

bDMARDs for psoriatic arthritis: utilisation analysis

Drug utilisation sub-committee (DUSC)

October 2015

Abstract

Purpose

To examine the PBS utilisation of biological disease modifying anti-rheumatic drugs (bDMARDs) for the treatment of psoriatic arthritis.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

- Adalimumab: 1 August 2006
- Etanercept: 1 August 2006
- Infliximab: 1 August 2006
- Golimumab: 1 August 2010
- Certolizumab pegol: 1 April 2015

Data Source / methodology

The Department of Human Services (DHS) Authority Approvals database was used for the majority of the analyses. The DHS prescription database and DUSC Highly Specialised Drugs database were used for prescription count and expenditure analyses.

Key Findings

- The number of patients on bDMARD treatment for psoriatic arthritis has increased from the time of listing, from about 900 in 2007 to nearly 5,000 in 2014.
- The number of new patients per year has also increased from about 570 in 2007 to about 1,000 in 2014 with no indication of stabilising.
- Adalimumab is the most commonly used bDMARD, followed by etanercept then golimumab. Infliximab has low and stable use. Certolizumab pegol was only recently listed and has yet to establish market share.
- Treatment continuation is high with 76-84% of new patients receiving a second authority approval for their initial bDMARD, and 94% receiving a second approval for any bDMARD.
- The majority of people remain on bDMARD therapy for long durations. For example, 73% of patients who began treatment in 2009 have received at least 10 authority approvals.

- Between 45% and 60% of patients who commenced bDMARD therapy prior to 2014 have received an authority for a single bDMARD, with 25-30% receiving authority approvals for one additional bDMARD, 10-15% for two additional bDMARDs, and 3-7% for three or more bDMARDs.
- Commonwealth expenditure increased by between \$5 million and \$10 million per year in for first six years of listing, and increased by \$12 million in the seventh year, and \$14 million in the eighth year of listing (to 30 September 2014). In 2014, Commonwealth expenditure on bDMARDs for psoriatic arthritis was \$86.5 million.

Background

Pharmacology

Adalimumab¹, etanercept², golimumab³, infliximab⁴ and certolizumab⁵ are biologic therapies that bind to tumour necrosis factor (TNF-alpha) or its cell surface targets and inhibit its inflammatory action.

Therapeutic Goods Administration (TGA) approved indications

Adalimumab is indicated for the signs and symptoms, as well as inhibiting the progression of structural damage, of moderate to severely active psoriatic arthritis in adult patients where the response to previous DMARDs has been inadequate.

Certolizumab pegol is for indicated the treatment of adult patients with active psoriatic arthritis where response to previous DMARDs has been inadequate.

Etanercept is indicated for the signs and symptoms of active and progressive psoriatic arthritis in adults, where response to previous DMARDs has been inadequate.

Golimumab is indicated for use, alone or in combination with methotrexate, for treatment of active and progressive psoriatic arthritis in adult patients where the previous response to DMARDs has been inadequate.

Infliximab is indicated for the treatment of the signs and symptoms, as well as improvement in physical function in adult patients, of active and progressive psoriatic arthritis who have not responded adequately to DMARDs.

¹ Adalimumab (Humira®), Australian Approved Product Information. Sydney: AbbVie Pty Ltd. Approved 10 December 2003, updated 14 May 2015. Available from <<https://www.ebs.tga.gov.au/>>.

² Certolizumab pegol (Cimzia®), Australian Approved Product Information. Melbourne: UCB Australia Pty Ltd. Approved 20 January 2010, updated 24 February 2015. Available <<https://www.ebs.tga.gov.au/>>

³ Etanercept (Enbrel®), Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 8 September 2000, updated 17 April 2015. Available from <<https://www.ebs.tga.gov.au/>>

⁴ Golimumab (Simponi®), Australian Approved Product Information. Sydney: Janssen-Cilag Pty Ltd. Approved 13 November 2009, updated 7 July 2014. Available from <<https://www.ebs.tga.gov.au/>>

⁵ Infliximab (Remicade®), Australian Approved Product Information. Sydney: Janssen-Cilag Pty Ltd. Approved 2 August 2000, updated 11 February 2015. Available from <<https://www.ebs.tga.gov.au/>>

All of the drugs are also indicated for the treatment of other inflammatory conditions.

Dosage and administration

Table 1: Dose and administration of bDMARDs for Psoriatic Arthritis⁶

Drug, brand name and sponsor	Dose and frequency of administration
Adalimumab Humira®, AbbVie Pty Ltd	40mg solution in pre-filled syringe or cartridge for once-fortnightly subcutaneous administration.
Certolizumab pegol Cimzia®, UCB Australia Pty Ltd	200mg/mL solution in pre-filled syringe for fortnightly subcutaneous administration Loading dose of 400mg (2 subcutaneous injections) at weeks 0, 2 and 4.
Etanercept Enbrel®, Pfizer Australia Pty Ltd	25mg solution in pre-filled syringe for twice-weekly subcutaneous administration 50mg solution for injection, as pre-filled syringe or cartridge for auto-injector for once-weekly subcutaneous administration.
Golimumab Simponi®, Janssen-Cilag Pty Ltd	50mg solution for injection, as pre-filled syringe or injection pen for once-monthly subcutaneous administration.
Infliximab Remicade®, Janssen-Cilag Pty Ltd	5mg/kg given as IV infusion followed by 5mg/kg doses at 2 and 6 weeks after initiation, then every 8 weeks after.

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 (as at 26 August 2015)

The PBS listing details of bDMARDs for severe psoriatic arthritis are presented in Table 2. Infliximab, administered as an infusion, has a Section 100 Highly Specialised Drugs Program listing. All others have General Schedule listings. All five medicines require written Authority Approval by the Department of Human Services (DHS) Medicare prior to prescribing.

⁶ Source: adalimumab (Humira®) Product Information, accessed 2 July 2015; certilzumab pegol (Cimzia®) Product Information, Accessed 2 July 2015; etanercept (Enbrel®) Product Information, accessed 2 July 2015; golimumab (Simponi®) Product Information, accessed 2 July 2015; infliximab (Remicade®) Product Information, accessed 2 July 2015.

