

Golimumab for non-radiographic axial spondyloarthritis: analysis of predicted versus actual utilisation

Drug utilisation sub-committee (DUSC)

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Abstract

Purpose

To compare the predicted and actual utilisation of golimumab for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) in the first 24 months of Pharmaceutical Benefits Scheme (PBS) listing.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Golimumab was first listed on the PBS 1 August 2010, and first listed for nr-axSpA on 1 December 2018.

Data Source / methodology

Data were extracted from the Services Australia Supplied Prescription database.

Key Findings

- There were 225 and 413 patients treated with golimumab for nr-axSpA during the first and second year of listing respectively, which was lower than predicted.
- There were 1,013 and 2,331 prescriptions dispensed for golimumab for nr-axSpA during the first and second year of listing respectively, which was lower than predicted.
- The most common age group in patients beginning golimumab treatment for nr-axSpA treatment were those aged between 30-35 years old with 54% of initiating patients being female.
- Other biologic therapies for nr-axSpA, such as certolizumab pegol and secukinumab, are gaining market share.

Purpose of analysis

To compare the predicted and actual utilisation of golimumab for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) in the first 24 months of Pharmaceutical Benefits Scheme (PBS) listing.

Background

Clinical situation

Axial spondyloarthritis (axSpA) includes types of inflammatory arthritis that primarily affect the spine and the sacroiliac joints in the pelvis. It is comprised of patients with both radiographic features (also known as ankylosing spondylitis) and non-radiographic features (nr-axSpA).¹ The Assessment of SpondyloArthritis international Society (ASAS) classification system for axSpA is based on whether patients meet clinical criteria or imaging criteria.² Patients who meet the ASAS criteria for axSpA and do not meet the modified New York criteria for radiographic sacroiliitis are considered to have non-radiographic axSpA (nr-axSpA).²

It is estimated that nr-axSpA affects around 30,000 Australians.³

Pharmacology

Golimumab is a human IgG1k monoclonal antibody produced by a murine hybridoma cell line with recombinant DNA technology.⁴ Monoclonal antibodies are proteins that recognise and bind to other specific proteins in the body. Golimumab acts by binding to a specific protein in the body called tumour necrosis factor (TNF) alpha. In people with diseases such as rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, the body produces too much TNF, which can cause the body's immune system to attack normal healthy parts of the body. Golimumab can block the damage caused by too much TNF.⁵

¹ Quinn S., Maguire S., O'shea F.B., O'Neill L., Molloy E., Fearon U. et.al. Characteristics and burden of disease in patients with radiographic versus nonradiographic axial spondyloarthritis in the ankylosing spondylitis registry of Ireland cohort. *Annals of the Rheumatic Diseases* 2021; 80:747.

² Maksymowych, W.P., Wichuk, S., Dougados, M., Jones H., Szumski A., Bukowski J.F., et al. MRI evidence of structural changes in the sacroiliac joints of patients with non-radiographic axial spondyloarthritis even in the absence of MRI inflammation. *Arthritis Res Ther* 2017;19: 126. <https://doi.org/10.1186/s13075-017-1342-9>

³ Arthritis Australia. Accessed on 17 August 2021 at: [Non-radiographic Axial Spondyloarthritis — Arthritis Australia](#)

⁴ Simponi® (golimumab). Australian Approved Product Information. Macquarie Park: Janssen-Cilag. Approved 13 November 2009, updated 8 February 2021. Available from <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-PI-03025-3&d=20210811172310101>

⁵ Simponi® (golimumab). Australian Approved Consumer Medicine Information. Macquarie Park: Janssen-Cilag. Date of preparation November 2019. Available from <https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-CMI-03026-3>

Therapeutic Goods Administration (TGA) approved indications

Golimumab is indicated for the treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence, who have had an inadequate response to, or are intolerant to, nonsteroidal anti-inflammatory drugs (NSAIDs).⁴

Golimumab is also indicated for

- Rheumatoid arthritis,
- Psoriatic arthritis,
- Ankylosing spondylitis, and
- Ulcerative colitis.

Dosage and administration

Table 1: Dosage and administration of golimumab for nr-axSpA

| Brand name and sponsor | Product | Dose and frequency of administration |
|-----------------------------------|---|--|
| Simponi® Janssen-Cilag Pty Ltd | Golimumab 50 mg/0.5 mL injection, 0.5 mL syringe Golimumab 50 mg/0.5 mL injection, 0.5 mL pen device | Golimumab 50 mg given as a subcutaneous injection once a month, on the same date each month. Available data in nr-axSpA suggest that clinical response is usually achieved within 12 to 14 weeks of treatment (after 3-4 doses). Continued therapy should be reconsidered in patients who show no evidence of therapeutic benefit within this time period. |

Source: Product Information⁴

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from [the TGA \(Product Information\)](#) and [the TGA \(Consumer Medicines Information\)](#).

PBS listing details

Table 2: PBS listing of golimumab (as at 1 July 2021)

| Item | Name, form & strength, pack size | Max. quant. | Rpts | DPMQ | Brand name and manufacturer |
|--------|---|-------------|------|------------|-----------------------------------|
| 11516D | golimumab 50 mg/0.5 mL injection, 0.5 mL syringe | 1 | 5 | \$1,160.58 | Simponi® Janssen-Cilag Pty Ltd |
| 11560K | golimumab 50 mg/0.5 mL injection, 0.5 mL syringe | 1 | 5 | \$1,160.58 | |
| 11521J | golimumab 50 mg/0.5 mL injection, 0.5 mL pen device | 1 | 5 | \$1,160.58 | |
| 11538G | golimumab 50 mg/0.5 mL injection, 0.5 mL pen device | 1 | 5 | \$1,160.58 | |

Source: the [PBS website](#). Special Pricing Arrangements apply.

