome.[8]

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Patient Group

Disease Area and Clinical Need

Sjögren's syndrome is a systemic autoimmune disorder, notably characterised by disruption and damage to the exocrine glands.[9] Whilst the cause of this autoimmune response is not currently fully understood, it is believed to be linked to genetic and environmental causes.[10] The symptoms of Sjögren's syndrome can vary between individuals, as can the severity of symptoms, but some common symptoms include: dry eyes and mouth, aching muscles and joint pain and extreme tiredness. Other symptoms of Sjögren's syndrome can include dry or itchy skin, persistent coughs, a quiet or hoarse voice and swelling of the glands of the cheeks, neck or under the jaw.[10] Although Sjögren's syndrome is not likely to lower an individual's life expectancy, the symptoms can have a sustained negative impact on quality of life with the condition having been associated with fatigue, pain or articular discomfort, ocular and oral impairment, sexual dysfunction, impaired sleep as well as pulmonary manifestations and psychological distress.[10,11]

Primary Sjögren's syndrome is believed to affect between 0.1%–0.6% of the general adult population. It is more prevalent in women, with a female to male ratio of at least 9:1, and a mean age of diagnosis of around 50 years of age.[9] In England, 2023-24, there were 752 finished consultant episodes (FCE) and 695 admissions for Sjögren's syndrome (ICD-10 code M35.0) which resulted in 535 FCE bed days and 631 day cases.[12]

Recommended Treatment Options

NICE currently does not recommend any treatments specific to Sjögren's syndrome.[13] However NICE do recommend ciclosporin for treating dry eyes, a common symptom of Sjögren's syndrome, if primary treatment with artificial tears has not been sufficient.[14]

Clinical Trial Information

Trial	**NEPTUNUS-2;** NCT05349214; A Randomized, Double-blind, Placebo Controlled, 3-arm Multicenter Phase 3 Study to Assess the Efficacy and Safety of Ianalumab in Patients With Active Sjogren's Syndrome **Phase III** - Active, not recruiting **Location(s) –** 10 EU Countries, UK, USA and other countries **Primary completion date –** May 2025
Trial Design	Randomised, quadruple-blinded, parallel assignment
Population	N=506 (actual), women and men ≥ 18 years of age with a classification of Sjögren's syndrome according to the ACR/EULAR 2016 criteria, who have been diagnosed with Sjögren's ≤ 7.5 years before screening
Intervention(s)	SC ianalumab (exposure level 1 and 2)
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: Change from baseline in EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) score at week 48 as compared to placebo See trial record for full list of other outcomes

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Results (efficacy)	-
Results (safety)	-

Trial	**NEPTUNUS-1;** NCT05350072; A Randomized, Double-blind, Placebo Controlled, 2-arm Multicenter Phase 3 Study to Assess the Efficacy and Safety of Ianalumab in Patients With Active Sjogren's Syndrome **Phase III -** Active, not recruiting **Location(s) –** 10 EU Countries, USA and other countries **Primary completion date –** May 2025
Trial Design	Randomised, quadruple-blinded, parallel assignment
Population	N=277 (actual), women and men ≥ 18 years of age with a classification of Sjögren's syndrome according to the ACR/EULAR 2016 criteria, who have been diagnosed with Sjögren's ≤ 7.5 years before screening
Intervention(s)	SC ianalumab
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: Change from baseline in ESSDAI score at week 48 as compared to placebo See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of ianalumab is not yet known.

Relevant Guidance

NICE Guidance

There is currently no NICE guidance for Sjögren's syndrome.

NHS England (Policy/Commissioning) Guidance

- NHS England. NHS standard contract for specialised rheumatology services (adult) A13/S/a. 2014

Other Guidance

- European League Against Rheumatism (EULAR). EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. 2020.[15]
- The British Society for Rheumatology. The British Society for Rheumatology guideline for the management of adults with primary Sjögren's Syndrome. 2017.[16]

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References

1 ClinicalTrials.gov. *A Randomized, Double-blind, Placebo Controlled, 2-arm Multicenter Phase 3 Study to Assess the Efficacy and Safety of Ianalumab in Patients With Active Sjogren's Syndrome (NEPTUNUS-1)*. *Trial ID: NCT05350072*. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/study/NCT05350072 [Accessed 21 January 2025].