Table 2: PBS listing of bDMARDs for psoriatic arthritis (as at 1 August 2015)**

Name	Item Codes	Forms and strengths	Qty and Rpts	DPMQ	Brand name and manufacturer
ADALIMUMAB	Initial: 9033K; 9101B; Continuing: 9034L; 9102C;	40mg/0.8mL injection, 2x 0.8mL Available as syringe or cartridge	Max Qty: 1 Repeats: Initial: 3 Cont: 5	\$1,763.56	Humira® AbbVie Pty Ltd
CERTOLIZUMAB PEGOL	10238W*	200mg/mL injection, 2x 1mL syringes	Max Qty: 2 Repeats: 5	\$1,698.16	Cimzia® UCB Australia Pty Ltd
ETANERCEPT	Initial: 9035M; 9087G; 9457R Continuing: 9036N; 9088H; 9458T	25mg injection (4x 25mg vials) & inert substance diluent (4x 1mL syringes) 50mg injection (4x 25mg vials) & inert substance diluent (4x 1mL syringes) 50mg injection in 1mL single use auto-injector	Max Qty: 25mg: 2 50mg: 1 Repeats: Initial: 3 Cont: 5	\$1,763.56	Enbrel® Pfizer Australia Pty Ltd
GOLIMUMAB	Initial: 3430M; 3431N Continuing: 3432P; 3433Q	50mg/0.5mL injection, 1x 0.5mL syringe	Max Qty: 2 Repeats: Initial: 3 Cont: 5	\$1,766.48	Simponi® Janssen-Cilag Pty Ltd
INFLIXIMAB	S100 Public: 5756Y S100 Private: 6496X	100mg injection, 1x 100mg vial	Max Qty: 1 Repeats: 0	Public: \$751.70 Private: \$788.70	Remicade® Janssen-Cilag Pty Ltd

Source: the [PBS website](#). * = special pricing arrangement is in place.

** DPMQ incorporates the new Administration, Handling and Infrastructure fee.

Restriction (abridged)

Restrictions for initiating treatment:

There are two initial restrictions for patients commencing therapy on biological medicines for psoriatic arthritis: Initial 1, for patients new to therapy or commencing a new treatment cycle; and Initial 2, for patients switching therapy within a treatment cycle.

A treatment cycle is the period where patients have either failed or ceased to sustain a response to three PBS subsidised bDMARDs, and must have, at minimum, a 5 year break in PBS-subsidised biological therapy. Patients who complete a treatment cycle and wait the requisite timeframe are considered to be initiating (Initial 1) patients if they recommence therapy. Both types of initial restriction are shared under single PBS item numbers for each medicine.

For patients initiating therapy for all drugs listed in Table 1 under the Initial 1 restriction, patients must have severe active psoriatic arthritis and meet the following criteria:

- Treatment is to be initiated by a rheumatologist or clinical immunologist with expertise in the management of psoriatic arthritis;
- Patients must have failed to achieve an adequate response to methotrexate at a dose of at least 20mg weekly for a minimum period of 3 months and failed to achieve an adequate response from either >2g per day sulfasalazine or up to 20mg of leflunomide per day for a minimum period of 3 months.
- Patients must have an Erythrocyte sedimentation rate (ESR) of >25mm/hr or a C-reactive protein (CRP) level of >15mg/L; and either
- An active joint count of at least 20 active (swollen and tender) joints; or
- At least 4 active joints from the following major joints: elbow, wrist, knee and/or ankle, and shoulder or hip.

Consideration may be given if elevated ESR or CRP thresholds cannot be met, by means of written application.

For patients commencing therapy under the Initial 2 restriction, patients must have a documented history of severe active psoriatic arthritis, must not have failed or not responded to treatment with 3 bDMARDs within the treatment cycle, and have not already failed or ceased to respond to treatment with that bDMARD during the treatment cycle.

Under the initial authority approval codes, patients are able to access a maximum of 16 weeks treatment for adalimumab, etanercept and golimumab, 18-20 weeks for certolizumab pegol (depending on dosage regimen), and up to 22 weeks treatment with infliximab under this restriction. Certolizumab pegol also has grandfathering provisions, with patients on non-subsidised treatment able to access up to 24 weeks of PBS-subsidised therapy.

Restrictions for continuing treatment:

To be eligible for ongoing treatment for all therapies, patients are required to demonstrate an adequate response to treatment defined as:

- An ESR of ≤ 25 mm/hr or CRP of ≤ 15 mg/L; or
- A minimum reduction of 20% of ESR or CRP from baseline levels and either;
- A reduction in total active joint count by $\geq 50\%$ from baseline (where the baseline is at least 20 active joints); or
- A reduction in the number of swollen major joints (from at least 4) by at least 50%.

Continuing treatment authority approvals provide up to 24 weeks of treatment.

For an example of a full restriction text for listings, refer to the [initial treatment item for adalimumab](#) and the [continuing treatment item for adalimumab](#).

For details of the current PBS listings refer to the [PBS website](#).

Date of listing on PBS for psoriatic arthritis

- Adalimumab: 1 August 2006
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- Golimumab: 1 August 2010
- Certolizumab pegol: 1 April 2015

Changes to listing

On 1 July 2008, the psoriatic arthritis bDMARD restrictions were amended to permit failure to achieve a response to leflunomide as an alternative to sulfasalazine.

There have been a number of minor restriction text changes as new medicines have become available, and the listing of new presentations such as auto-injectors.

The grandfathering restrictions for adalimumab, etanercept and infliximab were removed on 31 July 2010.

Current PBS listing details are available from the [PBS website](#).

Clinical Guidelines

The Australian Rheumatology Association's (ARA) published recommendations for the use of biologics for the treatment of psoriatic arthritis recommend clinicians consider a number of factors when determining appropriate treatment regimens. The ARA acknowledges that its recommended indications and criteria differ from the current eligibility for PBS-subsidised bDMARDs. The most recent advice on the use of bDMARDs differs in the following key ways from the PBS restrictions⁷:

- Consideration of each component of the disease and patient quality of life outcomes, and not simply rely on the number of swollen joints;
- TNF inhibitor therapy should be considered in patients with a history of psoriasis, an inadequate response to NSAIDs and/or steroid injections, with at least 5 or more swollen and 5 or more tender or painful joints / entheses / dactylitis sites in the setting of psoriatic spondyloarthropathy, after failing an adequate trial of methotrexate and /or leflunomide therapy. Sulfasalazine has a weak DMARD role in PsA; and
- ESR and/or CRP measurements are often in normal ranges in active severe cases of psoriatic arthritis.