Restriction

Clinical criteria:

Patient must not have received PBS-subsidised treatment with a biological medicine for this condition,

AND

Patient must have had chronic lower back pain and stiffness for 3 or more months that is relieved by exercise but not rest,

AND

Patient must have failed to achieve an adequate response following treatment with at least 2 non-steroidal anti-inflammatory drugs (NSAIDs), whilst completing an appropriate exercise program, for a total period of 3 months,

AND

Patient must have one or more of the following: (a) enthesitis (heel); (b) uveitis; (c) dactylitis; (d) psoriasis; (e) inflammatory bowel disease; or (f) positive for Human Leukocyte Antigen B27 (HLA-B27),

AND

The condition must not be radiographically evidenced on plain x-ray of Grade II bilateral sacroiliitis or Grade III or IV unilateral sacroiliitis,

AND

The condition must be non-radiographic axial spondyloarthritis, as defined by Assessment of Spondyloarthritis International Society (ASAS) criteria,

AND

The condition must be sacroiliitis with active inflammation and/or oedema on non-contrast Magnetic Resonance Imaging (MRI),

AND

The condition must have presence of Bone Marrow Oedema (BMO) depicted as a hyperintense signal on a Short Tau Inversion Recovery (STIR) image (or equivalent),

AND

The condition must have BMO depicted as a hypointense signal on a T1 weighted image (without gadolinium),

AND

The treatment must not exceed a maximum of 16 weeks with this drug under this restriction.

Population criteria:

Patient must be aged 18 years or older.

Treatment criteria:

Must be treated by a rheumatologist; OR

Must be treated by a clinical immunologist with expertise in the management of non-radiographic axial spondyloarthritis.

For details of the current PBS listing and related notes, refer to the [PBS website](#).

Date of listing on PBS

Golimumab was first listed on the PBS 1 August 2010, and first listed for nr-axSpA on 1 December 2018.

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

PBAC November 2017

Golimumab was rejected for nr-axSpA at the November 2017 PBAC meeting. The submission requested an Authority Required listing for golimumab for the treatment of nr-axSpA. The requested basis for listing was a cost-utility analysis of golimumab and background non-steroidal anti-inflammatory drugs (NSAIDs) versus conventional care (as represented by placebo plus background NSAIDs).

The submission appropriately used an epidemiological approach to estimate the financial implications of listing golimumab on the PBS for patients with nr-axSpA with objective signs of inflammation (OSI).

The evaluation considered that the accuracy of the estimates was unclear due to:

- only 18-44 year olds were considered; with no consideration of use in patients 45 years or older who may have been diagnosed aged <45 years (under-estimate). DUSC agreed with the evaluation and considered that patients 45 years or older who were diagnosed before the age of 45 should be included in the estimated patient numbers. DUSC considered that the magnitude of this was unclear but likely sizeable;
- many of the assumptions (the prevalence of axSpA (0.70%), axSpA cases diagnosed (76%), prevalence of nr-axSpA (50%), prevalence nr-axSpA cases diagnosed with complete radiographic data (88.6%)) were derived from a US study, and it was unclear whether these estimates were relevant to the Australian population;
- the assumption of the proportion of nr-axSpA patients that would be eligible for treatment may not have been accurate as the value was derived from countries where nr-axSpA is classified without formal criteria. DUSC agreed with the evaluation that the applicability of this rate to the likely Australian population was unclear;
- the submission provided no details as to how the uptake rates were derived. Further, the DUSC noted that two separate uptake rates were included and considered that this likely underestimated the number of treated patients;
- the estimates only account for 16 weeks of initial treatment which was inconsistent with the requested listing of 20 weeks (under-estimate);
- the estimated cost-offsets to the PBS in terms of nr-axSpA treatment medications are derived from an Australian cost of illness study (Tilden 2004) for AS. The publication provided no detailed information on the methodology of the study (for example, the healthcare resource-use questions included in the survey, the characteristics of the sample population and whether any eligibility criteria were applied) nor details of the specific costs included. The costs were applied based on BASFI scores and its associated regression equation within the 'responder' and 'non-responder' health states of the modelled economic evaluation to estimate costs;
- whether any costs applicable to hospitals represent a real cost-offset (may lead to under-estimate of net cost to Government); and
- there was potential for considerable use outside of the proposed PBS indication, in particular in patients with non-specific back pain without OSI.

DUSC considered the estimates presented in the submission to be underestimated. The main issues were:

- The prevalence of nr-axSpA in Australia is unknown and the use of US prevalence data introduces uncertainty to the estimates.
- The submission estimates were unnecessarily complicated, mainly due to the linkage to and from the economic evaluation provided in the submission.

- The estimates were artificially reduced through the inclusion of several unnecessary modelling steps, including applying diagnosis rates and separate prevalence rates for axSpA and nr-axSpA.

For further details refer to the [Public Summary Document](#) from the November 2017 PBAC meeting.

PBAC July 2018

Golimumab was recommended for nr-axSpA at the July 2018 PBAC meeting. The resubmission requested an Authority Required listing for golimumab for the treatment of nr-axSpA.

