REVIEW ARTICLE

Drug Safety 2006; 29 (8): 675-685
0114-5916/06/0008-0675/$39.95/0

Safety of Etanercept in Psoriasis
A Critical Review

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Contents

Abstract

Conventional systemic treatments for patients with psoriasis are associated with multiple adverse effects that require continuous monitoring. The introduction of new biological agents such as etanercept, a fully human fusion protein, has permitted individualisation of patients' treatment according to disease stage. The drug is a competitive inhibitor of tumour necrosis factor-α (TNFα) that prevents interaction between this cytokine and its cell surface receptors. Etanercept also modulates the activity of other inflammatory cytokines and does not induce complement-mediated cell lysis *in vitro*.

The main source of information regarding etanercept safety comes from studies in patients with rheumatoid arthritis. The most common adverse effect during drug administration is mild injection site reactions. There is no increase in the overall incidence of infections compared with placebo, although there have been several reports of infections caused by intracellular organisms (*Mycobacterium tuberculosis*, *Listeria monocytogenes*, and *Mycobacterium avium intracellu-*

lare). Therefore, combination of this drug with corticosteroids must be carefully monitored and should be avoided in patients with established sepsis.

There are no data showing that treatment with etanercept results in an increase in the occurrence of malignant neoplasms. However, caution is recommended in use of etanercept in patients with a current or past history of demyelinating disease. Etanercept must be used with extreme caution in patients with heart failure because of several reports indicating a worsening or *de novo* occurrence of congestive heart failure while receiving the drug. Monitoring of autoantibodies is not currently considered necessary as they do not predict response, toxicity or autoimmune events. The presence of non-neutralising antibodies to the TNF receptor fragment or other protein components of etanercept has not been related to a decrease in drug response or adverse reactions. Etanercept does not generally modify the course of inflammatory bowel disease. When combined with other systemic therapies for psoriasis, current data do not show an increase in adverse events.

In patients with hepatitis C viral infection, etanercept does not increase transaminase levels or viral load and in some instances has allowed the concomitant use of interferon which had previously been discontinued because of a worsening of psoriasis. Etanercept is rated as a US FDA category B drug in pregnancy. However, its use is not recommended in pregnant women unless the benefit-risk ratio greatly favours its use. Etanercept is not recommended for use in lactating women.

Etanercept represents a relevant treatment for psoriasis, efficacious over many weeks and safe but special care should be taken to avoid the potential risks.

Psoriasis is a chronic disease that involves the skin and joints and affects approximately 1–3% of the world's population.[1] The most common clinical presentation of this condition is plaque psoriasis, which occurs in >80% of cases. Other forms of the disease include guttate (affecting 10% of patients), erythrodermic (0.6–1% of patients) and pustular psoriasis (<3% of patients).[2] Psoriatic arthritis is present in 5–42% of patients with psoriasis and may follow a destructive course that can lead to disabling joint disease.[3]

Currently, T cells are considered to play a prominent role in the pathogenesis of psoriasis.[4] Naive T cells are activated by antigen presenting cells (APC) presenting unidentified antigens exposed on class I (for intracellular antigens) or class II (for extracellular antigens) major histocompatibility complex; after several stages, these activated T cells evolve into memory cells. Binding of memory T cells to their specific antigens induces massive secretion of type-1 cytokines, interferon-γ, interleukin (IL)-2 and tumour necrosis factor-α (TNFα).[4] TNFα is a critical proinflammatory cytokine that mediates many inflammatory processes, including immune-cell activation and proliferation, apoptosis and regulation of leukocyte movement.[5] It also plays a key role in the development, proliferation and maintenance of psoriatic plaques[6] and in the joint damage of psoriatic arthritis,[7] promoting activation of T cells and other cytokines and thus leading to further inflammation.[8]

The classical treatment of psoriasis ranges from topical therapies for mild disease to systemic therapies for more widespread conditions. Systemic therapies, such as methotrexate, acitretin and ciclosporin, are used only in severe cases of psoriasis and psoriatic arthritis after failure of conventional therapy or in patients with disease too extensive for topical treatment. However, these treatments are limited by their cumulative toxicity[8]

Table I. Human tumour necrosis factor-α (TNFα) antagonists

Structure	Components	Target	Derivation
Infliximab	Chimeric IgG1 mAb comprising a human Fc portion and murine Fv	TNF	Mouse and human
Adalimumab	Fully humanised IgG1 mAb made by phage display from human components	TNF	Human
Etanercept	Dimer of p75 component of human TNF-R fused to human IgG Fc	TNF, lymphotoxin-α	Human
Lenercept	Dimer of p55 component of human TNF-R fused to human IgG Fc	TNF, lymphotoxin-α	Human

Fc = constant region; **Fv** = variable region; **mAb** = monoclonal antibody; **TNF-R** = TNF receptor.

and, therefore, are not appropriate strategies for treating chronic forms of the disease.