⁷ Australian Rheumatology Association (2011), Updated Recommendations for the Use of Biological Agents for the Treatment of Rheumatic Diseases. Available at: https://rheumatology.org.au/downloads/FINAL-BiologicalRecommendations060111_000.pdf Accessed July 6 2015.

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

Etanercept: Was recommended at the March 2005 PBAC meeting for psoriatic arthritis on the basis of acceptable cost-effectiveness if the same indices of disease severity that applied to the current listing in rheumatoid arthritis apply in psoriatic arthritis. In [July 2008](#), PBAC rejected a submission to reduce the swollen joint threshold from 20 to 10 and halve the ESR and CRP thresholds on the basis of uncertain clinical effectiveness and uncertain and high cost-effectiveness.

Infliximab: In [March 2006](#), PBAC recommended the listing of infliximab for use in psoriatic arthritis on a cost-minimisation basis concluding that the indirect comparison showed that infliximab is no worse than etanercept in terms of effectiveness and safety when used for the treatment of psoriatic arthritis.

Adalimumab: First considered at the [March 2006](#) meeting for psoriatic arthritis, and recommended on a cost-minimisation basis with the PBAC concluding that the indirect comparison showed that adalimumab is no worse than etanercept in terms of effectiveness and safety when used for the treatment of psoriatic arthritis.

Golimumab: The PBAC recommended listing of golimumab for psoriatic arthritis at the [March 2010](#) meeting, on a cost-minimisation basis with adalimumab and etanercept.

Certolizumab pegol: The PBAC recommended certolizumab pegol for psoriatic arthritis at the [November 2014](#) meeting on a cost-minimisation basis with adalimumab.

At the July 2014 meeting, the PBAC deferred a decision on whether to recommend relaxing authority restrictions for continuing patients to streamlined authority, pending the outcomes of a post-market review into PBS Authorities.

Previous reviews by the DUSC

The DUSC reviewed the utilisation of bDMARDS for psoriatic arthritis at the February 2009 meeting. The review found that initial approvals for adalimumab had exceeded those for etanercept after the first a few months of listing. Infliximab had consistently taken a smaller market share for this indication for the entire period of listing. First time continuations were found to be in the range of 71-75%.

Methods

The DHS Authority Approvals database was used to determine the number of patients, proportion of patients continuing treatment after their initial course of therapy, and the sequence of bDMARD use. Patients were counted as receiving treatment in a particular year if they received an authority approval that year. It is assumed patients will receive at least one approval a year as no more than 24 weeks of treatment is approved for psoriatic arthritis at a time. This may result in a small overestimate because some patients who receive an authority may not have the medicine dispensed.

The DHS prescription database was used for the number of dispensed prescriptions and expenditure for adalimumab, etanercept and golimumab. The Highly Specialised Drugs Database was used for quantity supplied and expenditure data for infliximab. As certolizumab pegol was listed on the PBS on 1 April 2015, no prescription data were available, and only limited authority data were available.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Department of Human Services (DHS) PBS date of processing data.⁸

Results

Analysis of drug utilisation

Number of Prescriptions

Figure 1 provides the total number of prescriptions dispensed for the four bDMARDs listed on the PBS for psoriatic arthritis available before 31 March 2015.

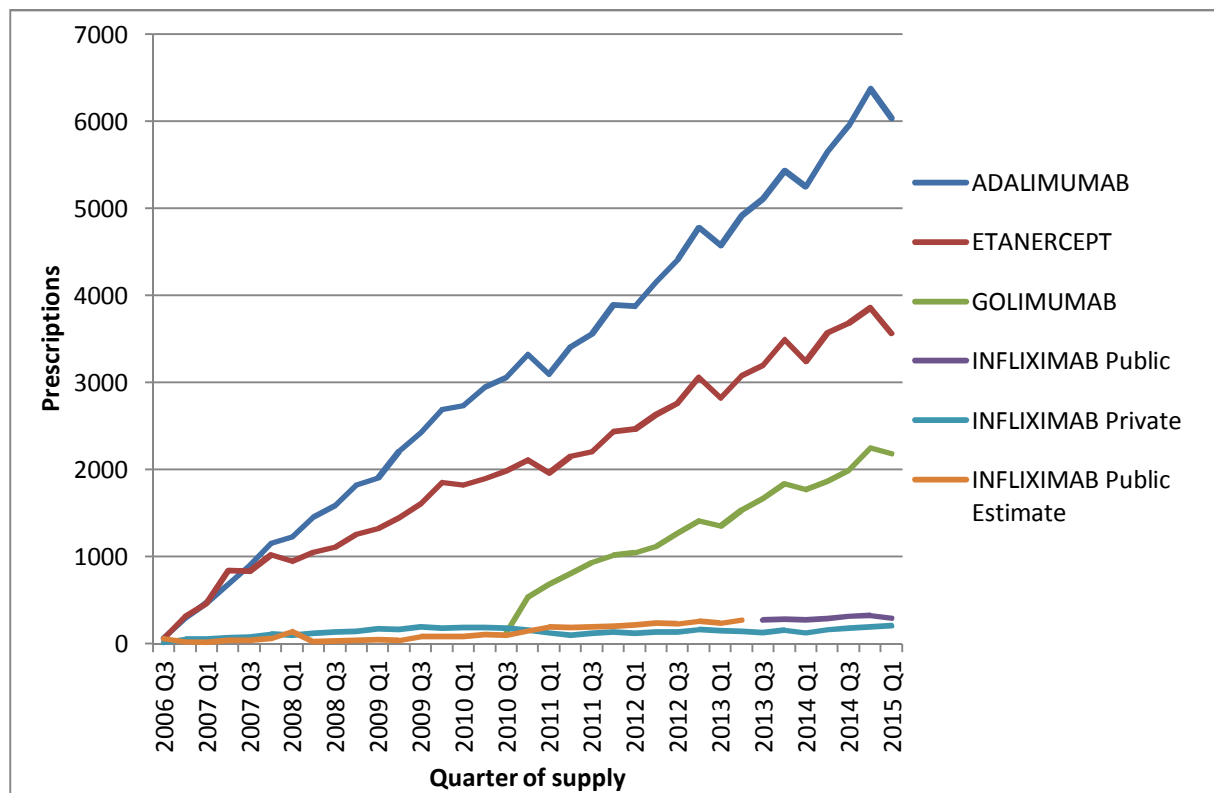


Figure 1 – bDMARD prescriptions for psoriatic arthritis, 2006-2015⁹

Source: DUSC database; infliximab data from DUSC HSD database, extracted July 2015

⁸ PBS statistics. Australian Government Department of Human Services Medicare. Canberra. Available from <<http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>>.