2 ClinicalTrials.gov. *A Randomized, Double-blind, Placebo Controlled, 3-arm Multicenter Phase 3 Study to Assess the Efficacy and Safety of Ianalumab in Patients With Active Sjogren's Syndrome (NEPTUNUS-2)*. *Trial ID: NCT05349214*. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/study/NCT05349214 [Accessed 21 January 2025].

3 Bowman S, Fox R, Dörner T, Mariette X, Papas A, Grader-Beck T, et al. Safety and efficacy of subcutaneous ianalumab (VAY736) in patients with primary Sjögren's syndrome: a randomised, double-blind, placebo-controlled, phase 2b dose-finding trial. *The Lancet*. 2022;399(10320):161-71. Available from: https://doi.org/10.1016/S0140-6736(21)02251-0.

4 Dörner T, Posch M, Li Y, Gram H, Wagner F, Oliver S, et al. Treatment of primary Sjögren's syndrome with ianalumab (VAY736) targeting B cells by BAFF receptor blockade coupled with enhanced, antibody-dependent cellular cytotoxicity. *Annals of the Rheumatic Diseases*. 2019;78(5):641-7. Available from: https://doi.org/10.1136/annrheumdis-2018-214720.

5 Ambrus J, Suresh L, Peck A. Multiple Roles for B-Lymphocytes in Sjogren's Syndrome. *Journal of Clinical Medicine*. 2016;5(10):87. Available from: https://doi.org/10.3390/jcm5100087.

6 National Institute for Health and Care Excellence (NICE). *A search for NICE recomendations for Sjögren's syndrome* 2025. Available from: https://www.nice.org.uk/search?q=Sjogren%27s+Syndrome [Accessed 23 January 2025].

7 ClinicalTrials.gov. *A filtered search for ongoing phase II or III clinical trials involving Ianalumab*. 2025. Available from: https://clinicaltrials.gov/search?intr=Ianalumab&term=Novartis&aggFilters=phase:2%203,status:act%20com%20not%20rec [Accessed 7 February 2025].

8 Novartis. *Novartis pipeline 2022 annual report*. 2022. Available from: https://www.novartis.com/sites/novartis_com/files/novartis-pipeline-2022-annual-report.pdf [Accessed 26 February 2025].

9 Bowman S. Primary Sjögren's syndrome. *Lupus*. 2018;27(1 (suplimental)):32-5. Available from: https://doi.org/10.1177/0961203318801673.

10 National Health Service (NHS). *Sjögren's syndrome*. 2025. Available from: https://www.nhs.uk/conditions/sjogrens-syndrome/ [Accessed 13 February 2025].

11 Miyamoto S, Valim V, Fisher B. Health-related quality of life and costs in Sjögren's syndrome. *Rheumatology*. 2021;60(6):2588–601. Available from: https://doi.org/https://doi.org/10.1093/rheumatology/key370.

12 National Health Service Digital. *Hospital Admitted Patient Care Activity, 2023-24*. 2024. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2023-24 [Accessed 13 February 2025].

13 National Institute for Health and Care Excellence (NICE). *A Search for NICE recomendations for Sjögren's syndrome*. 2025. Available from: https://www.nice.org.uk/search?q=Sj%C3%B6gren%27s+syndrome+ [Accessed 13 February 2025].

14 National Institute for Health and Care Excellence (NICE). *Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears*. 2015. Available from: https://www.nice.org.uk/guidance/ta369 [Accessed 13 February 2025].

15 Ramos-Casals M, Brito-Zerón P, Bombardieri S, Bootsma H, De Vita S, Dörner T, et al. EULAR recommendations for the management of Sjögren's syndrome with topical and systemic

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therapies. *Annals of the Rheumatic Diseases*. 2020;79:3-18. Available from: https://doi.org/10.1136/annrheumdis-2019-216114.

16 Price E, Rauz S, Tappuni A, Sutcliffe N, Hackett K, Barone F, et al. The British Society for Rheumatology guideline for the management of adults with primary Sjögren's Syndrome. *Rheumatology*. 2017;56(10):1828. Available from: https://doi.org/10.1093/rheumatology/kex375.

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