Concise report

Analysis of 4-year Dutch reimbursement application data of biological therapies for psoriatic arthritis

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Abstract

Objectives. To get the approval for reimbursement of biological therapies for PsA, patients need to fulfill specific criteria in many countries. The aim of this study was to evaluate the 4-year Dutch reimbursement application data, including the diagnostic, disease activity and response criteria that were applied for treatment of PsA with biologics.

Methods. All initial and follow-up applications for approval of treatment with biologics were included for investigation. Data were analysed descriptively with regard to application characteristics, patient characteristics and response to therapy.

Results. In the period studied, 3723 application forms of 1991 patients were received. This concerned 2118 initial treatment applications and 1605 follow-up applications. Of all initial treatment applications, 2003 (94.6%) were approved. The major part of all applications concerned requests for etanercept (59.1%), followed by adalimumab (38.2%). Patients were suffering from polyarthritis in most cases (63.1%). MTX was used by nearly all patients, but only 55.8% had used the required dosage of 25 mg/week. Approximately 79.4% of all patients met the response criteria after 3 months of treatment. The mean number of affected joints declined from 7.7 at first application to 1.4 at follow-up. The initial visual analogue scale (VAS) score indicated by patients decreased from 71.2 to 24.1 at follow-up. The VAS score indicated by physicians decreased from 66.0 to 18.4.

Conclusions. Biologics are expensive, but highly effective in the treatment of PsA. Careful compilation of treatment and reimbursement criteria is important for patients as well as for physicians and health insurance companies.

Key words: Psoriatic arthritis, Biologic, Etanercept, Adalimumab, Infliximab, Reimbursement, Criteria, Methotrexate, Joint.

Introduction

PsA is a seronegative inflammatory joint disease associated with psoriasis. Mild PsA can be successfully treated with NSAIDs or IA corticosteroid injections. In the case of severe PsA, synthetic or biological DMARDs, or combinations of these therapies are needed to alleviate signs and symptoms, and to inhibit structural joint damage [1].

Currently, three anti-TNF-α agents are registered for the treatment of PsA, adalimumab, etanercept and infliximab. Biologics are expensive and therefore in many countries criteria are developed that patients need to fulfill to get approved for reimbursement of these therapies. Nevertheless, a recent pharmacoeconomic study on PsA showed that anti-TNF-α therapy is cost-effective in short-term clinical practice [2].

In the Netherlands, the reimbursement criteria for biological treatment for PsA as well as for other rheumatological indications are formulated by the Dutch Society for Rheumatology (Nederlandse Vereniging voor
Reumatologie), and subsequently authorized by the Health Care Insurance Board (College Voor Zorgverzekeringen). Which criteria are applicable is dependent on the type of PsA. At joint count, at least two inflamed joints should be found. Patients are eligible for reimbursement of biological treatment if they are not responsive to MTX at a dosage of at least 25 mg/week, or if they have a contraindication or intolerance for this therapy. Secondly, the global assessment of disease activity, measured on the basis of a visual analogue scale (VAS) of 0–10, should be at least 4 according to the physician as well as the patient. Thirdly, the arthritis should be persistent despite local (IA) therapy. In the case of polyarticular PsA (five or more joints affected), there should be at least five tender and five swollen joints, or a mutilating arthritis should be present. After 3 months of therapy, patients should have met the response criteria, implying a diminution of number of painful or swollen joints, in at least one affected joint in the case of oligoarticular PsA, or in at least 20% of the affected joints in the case of polyarticular PsA. Disease activity measures on psoriasis are left out of consideration.

From February 2004 to March 2008, evaluation of these diagnostic, disease activity and response criteria in the Netherlands occurred centrally by a subcommittee of an independent foundation [Landelijke Beoordeling Aanvragen Geneesmiddelen (LABAG), National Evaluation of Applications of Drugs]. This committee was appointed by health insurance companies and comprises representatives of rheumatologists, dermatologists, paediatricians, health insurance companies and the government. Applications for biological therapies for PsA could only be submitted by physicians with experience in treating patients with PsA.