⁹ As prescription data for public hospital use of infliximab were only available from 1 September 2013, an estimate of infliximab prescriptions from public hospitals before this date has been provided, as per the methods described in Appendix A.

Figure 1 shows a broadly linear increase in the number of prescriptions for adalimumab, etanercept and golimumab. The number of prescriptions per quarter continues to rise and shows no sign of stabilising.

Number of patients

Figure 2 provides the number of new and prevalent patients receiving bDMARD treatment for psoriatic arthritis per calendar year since listing on 1 August 2006.

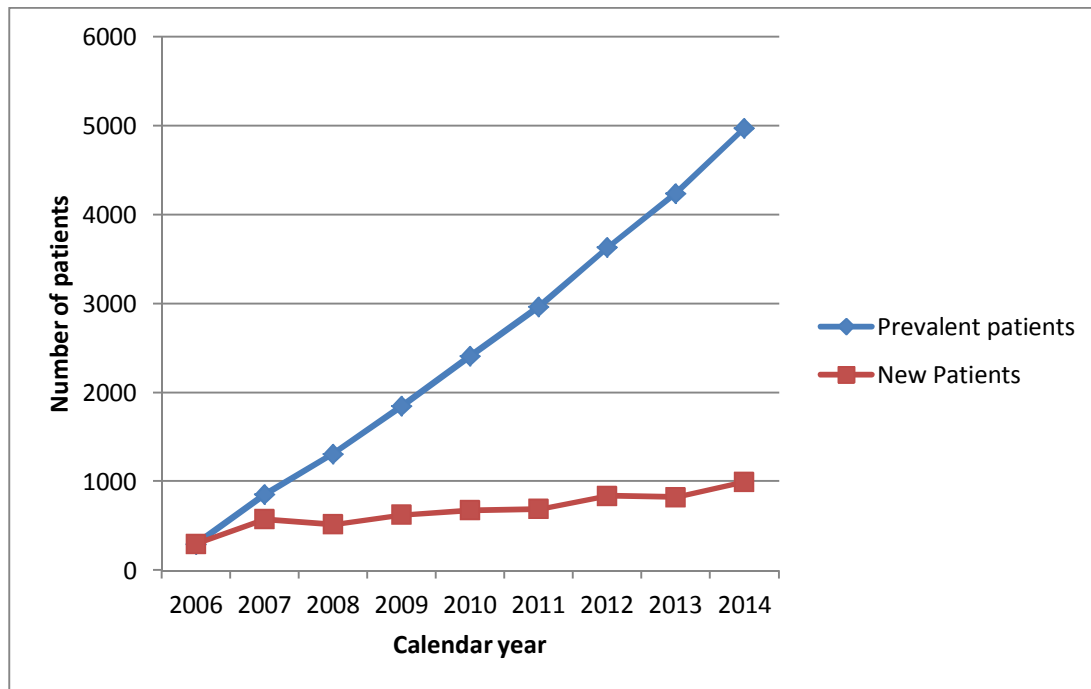


Figure 2 – New and prevalent patients receiving bDMARD treatment by year, 2006-2014

Source: DHS Authorities Database, extracted July 2015

Figure 2 shows an increasing number of prevalent patients receiving bDMARD therapy, with no sign of stabilising. The number of new patients has also increased steadily over the nine years since listing of the first bDMARD.

Figure 3 provides the number of patients initiating bDMARD treatment by initiating drug and calendar year. This captures only the first time a patient commenced bDMARD therapy.

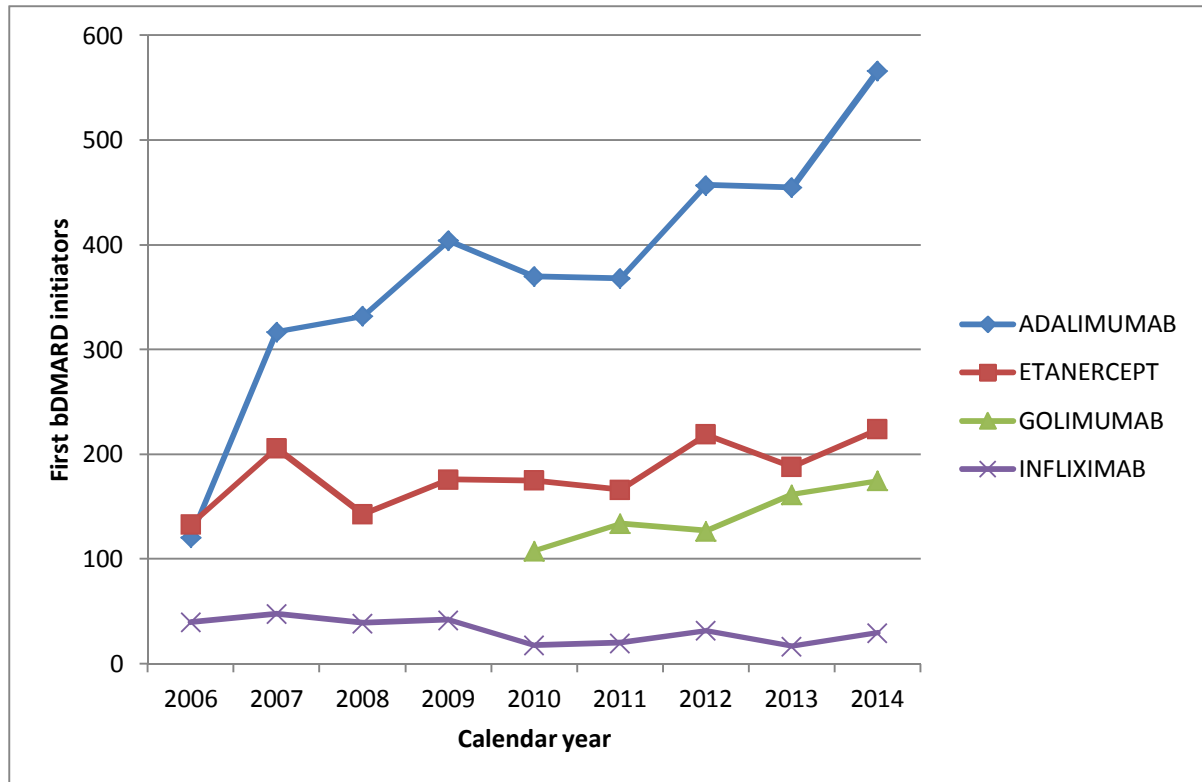


Figure 3 – bDMARD-naive initiations for psoriatic arthritis by drug and calendar year, 2006-2014