Advances in immunology and DNA biotechnology combined with a deeper knowledge of the aetiopathogenesis of psoriasis have resulted in the development of new therapeutic agents called 'biological therapies'. These treatments act at specific stages of the disease, minimising adverse effects.

Given that psoriasis is an inflammatory disease, blockade of the inflammatory cascade by specific drugs at several stages of the disease could, theoretically, improve the course of the disease with fewer adverse events. Because of its pivotal role in the inflammatory process, one of the specific targets for new biological therapies is TNFα.[9]

1. Tumour Necrosis Factor-α Antagonists

TNFα antagonists have been shown to be effective in the treatment of patients with psoriasis and psoriatic arthritis. Etanercept is currently approved by the US FDA and by the European Medicines Agency (EMEA) for the treatment of psoriasis and psoriatic arthritis, whereas infliximab has been approved for this indication only by the EMEA. In addition, several other TNFα antagonists are being developed and tested in humans (table I), without as yet having been approved for use in psoriasis.[10]

Infliximab is a TNFα monoclonal antibody formed with a human constant and a mouse variable region of IgG1.[11] Adalimumab is a fully humanised IgG1 monoclonal antibody made by phage display from human components.

Etanercept, a disease-modifying drug, is a fully human dimeric fusion protein consisting of the extracellular ligand-binding domain of the 75kDa (p75) TNF receptor linked to the constant region of IgG1. It is synthesised by recombinant DNA technology in Chinese hamster ovary-cell lines and exhibits a longer half-life than the native soluble receptor.[12,13] Etanercept acts as a competitive inhibitor of TNFα by binding to this cytokine and preventing interactions with its cell surface receptors.[12-14] It also modulates the activity of other inflammatory cytokines,[12-14] such as lymphotoxin-α, a cytokine that is structurally similar to TNF and with similar activities.[5] Unlike other TNFα antagonists, etanercept does not induce complement-mediated cell lysis *in vitro*.[12] The dimeric nature of etanercept means its affinity for TNFα is 50–1000 times greater than that of soluble monomeric forms of TNFα receptor.[14]

TNF exists in soluble and membrane-bound forms. There are two TNF receptors, p55 and p75, which also exist in both soluble and membrane-bound forms. Lenercept is similar to etanercept in its dimeric structure but is compounded by two p55 TNF soluble receptors. It has not been further developed for human use because it induces anti-lenercept antibodies.[10]

2. Objective and Search Methodology

The aim of this article is to review the safety of etanercept in psoriasis, based on currently available clinical data published in the literature. We searched MEDLINE from January 1991 to October 2005 using the terms 'psoriasis' and 'etanercept'. All articles identified by this search, including case reports, cohort studies, randomised controlled trials,

letters, meta-analyses and review articles, were reviewed. Emphasis was placed on studies that evaluated the safety of TNFα inhibitors; the most relevant articles (in the authors' opinion) and the main sources of data referenced by those articles were included (the search generated 180 articles of which 63 were reviewed for this paper).

3. Safety of Etanercept

There is long clinical experience with etanercept, including data from controlled clinical trials dating from 1993 and postmarketing data collected since 1998. More than 130 000 patient-years of exposure to etanercept have demonstrated the safety of this drug.[12] The main source of information regarding the safety of etanercept comes from studies of use of the drug for rheumatoid arthritis (RA). In one of these, a long-term (5-year) study, the rate of infection requiring hospitalisation or intravenous antibacterial therapy in the group receiving etanercept was the same as that found in the placebo control group (0.04 vs 0.04 events per patient/year, respectively).[15] Etanercept has also been used in patients with psoriatic arthritis, with or without skin lesions, for up to 6 years without any safety issues specific to the psoriatic arthritis population having been identified.[16]

Nevertheless, as with other TNFα antagonist drugs, there is the potential risk for infections, neoplasms, demyelinating disease, heart failure and autoimmune diseases with long-term use of etanercept. In the following sections, we review the available data relating to these potentially serious adverse events of etanercept, together with what is known about other less severe but more common adverse effects of the drug.