The requested basis for listing was a cost-utility analysis of golimumab and background non-steroidal anti-inflammatory drugs (NSAIDs) versus conventional care (as represented by placebo plus background NSAIDs).

Numerous changes were made to the financial estimates provided in the resubmission:

- increased the estimated prevalent population with nr-axSpA in Australia by 5% in acknowledgement that some patients treated with golimumab may be aged over 45 years
- estimated the eligibility of the prevalent patient pool for golimumab from the OSI population in the GO-AHEAD trial who had elevated CRP, positive evidence of sacroiliitis on MRI, one or more SPA features (other than arthritis and family history), and who were positive for the HLA-B27 gene
- removed the previous subtraction of patients from the prevalent patient pool who had progressed to AS
- based the estimated continuation rate of golimumab on estimates from the GOAHEAD trial rather than from Wang 2016
- increased the market uptake rate due to the more specific at risk population requested in the PBS listing, and removed the previous 'patients electing to receive treatment rate' based on the Sieper 2016 study
- removed the cost savings associated with changes in the use of other PBS medicines assumed in the previous submission (based on Tilden 2004)
- no longer subtracted the cost of conventional care (in regard to 'other PBS' or MBS items) from the financial estimates
- did not include any costs for inpatient hospital costs for golimumab or conventional care
- included an annual Group A GP consultation MBS fee for women
- used the reduced DPMQ of [REDACTED] and an updated weighted average co-payment to calculate revised financial estimates
- no longer specifically requested a special pricing arrangement, although in Section 1 the resubmission stated that the Sponsor proposed to work with the Department to incorporate the final negotiated price for patients with nr-axSpA into the weighted price calculation that currently exists for golimumab across the PBS listed indications.

The resubmission also underestimated the number of patients who would be eligible for treatment under the proposed restriction by assuming that all eligible patients must have the HLA-B27 gene. That is, the eligible patient population was calculated from the GO-AHEAD trial by estimating the proportion of patients in the OSI population who had elevated CRP, positive sacroiliitis on MRI, one or more SPA features (excluding family history and arthritis) and HLA-B27 gene positivity. The evaluation considered that the resubmission's approach was inappropriate, as positivity for the gene was not an absolute requirement under the proposed restriction. This reduced the proportion of OSI patients eligible for golimumab.

The resubmission stated that it anticipated that there would be patients enrolled in a patient familiarisation program and that these patients were expected to continue golimumab should it be listed on the PBS. The resubmission stated that grandfathered patients were assumed to be part of the Year 1 initiating cohort estimated through the epidemiological approach, and thus were not separately added into the number of treated patients.

Overall, the financial estimates were considered to be highly uncertain given the lack of certainty surrounding the prevalence of nr-axSpA and the likely uptake of golimumab. The ESC considered that the estimated patient numbers and prescription volumes were overestimated compared with the population intended by the PBAC in its November 2017 consideration and if a stopping rule were applied.

The ESC considered there to be a continued risk of golimumab use beyond the proposed population in patients with chronic back pain. While the proposed restriction narrowed the patient population compared to the previously proposed restriction, it may not sufficiently restrict use to the patient population likely to benefit the most.

The pre-PBAC response acknowledged that there was uncertainty in the financial estimates given the lack of reliable data to estimate the size of the patient population intended by the PBAC in its previous consideration. To address this, the pre-PBAC response proposed an RSA.

The PBAC noted that the financial estimates did not include the increased number of MRIs that would be required to determine patient eligibility for PBS subsidy (PBS eligibility).

The PBAC noted the DUSC report for ankylosing spondylitis showed an increase in the number of scripts for bDMARDs for ankylosing spondylitis, and that there may already be usage across indications.

For further details refer to the [Public Summary Document](#) from the July 2018 PBAC meeting.

Approach taken to estimate utilisation

The resubmission took an epidemiological approach to estimate utilisation. It noted that there were no studies published on the incidence or prevalence of nr-axSpA in Australia, and that the prevalence of nr-axSpA was difficult to estimate due to the multifactorial aetiology and recently established clinical definitions of the condition.

The prior submission had assumed patients would be aged 18 to 45, but the resubmission followed the advice of PBAC and allowed 5% of patients to be aged over 45 years.

Overall, the resubmission estimated there were approximately 30,000 to 35,000 nr-axSpA prevalent patients per year, and that 18.9% of these would be eligible under the PBS restriction (71.5% would be candidates for biologic therapy as they have objective signs of disease and 26.4% would have both elevated C reactive protein (CRP) and sacroiliitis on magnetic resonance imaging (MRI)).

The resubmission applied an uptake rate to the estimated eligible prevalent patients to predict the number of treated patients of 50% in year 1, increasing to 70% in years 4 to 6. The number of initiating patients was calculated by subtracting the treated patients in that year from the number of treated patients in the previous year.

Previous reviews by the DUSC

This is the first DUSC review of nr-axSpA.

Methods

Data extracted from the PBS claims database maintained by the Department of Health and processed by Services Australia were used for the analyses. Prescription data were extracted from the PBS listing of golimumab on 1 December 2018 up to and including 30 June 2021. Additional data of golimumab, secukinumab and certolizumab pegol were extracted from 1 December 2016 up to and including 30 June 2021. Data were extracted on 9 August 2021.

These data were used to determine the number of incident and prevalent patients, number of prescriptions supplied and to analyse patient demographics such as age and gender. Initiating and prevalent patients were counted by quarter of supply. An initiating patient was defined based on their first date of supply of golimumab (or secukinumab/certolizumab pegol).