Source: DHS Authority Approvals Database, extracted July 2015

The majority of people commencing a bDMARD for psoriatic arthritis for the first time are prescribed adalimumab. Infliximab, which requires infusion, is used as the first bDMARD in only a small number of patients.

Figure 4 shows the number of patients with a first approval for a bDMARD. As patients are able to initiate more than one bDMARD in any year, the total number of patients is higher than the number of patients on bDMARD therapy in a given year.

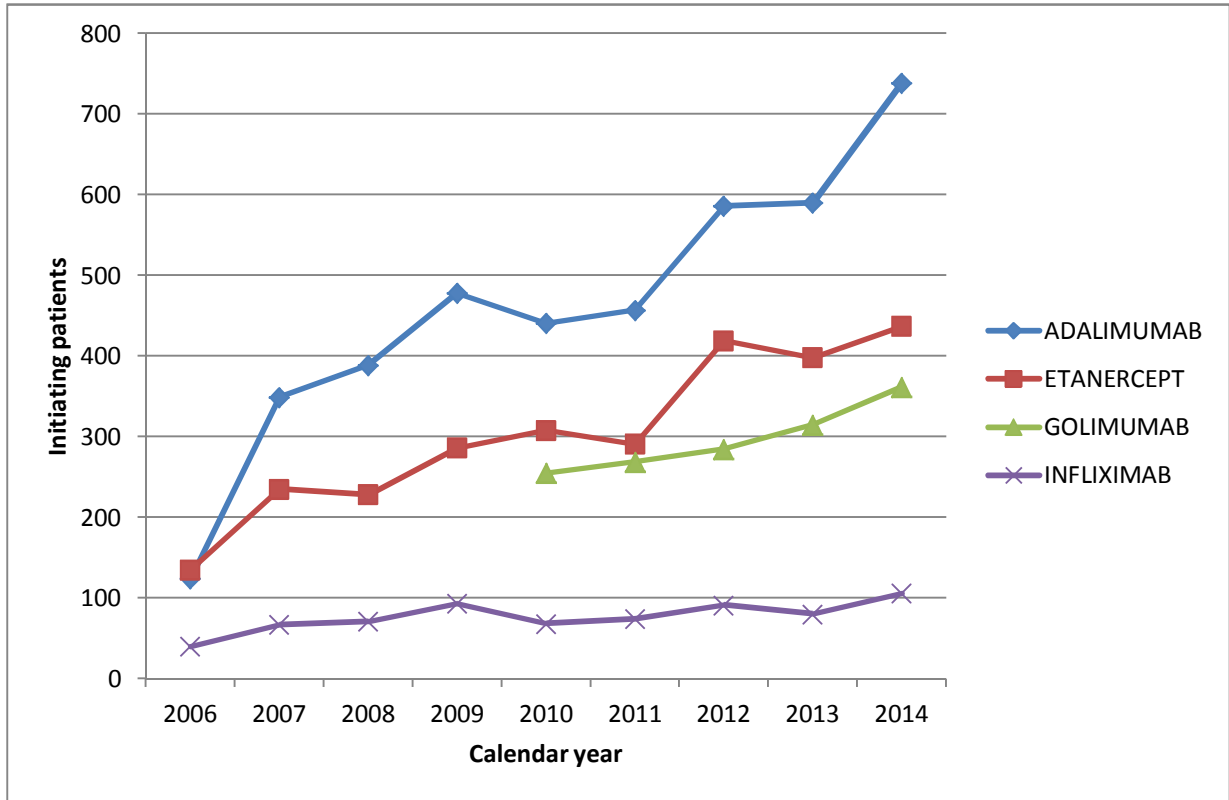


Figure 4 – Number of patients initiating each bDMARD, 2006-2014

Source: DHS Authority Approvals Database, extracted July 2015

The number of patients starting a new bDMARD (which includes patients switching drugs) has increased since listing on 1 August 2006. The patterns of initiations to each drug (Figure 4) do not differ much from the patterns in patients new to bDMARD therapy (Figure 3) because many patients remain on the first bDMARD for a long period of time. Further information on duration is provided later in this report. In 2014, the difference between first time initiating patients and total initiating patients was about 200 each for adalimumab, etanercept and golimumab, and about 50 for infliximab.

Continuation

Figure 5 presents the proportion of bDMARD naïve patients who started treatment in 2012 by the number of approvals received. The 2012 calendar year cohort is presented to balance recent practice with an adequate period of follow-up data. A first authority approval generally provides sufficient therapy for 16 weeks (adalimumab, etanercept, golimumab) or 22 weeks (infliximab). Continuing authority approvals generally provide 24 weeks of treatment.