3.1 Allergic Reactions

3.1.1 Injection Site Reactions

An injection site reaction is the most common adverse event during administration of etanercept, occurring in approximately one-third of patients.[17] These reactions are usually mild, occur in the first few weeks of treatment at the site of the last injection, and exhibit a recall phenomenon (i.e. occurrence of lesions at prior injection sites). Topical corticosteroids, moisturisers and histamine H_1 receptor antagonists (antihistamines) may be used to manage the symptoms, which usually resolve with continued treatment over a few months. Gottlieb et al.[16] found that etanercept injection-site reactions were mild to moderate and dissipated with time, with most patients experiencing two or less reactions. Recent studies have shown that these lesions are composed of an inflammatory infiltrate that predominantly consists of CD8+ T cells.[18,19]

3.1.2 Urticaria and Angioedema Reactions

Although etanercept is an exogenous fusion protein and has potential immunogenicity, there are few reports in the literature of immediate allergic reactions such as urticaria or angioedema with etanercept.[20] Anti-etanercept antibodies are detected in a small percentage of patients receiving the drug, but their significance is unclear (see section 3.7).[13]

3.2 Infections

The most common infection site in patients taking etanercept is the upper respiratory tract, which has been reported to affect 29% of etanercept-treated patients compared with 16% of those receiving placebo.[13] However, in controlled clinical trials that compared etanercept with placebo, the incidence of severe infections was similar in placebo- and drug-treated groups (1.3% vs 0.9%, respectively).[13] Furthermore, when Klareskog et al.[15] evaluated the safety of etanercept in 1960 patients treated with the drug for >5 years, they found no increase in mild or severe infections compared with the general population. Nevertheless, in postmarketing surveillance studies, there were early reports of serious infections (30 patients of 25 000 treated with etanercept), some of which proved fatal (6 of 30 patients died after receiving etanercept for 2–16 weeks).[21] Because of such reports, current prescribing guidelines suggest that patients should be monitored for signs and symptoms of infection when taking a TNFα inhibitor and that these agents should

not be used in patients with active, serious infections or chronic recurrent infections.[22]

One of the potential risks of TNFα antagonists is an increase in the risk of infections caused by intracellular microorganisms. This complication is secondary to inhibition of T lymphocytes, which are required for the formation of granulomas. One of the infections caused by such microorganisms that is most commonly reported in patients treated with these drugs is reactivation of, or primary infection by, *Mycobacterium tuberculosis*.[13,23,24] Most cases of this disease occur during the first few months of treatment. The chronology and strong association with endemic infections in reported cases suggest reactivation of latent tubercle bacilli from TNFα inhibition.[13,23] Some official organisations have included etanercept among the drugs for which a tuberculin test and a chest x-ray are advised before initiation of treatment.[23]

Other infections reported with the use of etanercept include two infections by *Listeria monocytogenes,*[25] a psoas abscess caused by *Mycobacterium avium intracellulare*, bacteraemia and a hip prosthesis infection.[26] It appears that certain comorbidities or the use of concomitant corticosteroid may predispose to severe infection,[13,27] and precaution is therefore advised when these two treatments are administered concomitantly. Another group of patients requiring special attention are those with established sepsis, in whom etanercept is not recommended because it increases mortality.[28]

3.3 Neoplasms and Haematological Disorders

Although there are no pre-clinical data demonstrating a causal relationship between TNFα antagonist therapies and the development of solid or lymphoid neoplasms,[15,29] there have been nine lymphomas in 5723 patients over approximately 11 201 patient-years of therapy in the controlled and open-label portions of clinical trials of etanercept in patients with Crohn's disease and RA.[30] Furthermore, when Wolfe and Michaud[31] prospectively studied a cohort of 18 572 RA patients treated with methotrexate, etanercept or infliximab, they identified a global standardised incidence ratio of 1.9 for lymphoma in patients with RA. The standardised incidence ratios of lymphoma in patients taking infliximab and etanercept were 2.6 and 3.8, respectively. However, Wolfe and Michaud[31] considered that the differences between therapies with respect to risk of lymphoma were slight and that the current data are insufficient to establish a causal relationship between RA treatments and the development of lymphoma. In contrast to the findings of the Wolfe and Michaud study,[31] Askling et al.[32] found that RA patients treated with TNFα antagonists did not have higher lymphoma risks than other RA patients. Further studies with longer follow-up periods are needed to clarify the relationship between TNFα antagonists and lymphoma.