The length of treatment was estimated using a Kaplan Meier method for patients who were only supplied golimumab for nr-axSpA. A patient was deemed to be continuing treatment (classified as censored in the Kaplan Meier analysis) at the end of the data period (i.e. the end of June 2021) if their last prescription was within three times the median time to resupply of this end date. Otherwise the patient was deemed to have ceased treatment with the treatment coverage end date being the supply date of their last prescription plus a median time to resupply.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Department of Human Services (DHS) Medicare date of processing data.⁶ The publicly available DHS Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included. The DHS Medicare data used in this report includes under co-payment prescriptions from 1 April 2012.

Results

Analysis of drug utilisation

Overall utilisation

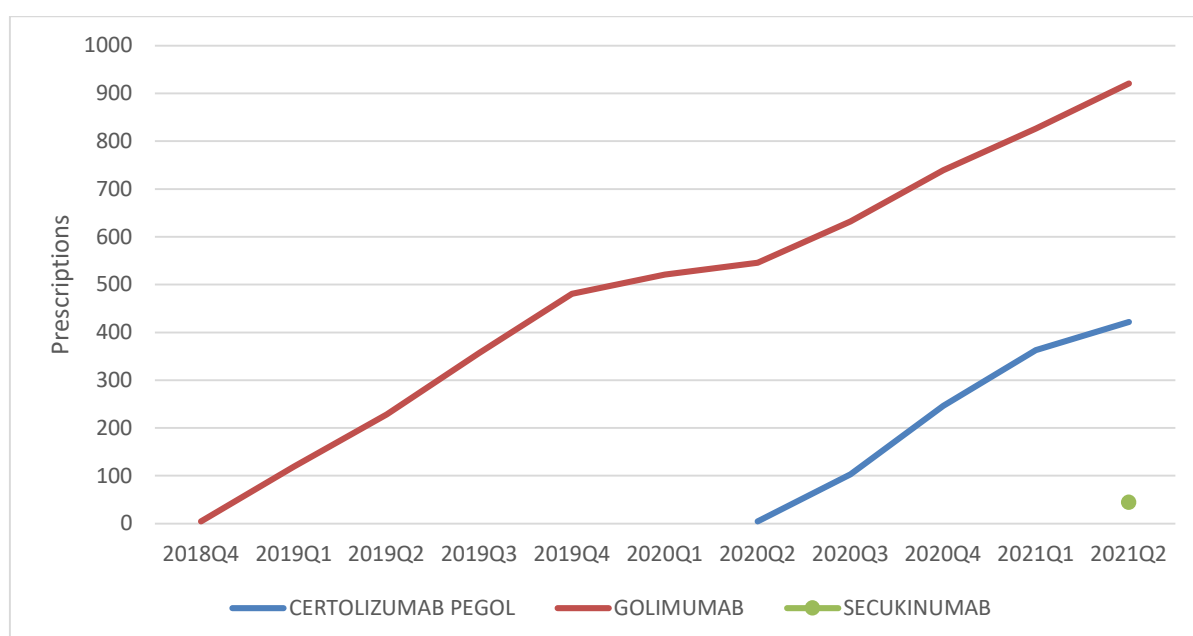


Figure 1: Prescriptions supplied for nr-axSpA medicines

Figure 1 shows the number of supplied prescriptions for golimumab for nr-axSpA, and the use of certolizumab pegol and secukinumab supplied for nr-axSpA for comparison. The number of supplied prescriptions of golimumab has increased each quarter since PBS listing, although the increases in quarters one and two of 2020 were relatively small. This may be due to the listing of certolizumab pegol in quarter two of 2020, and it is possible the beginning of the COVID-19 pandemic in Australia may have also affected utilisation.

⁶ PBS statistics. Australian Government Department of Human Services Medicare. Canberra. Available from <<http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>>.