The aim of this study was to evaluate the 4-year Dutch reimbursement application data, including the diagnostic, disease activity and response criteria that were applied for treatment of PsA with biological therapies.

Patients and methods

Requests for reimbursement of biologics were made by rheumatologists filling out an application form, which was submitted to the national committee (LABAG). This application form contained the patient’s demographic data, questions about the number of affected joints, specific questions about MTX use and dosage in history, type of PsA and VAS scores on global disease activity of patients and physicians. After 3 months of therapy, a second, identical form was filled out and submitted for evaluation of the response criteria.

All initial and follow-up applications for approval of treatment with biologics submitted to LABAG between February 2004 and March 2008 were included for investigation. Data were analysed descriptively with regard to application characteristics, patient characteristics and response to therapy. Patient characteristics were analysed from the patient perspective. Response to therapy was analysed from the treatment perspective.

Application characteristics

The number of application forms received and the number of patients concerned were calculated. The percentage of approved initial and follow-up treatment applications was computed.

Patient characteristics

Patient characteristics included gender, age at very first application, type of PsA, baseline VAS score and medication history with regard to MTX use.

Response to therapy

The assumption was made that rheumatologists did not submit a follow-up application when there was insufficient response or side effects to biological therapy. Therefore, the percentage of patients meeting the response criteria after 3 months of therapy was calculated by dividing the number of approved follow-up applications by the number of approved initial applications. Furthermore, the response to therapy was represented by the decline in the number of affected joints and the reduction in VAS scores of patients and physicians.

Results

Application characteristics

In the period studied, 3723 application forms were received by LABAG. This concerned 2118 initial treatment applications and 1605 follow-up applications. Of all initial treatment applications, 2003 (94.6%) were approved, 51 (2.4%) were rejected because reimbursement criteria were not fulfilled, 47 (2.2%) could not be taken into consideration due to insufficient data, 10 (0.5%) were withdrawn by physicians before approval, 3 (0.1%) were considered as reflecting no reason to treat, 2 (0.1%) had no decision status, 1 (0.0%) received no follow-up advice and 1 (0.0%) received neutral advice, meaning that direct consultation of the health insurance company by the prescribing physician was required. Of the 1605 follow-up applications, 1591 (99.1%) met the response criteria and were approved, 7 (0.4%) did not meet the response criteria and thus were rejected, 5 (0.3%) were withdrawn by the physician, 1 (0.1%) was considered as reflecting no reason to treat and 1 (0.1%) could not be taken into consideration due to insufficient data.

Of the 2118 initial treatment application forms, 1251 (59.1%) concerned an application for etanercept, 810 (38.2%) for adalimumab, 7 (0.3%) for infliximab, 1 (0.0%) for anakinra and in 49 (2.3%) forms the medication requested for was not discernible. The number of applications for infliximab was low, as this biologic, in contrast to etanercept and adalimumab, was not fully reimbursed by health insurance companies in the Netherlands.

Patient characteristics

Initial and follow-up application forms comprised 1991 patients. Of all patients, 1075 (54.0%) were males, 868 (43.6%) were females and for 48 (2.4%) the gender was not mentioned. Mean age at first application was
Response to therapy

A total of 2003 of all initial treatment applications and 1591 of all follow-up applications were approved by LABAG, indicating that ~79.4% (1591 out of 2003) of all patients had met the response criteria after 3 months of treatment. From the data it is unclear whether biological treatment was withdrawn because of unresponsiveness to the treatment, side effects or other reasons. Categorized for different biological therapies, the percentage of patients meeting the response criteria came down to ~80.1% (966 out of 1206) for patients treated with etanercept and ~83.3% (622 out of 747) of patients treated with adalimumab.

The mean number of affected joints declined from 7.7 (range 0.0–62.0; S.E.M. 0.1) at first application to 1.4 (range 0.0–28.0; S.E.M. 0.1) at follow-up, corresponding to an 81.8% decline in the number of affected joints in 3 months. The initial VAS score indicated by patients decreased from 71.2 (range 9.0–100.0; S.E.M. 0.3) to 24.1 (range 0.0–95.0; S.E.M. 0.4) at follow-up, i.e. a reduction of 66.2%. Likewise, the VAS score indicated by physicians decreased from 66.0 (range 8.0–100.0; S.E.M. 0.3) to 18.4 (range 0.0–90.0; S.E.M. 0.3; 72.1% reduction).