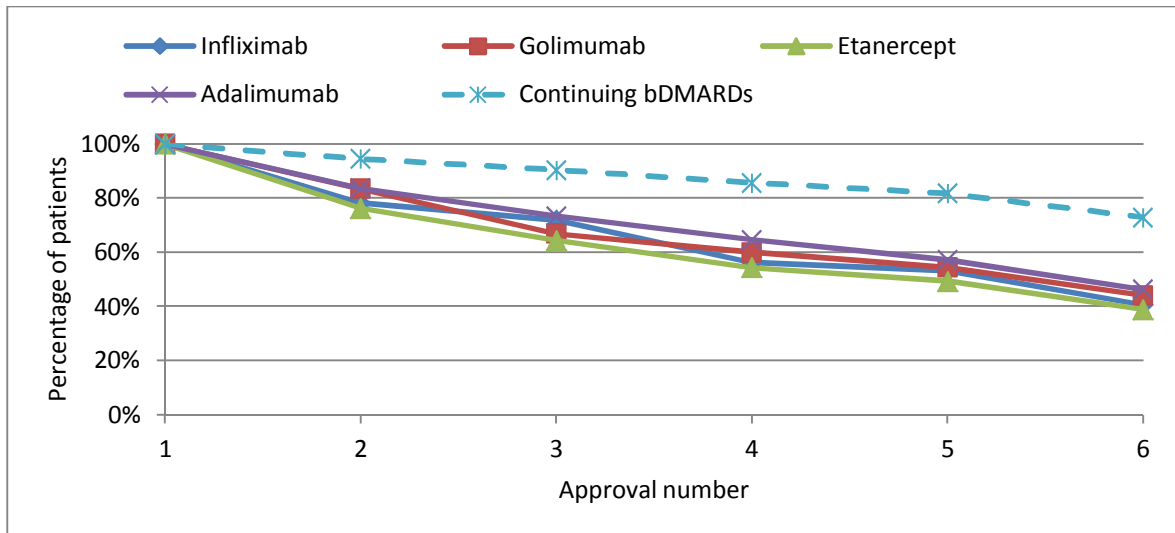


Figure 5: Continuation of bDMARDs for psoriatic arthritis – 2012 new patients (n=836)

Source: DHS Authority Approvals database, extracted July 2015

Note: Analysis cut at sixth Authority approval. Patients receiving their first approval late in 2012 may not have sufficient time to receive a seventh approval by the end of the data period. Median time to the sixth approval was 116 weeks.

The rates of continuation are broadly similar across the four medicines with between 76% and 84% of patients receiving a second authority approval for their first prescribed bDMARD; and 39-46% receiving at least six authority approvals. Continuation with any bDMARD therapy is substantially higher than continuation with any individual medicine, with 94% of patients starting bDMARD therapy receiving a second authority approval for any drug and 73% with at least 6 authority approvals. This is consistent across the years with >90% of patients who start treatment between 2010 and 2014 receiving a continuing authority approval (data not shown).

To consider continuation on treatment over a longer time period, Figure 6 presents the rate of continuation with bDMARD treatment for an earlier cohort of patients who started treatment in 2009. At the time of data extract, these patients had sufficient time to receive their tenth authority approval.

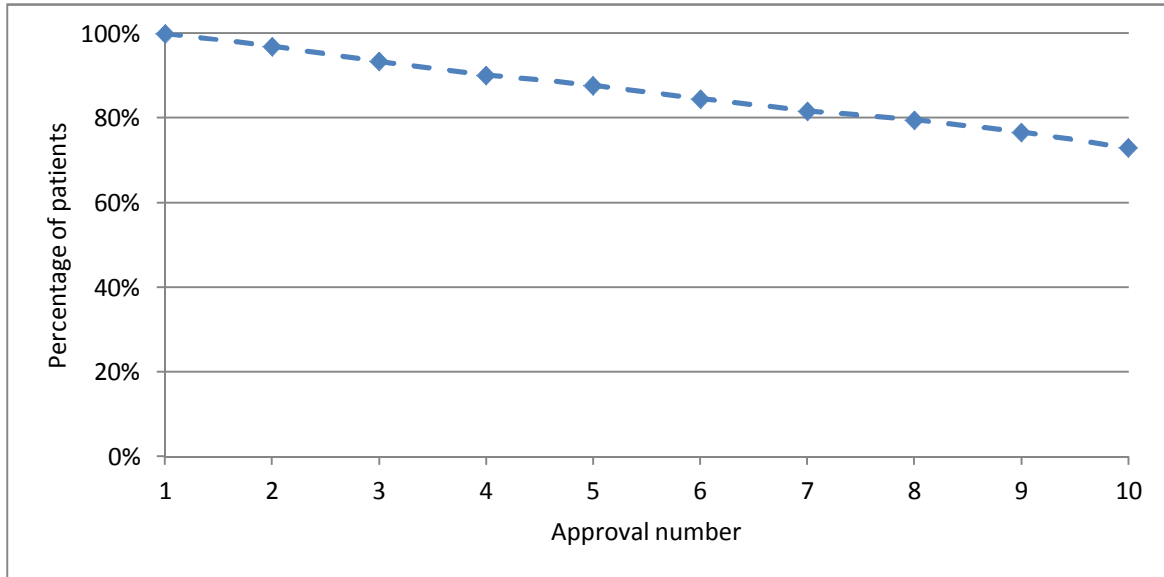


Figure 6: Continuation of bDMARDs of psoriatic arthritis – 2009 patients (n=622)

Source: DHS Authority Approvals database, extracted July 2015

Note: Median time to the tenth approval was 218 weeks.

The majority of patients (73%) who started their first bDMARD for psoriatic arthritis in 2009 received a tenth bDMARD authority approval.

bDMARD utilisation patterns

Table 3 presents patterns of bDMARD use and switching based on patients who received authorities for one or more bDMARDs. The analysis counts patients who received their first bDMARD approval before 1 January 2014, meaning patients had a minimum of 18 months to have received an authority for additional bDMARDs. The data includes subsequent authorities for this cohort up to 30 June 2015. As such, certolizumab pegol approvals for this cohort have been included since its listing on 1 April 2015. As the number of patients continues to grow, substantially more patients have had shorter treatment durations, reducing their likelihood of having switched to other bDMARDs. As such, this analysis is only indicative of patterns of bDMARD use.