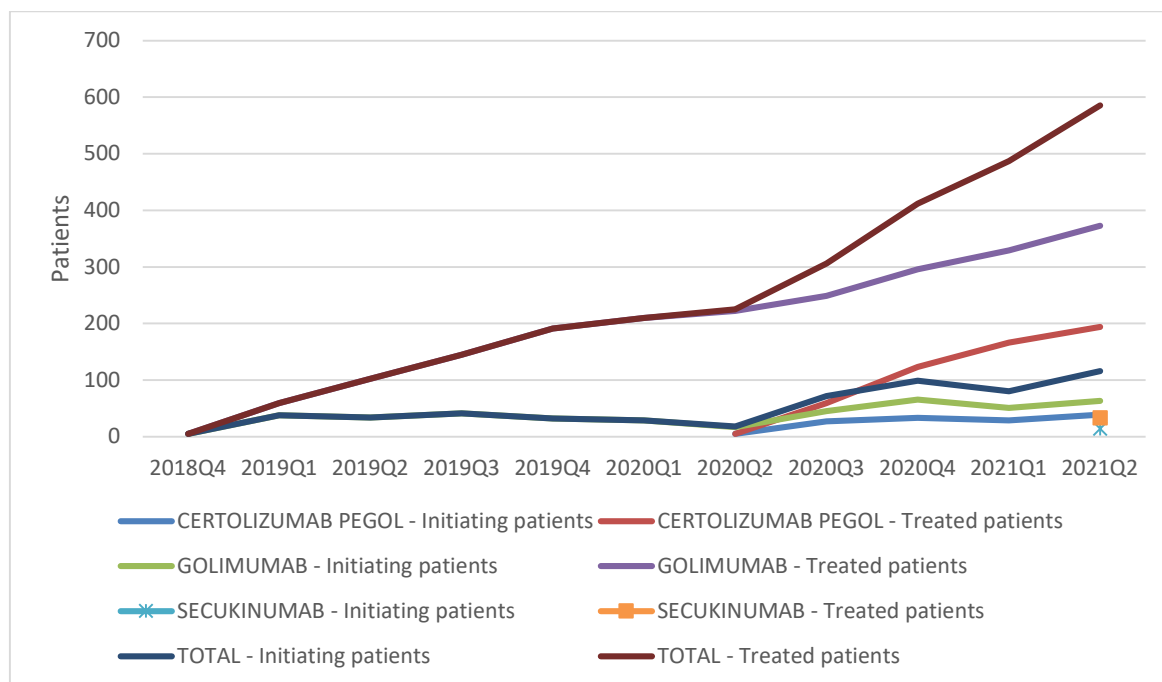


Figure 2: Initiating and treated patients supplied nr-axSpA medicines

Figure 2 shows initiating and treated patients supplied nr-axSpA medicines. Patients are counted as initiating the first time they receive a prescription for any of the three included medicines, and are only counted once. Patients may be counted more than once as treated patients. Figure 2 may suggest that the majority of patients have not switched to certolizumab pegol from golimumab, but are a new group of patients. The PBS restrictions state that the patient must not have received PBS-subsidised treatment with a biological medicine for this condition.

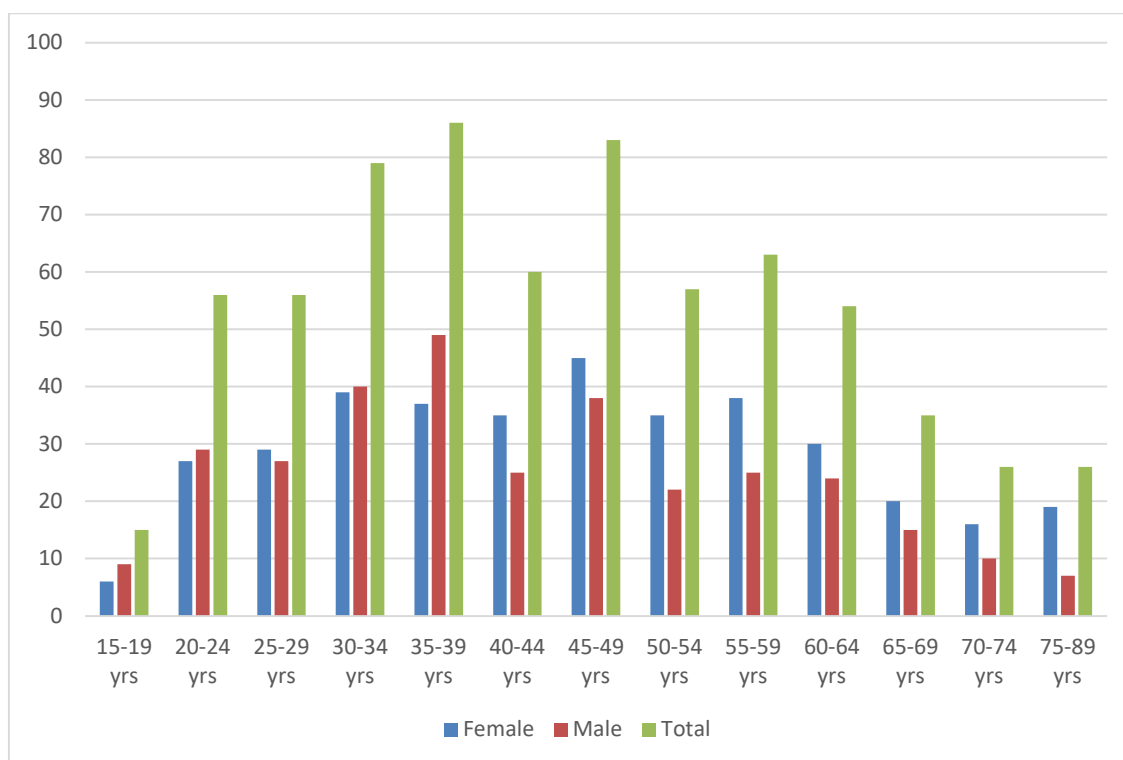


Figure 3: Age and sex of golimumab nr-axSpA patients at initiation

Figure 3 shows there were similar numbers of male and female patients who have initiated golimumab for nr-axSpA across age groups. There are fewer patients younger than 20 and older than 64, and the age groups with the highest number of initiating patients are 35-39 years, 45-49 years and 30-34 years, with 86, 83 and 79 patients respectively.

The youngest patient across all of these is 18, in line with the PBS population restriction that patients must be aged 18 years or older. However, more older patients may have initiated golimumab for nr-axSpA than was predicted by the submission.

The mean and median age of patients who received golimumab for nr-axSpA are summarised in Table 3, and the patients who received golimumab for nr-axSpA only are summarised in Table 4.