An increased risk of squamous cell carcinoma and basal cell carcinoma has been reported in patients with psoriasis.[33,34] It is not known if this increased risk can be attributed to psoriasis itself or to different treatment regimens; the clinical practice of rotational therapy makes it difficult to elucidate the causal agent.[16]

Other neoplasms, such as breast, prostate and lung carcinoma[13,16] have been reported in clinical trials and in postmarketing studies of etanercept.[13,16] However, it is not known whether etanercept may influence the development of such neoplasms.[13,35]

Seven cases of aplastic anaemia have been reported to the FDA, five of them with a fatal outcome, following treatment with etanercept.[13] The drug label therefore recommends caution with use of etanercept in patients with a history of blood dyscrasia.[13] However, a causal relationship between use of etanercept and aplastic anaemia could not be found.[13]

Taken together, the available data provide no evidence that use of etanercept results in an increased incidence of neoplasms or haematological conditions in patients with psoriasis.

3.4 Demyelinating Diseases

TNFα is an important mediator of disease in multiple sclerosis (MS). This cytokine has been

demonstrated in active foci of MS in autopsy specimens and is elevated in both the serum and cerebrospinal fluid (CSF) of patients with MS.[36-38] Moreover, levels of TNFα in the CSF are strongly correlated with MS activity.[36,37] However, failure of some approaches to the treatment of MS using TNFα antagonists has resulted in abandonment of all TNFα antagonists as candidate drugs for the treatment of MS.[39,40] In addition, several cases of demyelinating disease have been reported with the use of TNFα antagonists, although a causal relationship underlying these findings has not been established.[40-42] The FDA has received 15 postmarketing reports of demyelinating diseases in patients treated with etanercept[13,43] and the drug label thus recommends caution with use of etanercept in patients with a current or past history of demyelinating disease.[13]

3.5 Heart Failure

Early studies showed that serum TNFα concentration is elevated in patients with congestive heart failure (CHF) and that this concentration correlates directly with the severity of disease.[44-48] Subsequently, TNFα was shown to have negative inotropic effects, cause cardiomyocyte apoptosis, and worsen CHF and its prognosis, and it was hypothesised that inhibiting TNFα might reverse CHF and improve functional status in CHF patients.[44-48] Two small short-term studies (one involving administration of a single dose of etanercept, the other 3 months of biweekly infusions) showed a nonsignificant trend towards improved status in patients with CHF treated with etanercept compared with placebo.[49,50] However, the two largest clinical trials that evaluated the use of etanercept for the treatment of CHF (RECOVER [Randomized Etanercept North American Strategy to Study Antagonism of Cytokines] and RENAISSANCE [Research into Etanercept: Cytokine Antagonism in Ventricular Dysfunction]) were discontinued because of a lack of efficacy.[51] No significant differences were found in parameters of disease status when etanercept was compared with placebo. The FDA has not prohibited the use of etanercept in patients with heart failure because no worsening of the condition or increased mortality has been reported in patients receiving the drug. However, the increase in mortality found with other TNFα antagonists, such as infliximab[52] and reports of worsening or the *de novo* occurrence of CHF in patients treated with etanercept[51,53,54] means extreme caution should be exercised when etanercept is used in such patients.

3.6 Autoantibodies and Lupus Syndrome

Development of antinuclear antibodies with use of TNFα antagonists has been reported extensively in the literature.[1-3,5,22] Most of the data were obtained from patients with RA who were treated with these agents. RA is a disease in which a variable proportion of patients have underlying positive autoantibodies with unclear pathogenic significance. However, the presence of anti-dsDNA antibodies, found in 8–15% of patients treated with infliximab, 3–15% of patients treated with etanercept and 5.6% of patients receiving adalimumab, has been shown to be related more clearly to drug therapy than to underlying disease.[55] Nevertheless, the incidence of lupus syndrome induced by TNFα antagonists is low,[2,5] with only few reports in the literature.[56-59]

Monitoring of antinuclear antibodies during TNFα antagonist therapy is not currently deemed necessary because their appearance does not predict response, toxicity or autoimmune events.[2,5]

3.7 Anti-Etanercept Antibodies

Non-neutralising antibodies to the TNF receptor fragment or other protein components of etanercept have been detected in the serum of <5% of patients with RA or psoriatic arthritis participating in clinical trials with these agents.[13] The presence of such antibodies has not been related to a decreased drug response or adverse reactions.