Table 3: bDMARD sequence for psoriatic arthritis

Adalimumab initiators	Patients (%)	Etanercept initiators	Patients (%)	Infliximab initiators	Patients (%)	Golimumab initiators	Patients (%)
ADA only	1623 (57%)	ETN only	762 (54%)	INF only	119 (46%)	GOL only	299 (56%)
ADA -> ETN	480 (17%)	ETN -> ADA	333 (24%)	INF -> ADA	45 (18%)	GOL -> ADA	91 (17%)
ADA -> INF	73 (3%)	ETN -> INF	26 (2%)	INF -> ETN	17 (7%)	GOL -> ETN	67 (13%)
ADA -> GOL	187 (7%)	ETN -> GOL	81 (6%)	INF -> GOL	19 (7%)	GOL -> INF	< 5 (1%)
ADA -> CZP	< 5(0%)	ETN -> 2 bDMARDs	158 (11%)	INF -> CZP	<5 (0%)	GOL -> 2 bDMARDs	56 (11%)
ADA -> 2 bDMARDs	368 (13%)	ETN -> 3 or more bDMARD	43 (3%)	INF -> 2 more bDMARD	38 (15%)	GOL -> 3 or more bDMARDs	14 (3%)
ADA -> 3 or more bDMARDs	96 (3%)	-	-	INF -> 3 or more bDMARD	17 (7%)	-	-
Total	2829	Total	1403	Total	256	Total	531

Source: DHS Authority Approvals database, extracted July 2015

ADA = adalimumab, ETN = etanercept, INF = infliximab, GOL = golimumab CZP = certolizumab pegol.

The majority of patients continue treatment with their first bDMARD. Infliximab has a slightly smaller proportion of bDMARD naïve patients continuing treatment. Between 25% and 30% of patients have at some stage received an authority for a second bDMARD, usually adalimumab or etanercept. Between 10% and 15% have received an authority for a third bDMARD. A very small proportion of patients have received authorities for four or five bDMARDs.

Use of certolizumab pegol between 1 April 2015 and 30 June 2015 was low and the use so far has been in patients who have received prior bDMARD therapy.

Analysis of expenditure

The following table presents the total benefits paid for bDMARDs used for psoriatic arthritis per calendar year over between 2006 and 2014.

Table 11: bDMARD expenditure for psoriatic arthritis

Listing years	2006 ^a	2007	2008	2009	2010	2011	2012	2013	2014	2015 ^b
Adalimumab	\$620,202	\$5,515,582	\$10,523,249	\$16,140,923	\$21,093,665	\$24,406,808	\$30,122,916	\$35,050,823	\$40,605,775	\$10,543,785
Etanercept	\$664,429	\$5,073,081	\$7,609,278	\$10,954,658	\$13,706,972	\$15,384,057	\$19,133,032	\$22,085,705	\$25,183,507	\$6,243,871
Golimumab					\$1,156,369	\$6,016,532	\$8,493,423	\$11,218,781	\$13,809,353	\$3,819,898
Infliximab	\$622,279	\$1,725,977	\$2,579,847	\$3,479,691	\$4,149,234	\$4,597,757	\$5,453,060	\$5,992,971	\$6,908,805	\$1,884,020
Psoriatic arthritis total	\$1,564,749	\$11,744,529	\$19,884,908	\$29,679,876	\$38,522,146	\$47,528,243	\$59,720,052	\$72,449,723	\$86,507,440	\$22,491,573

Source: DUSC database; infliximab data from DUSC HSD database, extracted July 2015

^a This data is for part of the year. The first bDMARD for psoriatic arthritis was listed on 1 August 2006

^b Data complete to 31 March 2015

Total expenditure on bDMARDs for psoriatic arthritis has increased substantially from \$11,744,529 in 2007, the first full year of listing, to over \$86 million in 2014.

Discussion

The number of new patients initiating bDMARD therapy for psoriatic arthritis has increased steadily from approximately 550 in 2007 to almost 1,000 in 2014, and shows no sign of stabilising. As the majority of patients remain on therapy for many years, there has also been a steady increase in the total number of patients treated with bDMARDs. In 2007 approximately 1,000 patients received bDMARD therapy, and this number has increased to nearly 5,000 in 2014. The increasing incident treated population could reflect increasing familiarity with therapies, an increase in the incidence of severe psoriatic arthritis, or use in patients with less severe disease, particularly given differences between treatment guidelines and PBS criteria.

The majority (76-84%) of patients who start a bDMARD receive a second authority approval for the same bDMARD, and 94% of patients receive a second authority approval for any bDMARD. Continuation rates in practice are generally higher than in the clinical trials used as the basis for PBS listing. The key trials (such as IMPACT I and II, ADEPT, MO2-518, MO2-570, GO-REVEAL) indicated response rates of between 36 - 77% based on ACR20 and ACR50 responses at 12 to 24 weeks. The PBS criteria most closely align with ACR50. Higher than expected continuation rates in practice have been observed for bDMARDs used in other indications including [rheumatoid arthritis](#) and [psoriasis](#). The DUSC has previously considered that there may be a clinician or patient reluctance to withdraw a treatment where patients are achieving a partial response.

More than half of patients initiating bDMARD therapy between 2006 and 2013 have remained on their first bDMARD thus far. For patients who switch to another therapy, the most common switches are between adalimumab and etanercept. The number of patients moving to additional bDMARDs may increase in the future as there may be a loss of response to bDMARDs over time.

DUSC consideration

DUSC considered that the understanding of clinical manifestations of psoriatic arthritis has evolved since bDMARDs were first made available through the PBS in 2006. The PBAC restrictions only take into account peripheral joint involvement and not other manifestations such as enthesitis, dactylitis and axial involvement. DUSC also noted that the Australasian Rheumatology Association's recommendations for use of bDMARDs in psoriatic arthritis differ from the PBS restrictions and that this may affect use of these medicines in practice.

DUSC considered that there could be multiple reasons for the high and increasing utilisation of bDMARDs for psoriatic arthritis including:

- There is no local epidemiological data on the incidence and prevalence of severe psoriatic arthritis in Australia. DUSC considered that the population with severe psoriatic arthritis may have been underestimated at the time bDMARDs were first listed for this indication. Stakeholders considered that psoriatic arthritis has been underdiagnosed and undertreated.
- It was initially easier to access bDMARDs via the psoriatic arthritis indication, which may have led to reclassification of some seronegative rheumatoid arthritis patients as having psoriatic arthritis accounting for some of the early rapid uptake of bDMARDs for psoriatic arthritis. DUSC noted that this is no longer likely to be the case as there is a better understanding of the pathological mechanisms for the diseases, and patients with rheumatoid arthritis are now able to access up to five different bDMARDs before requiring a treatment break.
- The higher than expected retention rates on bDMARDs than predicted. DUSC considered that this could partly be due to inflexibility in the PBS restriction and continuation rules for the proportion of patients with psoriatic arthritis that follows a relapsing/remitting disease course. Currently the restriction does not allow for patients who have demonstrated a response to have a treatment break and recommence at a later date as part of the same treatment cycle.
- Treatment of milder disease. DUSC considered that this is possible and noted that TNF inhibitors are used to treat a broader range of clinical manifestations than conventional DMARDs (in particular spinal disease, skin and enthesitis).
- Increased familiarity with bDMARDs.