Table 3: Mean and median age of patients who received golimumab for nr-axSpA

| Patient sex | Number | Mean | Median | Youngest | Oldest |
|-------------|--------|------|--------|----------|--------|
| Female | 376 | 46.5 | 46 | 18 | 87 |
| Male | 320 | 43.2 | 40.5 | 18 | 88 |
| Total | 696 | 45.0 | 44 | 18 | 88 |

Table 4: Mean and median age of patients who received golimumab for nr-axSpA only

| Patient sex | Number | Mean | Median | Youngest | Oldest |
|-------------|--------|------|--------|----------|--------|
| Female | 211 | 40.0 | 40 | 18 | 72 |
| Male | 166 | 37.0 | 36 | 18 | 80 |
| Total | 377 | 38.7 | 37 | 18 | 80 |

Prescriber type**Table 5: Major specialty type of prescribers**

| | Initiating prescriptions | | Prescriptions | |
|---------------------------|--------------------------|-----|---------------|-----|
| Major specialty | Number | % | Number | % |
| Rheumatology | 316 | 84% | 3,299 | 85% |
| Internal Medicine | 30 | 8% | 324 | 8% |
| Immunology and Allergy | 8 | 2% | 68 | 2% |
| Palliative Medicine | 8 | 2% | 72 | 2% |
| Other (including unknown) | 15 | 4% | 129 | 3% |
| Total | 377 | | 3,892 | |

Analysis of prescriber type for the 377 patients who received golimumab for nr-axSpA only show that 84% of initiating prescriptions and 85% of overall prescriptions were prescribed by rheumatology specialists.

Indication switching

For the patients who were supplied golimumab under a PBS item code for nr-axSpA, the top 10 indication sequences, as determined from PBS item code, is below. This is including prescriptions supplied from 1 December 2016, two years prior to golimumab listing for nr-axSpA. Note that of the 696 patients supplied golimumab for nr-axSpA between December 2018 and June 2021, 583 patients are included in the top 10 indication sequences.

Table 6: Top 10 indication sequences for golimumab

| Indication sequence | Count patients |
|--|----------------|
| nr-axSpA | 377 |
| Ankylosing spondylitis>nr-axSpA>Ankylosing spondylitis | 49 |
| Rheumatoid arthritis>nr-axSpA>Rheumatoid arthritis | 45 |
| Psoriatic arthritis>nr-axSpA>Psoriatic arthritis | 34 |
| Ankylosing spondylitis>nr-axSpA | 24 |
| nr-axSpA>Ankylosing spondylitis | 14 |
| Psoriatic arthritis>nr-axSpA | 11 |
| Rheumatoid arthritis>nr-axSpA | 10 |
| nr-axSpA>Psoriatic arthritis | 10 |
| nr-axSpA>Rheumatoid arthritis | 9 |

For the patients who were supplied golimumab, certolizumab pegol or secukinumab under a PBS item code for nr-axSpA, the top 10 indication sequences, as determined from PBS item code, is below. Note that of the 960 patients supplied one of these three medicines for nr-axSpA between December 2018 and June 2021, 790 patients are included in the top 10 indication sequences.

Table 7: Top 10 indication sequences for nr-axSpA medicines

| Indication sequence | Count patients |
|--|----------------|
| nr-axSpA | 470 |
| Rheumatoid arthritis>nr-axSpA>Rheumatoid arthritis | 73 |
| Ankylosing spondylitis>nr-axSpA>Ankylosing spondylitis | 58 |
| Psoriatic arthritis>nr-axSpA>Psoriatic arthritis | 52 |
| Ankylosing spondylitis>nr-axSpA | 37 |
| Rheumatoid arthritis>nr-axSpA | 26 |
| nr-axSpA>Ankylosing spondylitis | 26 |
| Psoriatic arthritis>nr-axSpA | 17 |
| nr-axSpA>Psoriatic arthritis | 16 |
| nr-axSpA>Rheumatoid arthritis | 15 |

Overall:

- A total of 696 patients were supplied golimumab under a PBS item code for nr-axSpA. Of these 696 patients:
 - 377 were not supplied golimumab under a PBS item code for a different indication.
 - 428 were supplied golimumab for nr-axSpA before other indications.
- A total of 960 patients were supplied golimumab, certolizumab pegol or secukinumab under a PBS item code for nr-axSpA. Of these patients:
 - 470 were not been supplied any of these medicines under a PBS item code for a different indication.
 - 562 patients were supplied one of these medicines for nr-axSpA before other indications.

Medicine sequence

For the patients who were supplied golimumab, certolizumab pegol or secukinumab under a PBS item code for nr-axSpA, the top 10 medicine sequences for any indication from 1 December 2016, as determined from PBS item code, is below. Note that of the 960 patients supplied one of these three medicines for nr-axSpA between December 2018 and June 2021, 945 patients are included in the top 10 medicine sequences.

Table 8: Top 10 medicine sequences for nr-axSpA medicines for any indication

| Medicine sequence | Count patients |
|---------------------------------|----------------|
| GOLIMUMAB | 595 |
| CERTOLIZUMAB PEGOL | 207 |
| GOLIMUMAB>CERTOLIZUMAB PEGOL | 57 |
| GOLIMUMAB>SECUKINUMAB | 29 |
| SECUKINUMAB | 16 |
| CERTOLIZUMAB PEGOL>GOLIMUMAB | 11 |
| CERTOLIZUMAB PEGOL>SECUKINUMAB | 10 |
| SECUKINUMAB>CERTOLIZUMAB PEGOL | 8 |
| GOLIMUMAB>SECUKINUMAB>GOLIMUMAB | 6 |
| SECUKINUMAB>GOLIMUMAB | 6 |