3.8 Inflammatory Bowel Disease

Although etanercept does not generally modify the course of Crohn's disease, there has been a report suggesting that this agent may have contribut-

ed to the development of clinically significant inflammatory bowel disease.[3,5]

3.9 Etanercept Combined with Other Systemic Therapies for Psoriasis

Etanercept has been combined in small case series and isolated clinical cases with psoralen + UVA,[4,5] ciclosporin,[60] hydroxycarbamide (hydroxyurea)[5] and acitretin,[61] with no increase in adverse effects. Etanercept may also be used safely in combination with methotrexate for RA and psoriasis.[62] Further studies with other immunomodulatory drugs are required to reach a final conclusion regarding the safety profile of such combinations.

3.10 Etanercept in Special Populations

3.10.1 Paediatric Patients

Etanercept has been approved by the FDA for the treatment of juvenile chronic arthritis in patients >4 years of age. The adverse reactions that occur in children are similar in type and incidence to those occuring in adults: injection-site reactions (39%), upper respiratory tract infections (35%), headache (20%), rhinitis (16%), abdominal pain (16%), vomiting (14%), pharyngitis (14%), nausea (12%), digestive infection (12%) and exanthema (10%).[63]

The efficacy of etanercept in paediatric patients with moderate-to-severe psoriasis has been recently reported.[16] The drug was administered to ten paediatric patients at doses of 0.4 mg/kg twice a week for patients weighing <50kg and 25mg twice a week for patients weighing >50kg. The only adverse event registered was a mild reaction at the injection site.[5,7]

3.10.2 Hepatitis C-Infected Patients

Etanercept has been administered to a small series of patients with hepatitis C infection with no reports of subsequent increases in transaminase levels or viral load.[64] Moreover, treatment with etanercept permitted the concomitant use of interferon in such patients when the latter agent had previously been discontinued because of a psoriasis flare.[12,65] Recently, Zein et al.[66] reported the results of a randomised, double-blind, placebo-controlled study of etanercept as adjuvant therapy to interferon and ribavirin in treatment-naive patients with chronic hepatitis C and concluded that etanercept delivered for 24 weeks in combination with interferon/ribavirin increased the proportion of patients achieving and maintaining virological response. Further studies are necessary to elucidate the role of etanercept in patients with hepatitis C infection.

3.10.3 Pregnant and Lactating Women

The US FDA rates etanercept as a category B drug in pregnancy, i.e. a drug that may be assumed to have been used by only a limited number of pregnant women and women of child-bearing age, without any form of definite disturbance in the reproduction process having been noted so far. In a recent prospective study, the following three study groups were compared: (i) pregnant women with RA receiving TNFα antagonists (including etanercept but not methotrexate); (ii) pregnant women with RA receiving systemic treatments but no methotrexate or TNFα antagonists; and (iii) pregnant women without RA and without any treatment. No increase in the risk of major structural defects was detected in any of the three groups.[67] However, the weight of newborns with mothers with RA, regardless of the type of treatment, was statistically significantly lower than the weight of newborns of mothers without RA, suggesting a potential influence of the disease or the treatment. Until additional data become available, caution is recommended when using etanercept in pregnant women. Since many medications and immunoglobulins are excreted in breast milk and it is not known whether etanercept is excreted in breast milk, its use is not recommended in lactating women.[13,50]

3.11 Etanercept Compared with Other Biologic Therapies for Psoriasis

Alefacept is a human fusion protein consisting of a fragment of IgG1 fused with a fragment of lymphocyte function-associated antigen type 3 (LFA-3).[68] Alefacept inhibits T-cell activation and proliferation by binding with CD2 on T cells and

blocking the LFA3/CD2 interaction; it also induces T cell apoptosis mediated by natural killer cells. Because treatment with alefacept results in a selective reduction of memory cells, CD4 lymphocyte count should be monitored weekly and alefacept therapy is contraindicated in patients with CD4 T-lymphocyte counts below normal levels.[3,6]