Discussion

This report represents the 4-year Dutch national diagnostic, disease activity and response criteria data that were applied for reimbursement of treatment of PsA with biologics. Analysed application forms comprised data of 1991 patients who were potentially eligible for biological therapy. A previous analysis of the 3-year Dutch reimbursement application data that were applied for treatment of psoriasis with etanercept or efalizumab, concerned 1197 patients [3]. Thus, relatively more requests for biological treatment are made for PsA than for moderate to severe psoriasis. Several explanations for this can be given.

First of all, PsA may be more prevalent than moderate to severe psoriasis, although the exact prevalence of PsA is unknown. Data about the prevalence of inflammatory arthritis in patients with psoriasis vary from 6 to 42% [4]. Secondly, rheumatologists may be more inclined than dermatologists to prescribe systemic therapies, including biologics. Thirdly, the criteria for (initial) reimbursement of biologics may be easier to meet for PsA than for moderate to severe psoriasis, as only one systemic drug that must have been used in history (i.e. MTX) is specified. The criteria only encompass disease activity measures specific for PsA and do not include severity measures on psoriasis. Besides, the reimbursement criteria do not incorporate frequently used measures such as CRP or Disease Activity Score in 28 joints (DAS-28) [5]. Finally, PsA may be more disabling than psoriasis, necessitating intensive systemic therapy.

A high percentage of all initial and follow-up applications (94.6% and 99.1%, respectively) were approved, indicating that rheumatologists are familiar with the demanded criteria for reimbursement of biological therapies. The major part of all applications concerned requests for etanercept, followed by adalimumab. This is very likely related to the different moments of approval of reimbursement by health insurance companies of etanercept and adalimumab in the Netherlands, as etanercept has been reimbursed since December 2003 and adalimumab since October 2005. Likewise, as infliximab was not fully reimbursed, the number of applications for this pharmaceutical was low.

The patients considered were predominantly male (54.0%) and were suffering from polyarthritis in most cases (63.1%). The latter is in agreement with the literature [6], which says that polyarthritis is the most common type of PsA in patients with established disease. In the current study, the mean number of affected joints was 7.7. MTX was used by nearly all patients, but only 55.8% had used the required dosage of 25 mg/week.

Global disease activity, indicated on a VAS, was assessed higher by patients than by physicians at both moments of evaluation. In a publication by Nicolau et al. [7] on discrepancy in the perception of RA disease activity between patient and physician, the same difference was established in the majority of patients.

Interestingly, ~80% of all patients had met the response criteria after 3 months of treatment. This is much higher than the response percentages calculated by using the application data on biological therapies for psoriasis [3]. Like the initial criteria for reimbursement of biologics, the response criteria may also be easier to meet for PsA than for psoriasis. Nevertheless, in randomized controlled trials on biological therapies for PsA, the ACR20 response after 12 weeks, which roughly resembles the Dutch response criteria, was far lower than 80% [8]. Data from large registries may be valuable to establish the efficacy of biological therapies for PsA in daily practice [9, 10].

In conclusion, biologics are expensive but highly effective therapies for different immune-mediated diseases, including PsA. Currently, biological therapies are indicated exclusively for severely affected patients. Careful compilation of treatment and reimbursement criteria is of importance for patients as well as for physicians and health insurance companies. The Dutch protocol...
for reimbursement of biologics for PsA, with diagnostic, disease activity and response criteria, has facilitated that every rheumatologist could prescribe biologics for PsA. Moreover, it has increased the confidence between rheumatologists and health insurance authorities. Hence, the central evaluation of the criteria for reimbursement of treatment with biologics in the Netherlands by LABAG could be ceased in April 2008.

**Rheumatology key messages**

- Biologics are effective in the treatment of PsA.
- Compilation of treatment and reimbursement criteria for biologics is important.
- This study shows reimbursement application data on biologics for PsA.

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**References**