DUSC considered that a review of the restrictions for bDMARDs for psoriatic arthritis may be required. DUSC noted that the restrictions for psoriatic arthritis were based on those for rheumatoid arthritis but that understanding of the disease had advanced since that time. DUSC requested further consultation with stakeholders prior to the PBAC considering this matter.

DUSC noted that an assessment of the use of DMARDs for psoriatic arthritis was not presented in the report and considered that this would enhance the analysis. DUSC recommended that this be undertaken for a future meeting.

The DUSC noted a proposal from a sponsor regarding changing the restriction for second and subsequent continuing authorities for any single bDMARD. DUSC noted that this request is being considered in the context of the Post-market Review of Authority Required Medicines.

DUSC actions

The DUSC requested that:

- the report be provided to the PBAC.
- further consultation is undertaken regarding whether there is a need to review the PBS restrictions for psoriatic arthritis.
- an assessment of DMARD use prior to initiation on bDMARDs for psoriatic arthritis be undertaken and presented to DUSC at a future meeting.

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

AbbVie Pty Ltd: Further analysis undertaken by the sponsor showed that the pattern of rate of growth in utilisation of bDMARDs in prevalent patients is typical of the rate of growth observed with the introduction of new treatments generally. Indeed the rate of growth in initial years may be lower than would be expected for new therapies and higher in later years. This is likely due to the requirement for patients to have demonstrated failure to respond to DMARDs before qualifying for treatment with bDMARDs. Hence, it would be reasonable to expect rates of growth of bDMARDs used for PsA to continue to decline until the growth rate matches population growth rates. AbbVie believes the DUSC review shows that adalimumab is being used within the PBS restriction criteria deemed by the PBAC to be cost-effective.

Pfizer Pty Ltd: The sponsor has no comment.

Janssen-Cilag Pty Ltd: Janssen are committed to the appropriate and cost-effective use of its medicines, infliximab and golimumab, for the treatment of psoriatic arthritis. Janssen believes the DUSC review demonstrates that both golimumab and infliximab are being used within the PBS population determined to be cost-effective by the PBAC.

UCB Australia 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.

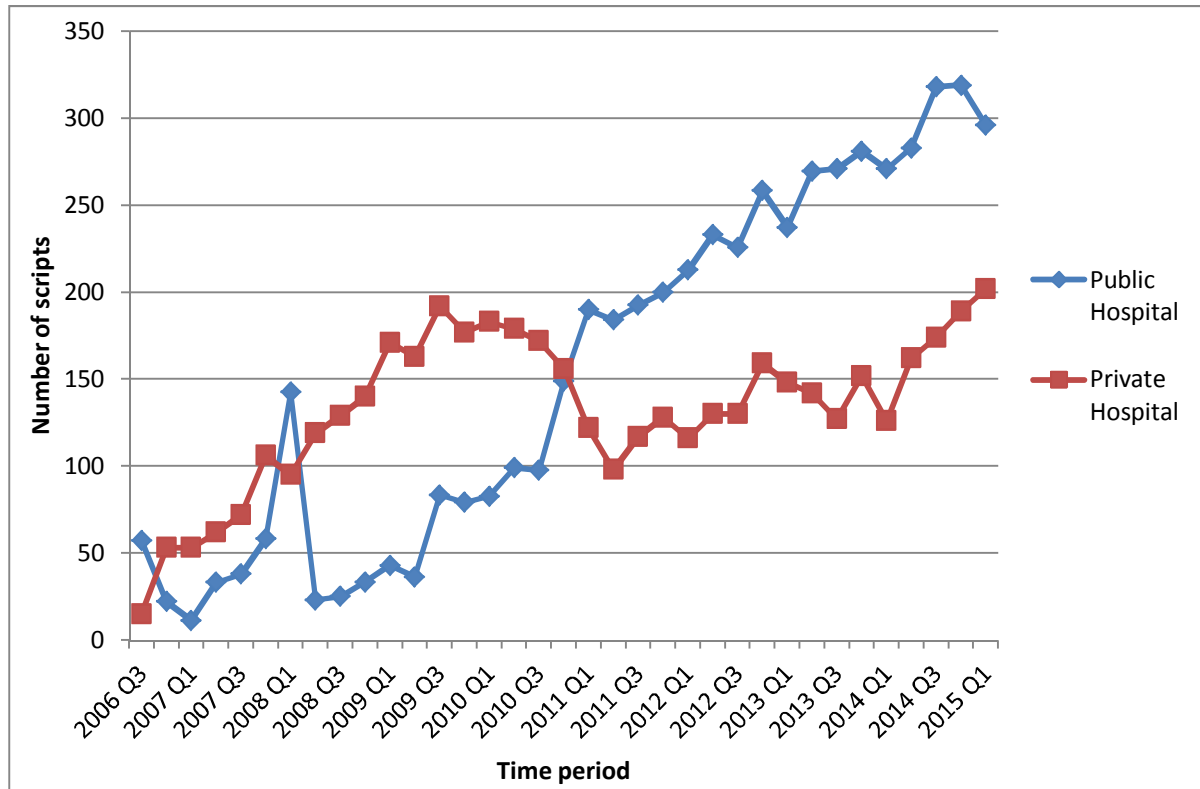
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Appendix A – methodology used to estimate public hospital infliximab prescriptions

Figure A provides the total number of prescriptions dispensed for infliximab, including an estimate of public hospital prescriptions before accurate data were available from quarter 3 2013, based on the average number of vials per prescription derived from the period data were available.

Figure A – Infliximab prescriptions for psoriatic arthritis, 2006-2015



Source: DUSC HSD Database, extracted July 2015

The figure shows the overall number of prescriptions is low, with the number of public hospital prescriptions growing from the second half of 2013 onwards. There is a level of uncertainty as to the exact number of prescriptions for public patients, as the actual data were unavailable before quarter 3 2013.