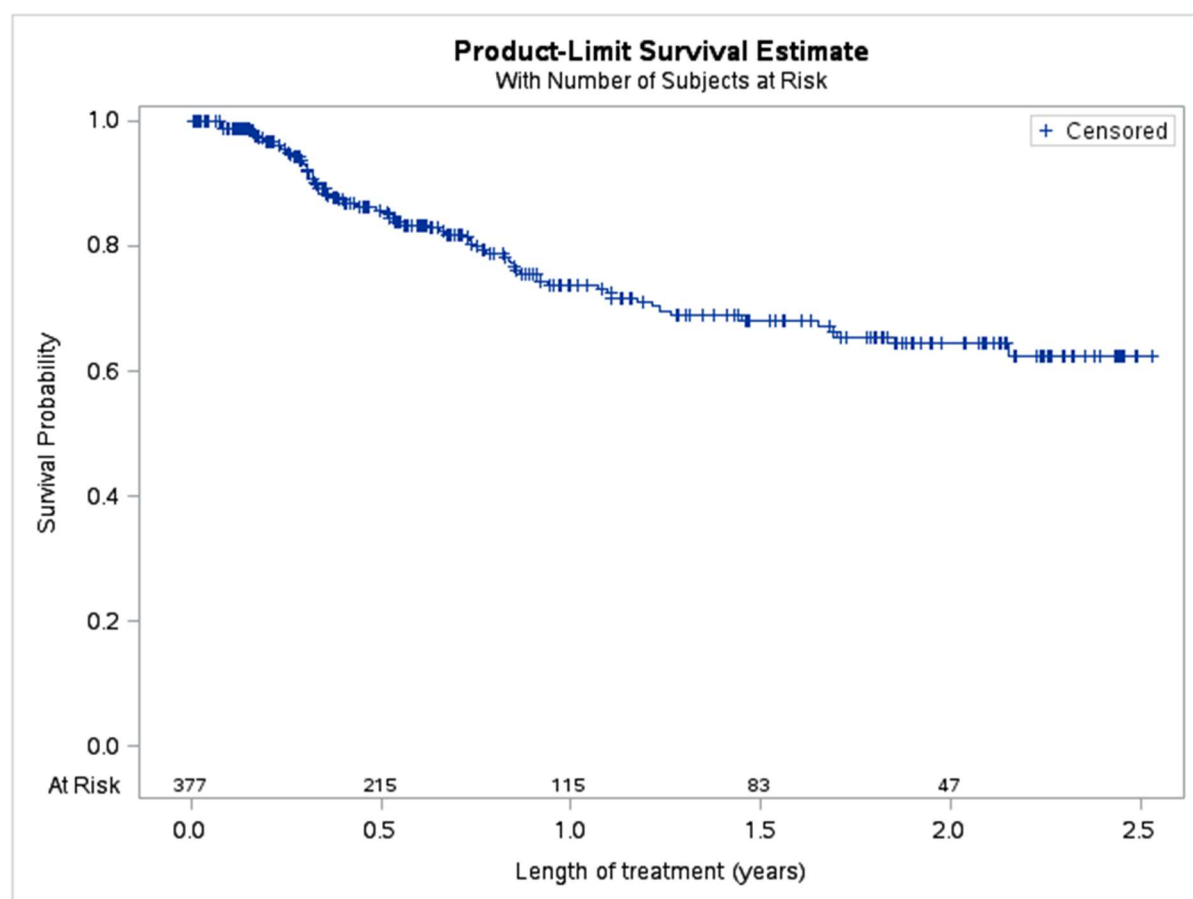
For the patients who were supplied golimumab, certolizumab pegol or secukinumab under a PBS item code for nr-axSpA, the top six medicine sequences for nr-axSpA, as determined from PBS item code, is below. Note that of the 960 patients supplied one of these three medicines for nr-axSpA between December 2018 and June 2021, 951 patients are included in the top six medicine sequences for nr-axSpA.

Table 9: Top 6 medicine sequences for nr-axSpA medicines for nr-axSpA

| Medicine sequence | Count patients |
|------------------------------|----------------|
| GOLIMUMAB | 634 |
| CERTOLIZUMAB PEGOL | 243 |
| GOLIMUMAB>CERTOLIZUMAB PEGOL | 40 |
| SECUKINUMAB | 17 |
| GOLIMUMAB>SECUKINUMAB | 10 |
| CERTOLIZUMAB PEGOL>GOLIMUMAB | 7 |

Length of treatment

Length of treatment was analysed using a Kaplan-Meier estimate for the 377 patients who were only supplied golimumab under nr-axSpA item codes.

**Figure 4: Kaplan-Meier estimates of length of treatment**

Length of treatment was analysed using a Kaplan-Meier estimate for the 377 patients who were only supplied golimumab under nr-axSpA item codes. The data were too immature to assess the treatment duration with golimumab, as the median time of therapy had not been reached. As at June 2021, the mean length of treatment was estimated to be 1.6 years with a standard error of 0.04838 years.

Analysis of actual versus predicted utilisation

Table 10: Analysis of actual versus predicted utilisation

| | | Year 1 | Year 2 | Year 3 |
|---------------------|------------|--------|--------|--------|
| Treated patients | Predicted | 2,955 | 3,306 | 3,668 |
| | Actual | 225 | 509 | 703 |
| | Difference | -92% | -85% | -81% |
| Initiating patients | Predicted | 2,955 | 351 | 362 |
| | Actual | 225 | 354 | 381 |
| | Difference | -92% | 1% | 5% |
| Prescriptions | Predicted | 27,511 | 21,824 | 22,667 |
| | Actual | 1,013 | 2,586 | 2,958 |
| | Difference | -96% | -88% | -87% |

Note: Year 3 is incomplete, December 2020 to June 2021 inclusive

Actual figures represent whole market of nr-axSpA

The submission predicted a large group of prevalent patients would be treated from Year 1, and that these patients would continue treatment in subsequent years. The number of patients who initiated in Year 1 was 92% less than predicted, and therefore the number of treated patients and the number of supplied prescriptions have been much lower than predicted.

It is unclear if the numbers were overestimated because the overall number of patients with nr-axSpA was overestimated, the number of patients who meet all the criteria was overestimated, or because the uptake was overestimated.

Discussion

New medicines such as certolizumab pegol may have gained some of the expected market of golimumab for nr-axSpA, however this use does not account for the large difference between the predicted and actual treated patients.

The submission predicted a large group of prevalent patients would be treated from year one, and calculated the initiating patients by subtracting the treated patients in that year from the number of treated patients in the previous year. Although this implies patients are continuing indefinitely, the prevalence estimate accounts for patients no longer being eligible.

Overall, the submission estimated there were approximately 30,000 to 35,000 nr-axSpA prevalent patients per year, and that 18.9% of these would be eligible under the PBS restriction. On its website, Arthritis Australia notes that around 30,000 Australians are affected by nr-axSpA. It is unclear why the predicted and actual number of treated patients were so different.

The submission originally predicted that all the patients would be aged 18-45 years old, but the resubmission allowed 5% of patients to be aged over 45 years. Figure 3 suggests more older patients may have initiated treatment than expected. It does appear from Tables 3

and 4 that, in line with the PBS restriction, prescribers are not prescribing golimumab to patients younger than 18 years old.

The analysis of prescriber type showed that 84% of initiating prescriptions and 85% of overall prescriptions were prescribed by rheumatology specialists. This appears to be in line with PBS restrictions, which state patients must be treated by a rheumatologist or by a clinical immunologist with expertise in the management of nr-axSpA. It is possible that prescribers who do not appear to fit the PBS treatment criteria may have more than one specialty.

DUSC consideration

DUSC noted the Pre-Sub-Committee Response (PSCR) provided by the sponsor, and feedback provided by Arthritis Australia (AA) and Australian Rheumatology Association (ARA).

DUSC noted the use by age and gender shows there are slightly more female than male patients, and that it appeared there had been more initiations in patients aged over 45 years than predicted. In its PSCR (p3) the sponsor noted that the analyses in the report showed that patients receiving golimumab were aligned with the restriction and demonstrate appropriate use.

DUSC noted the predicted versus actual review showed that the use of golimumab was lower than predicted. DUSC noted there were several areas of uncertainty in the estimates, and as the prevalence in Australia is unknown the US prevalence was used. DUSC noted the previous DUSC considerations suggested the accuracy of the estimates and their application to the Australian population was unclear.

The PSCR suggested several reasons for the overestimation:

- COVID-19 pandemic – the PSCR noted the growth rate of golimumab prescriptions declined when compared to those prior or after the first two quarters of 2020.
- The listing of certolizumab pegol for nr-axSpA in June 2020 – the PSCR noted it may have been appropriate to compare the predicted utilisation of golimumab to the overall nr-axSpA market.
- Awareness of disease, diagnosis and available treatment options – the PSCR noted that over time with more options and greater awareness, the actual use of these biologics including golimumab will continue to increase, closer to the predicted.
- Stringent PBS restrictions - the PSCR noted that listings are complex and restrictive and required written authorisation for initial and continuing therapy.

DUSC noted the report showed that certolizumab pegol and secukinumab had gained market share, and the overall trend of use increased when additional medicines were listed. DUSC noted from the AA response that if a patient was prescribed a biologic medicine for nr-axSpA and did not achieve a benefit, a rheumatologist would be likely to try a different biologic medicine, and that this could be contributing to the growth of the market.

DUSC noted the analysis of prescriber type showed initiation was overwhelmingly dominated (84%) by rheumatology. DUSC considered that one factor limiting use could be access to rheumatology specialists, particularly through the public system, and that once patients are referred to a specialist, they were likely triaged as routine, and could take years to be seen.

The response from AA commented that AS often takes as long as 10 years to diagnose, and that young adolescent men may mistakenly attribute their symptoms to sporting injuries, rather than seeking treatment and being diagnosed with axial spondyloarthritis early in their condition. The ARA also suggested there may be a delay in diagnosing young men, but commented this was more likely to affect those in physically challenging trades, which lead to back injuries, rather than sporting injuries. DUSC considered a similar delay may also be likely for nr-axSpA, and that part of the overestimate of use could be due to patients not being diagnosed.

DUSC commented that less severe patients may be reluctant to begin long term treatment with a biologic medicine when they do experience a benefit from anti-inflammatories, and that more severe or borderline nr-axSpA patients could be diagnosed with AS, which would give them more therapeutic options. DUSC considered these factors could also be contributing to the overestimate of use.

Overall DUSC considered the predicted patients and prescriptions may have been overestimated due to several factors, including access to specialists, understanding and awareness of the disease, and patients' reluctance to initiate biologic medicines. DUSC did not suggest changing or simplifying the PBS restriction.

DUSC actions

DUSC requested that the report be provided to the PBAC for consideration.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Janssen-Cilag Pty Ltd: The sponsor has no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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