Although alefacept was well tolerated in studies of patients with psoriasis vulgaris, treatment was effective in only one-third of patients and its onset of action was slow.[4,6,69-71] Studies of combined therapy indicate that the combination of alefacept with ciclosporin, methotrexate, acitretin or phototherapy may improve clinical outcomes with the drug, but this needs further investigation.[72,73] Such combination therapy would also add the safety limitations of classical treatments for psoriasis to those of alefacept. There are currently no data comparing the safety of etanercept with alefacept.

Efalizumab is a humanised monoclonal antibody of the α-1 integrin CD11a, which is a component of LFA-1 on the surface of T-cells. It acts by blocking the interaction between LFA-1 on T cells and intercellular adhesion molecule-1 (ICAM-1) on APC and endothelium, inhibiting the costimulation and migration of T cells, respectively.[74]

Studies of efalizumab show good tolerance with adverse events that subsided with subsequent doses and no significant increases in malignant diseases or any opportunistic infections; however, exacerbations of psoriasis have been reported after discontinuation of the drug.[75-77] There are currently no data comparing the safety of etanercept with efalizumab.

Infliximab is a chimeric monoclonal antibody specific for TNFα which consists of the human antibody constant region and a murine variable region.[78] It acts by binding to soluble and transmembrane TNFα, blocking its action and also stimulating cell lysis mediated by complement in cells expressing TNFα on their surface.[78]

Although infliximab is effective within 2 weeks and has been reported to achieve long-lasting remissions in patients with psoriasis, it has also been associated with several adverse events related to its chimeric nature; these include immediate infusion reactions (fever, chills and allergic reactions), serum sickness reactions and development of neutralising antibodies.[78-80] While addition of methotrexate could prevent the formation of anti-infliximab antibodies,[80] infliximab has been licensed as monotherapy for psoriasis.[81]

Like etanercept and other TNFα antagonists, infliximab is also associated with potential risks of drug-induced lupus, lymphomas, CHF and opportunistic infections, such as tuberculosis.[6,52,80,82] However, because of the higher incidence of tuberculosis in patients treated with infliximab compared with etanercept, the FDA requires tuberculosis screening before initiation of treatment with infliximab.[83]

Wallis et al.[84] found that the risk of granulomatous infection was 3.25-fold greater among patients who received infliximab than among those who received etanercept. The clustering of such reports shortly after initiation of treatment with infliximab is consistent with reactivation of latent infection. These data also demonstrate that, despite sharing a common therapeutic target, etanercept and infliximab differ in their effects on pre-existing granulomas. Indeed, given the multiple actions of TNFα in different immune pathways, further investigations are required to elucidate the differences between these two drugs. There are currently no data comparing the safety of etanercept with infliximab.

4. Conclusions

The different conventional systemic treatments used for psoriasis to date, including phototherapy,[85,86] are associated with multiple adverse events that require continuous monitoring of patients and their laboratory parameters. This causes significant inconvenience for patients and ultimately affects their quality of life. The problem has motivated the search for new, safe and effective long-term treatment options that do not impair patients' lifestyles.

Etanercept has demonstrated marked efficacy in the treatment of psoriasis and other inflammatory diseases such as psoriatic arthritis, rheumatoid arthritis and juvenile rheumatoid arthritis. The fast clinical response to treatment with etanercept underlines the important role of TNFα in such conditions

and the potent inhibitory effect of etanercept on this cytokine.[62,63] The drug is well tolerated and has been shown to have an excellent safety profile with long-term use; this manifests as a very low incidence of adverse events, including infections, malignancies, reactions at the injection site, laboratory test abnormalities and formation of anti-etanercept antibodies.

Another important consideration is that etanercept is easy to use and can be self-administered by the patient. This decreases the high number of ambulatory visits or laboratory monitoring tests required with other biological agents, e.g. infliximab, that require administration in the physician office, again clearly improving patient's quality of life. Furthermore, while the onset of action of etanercept may not be as rapid as that of infliximab, the available data suggest that etanercept is the safer drug.[79,80]

It is hoped that this review will encourage clinicians to reconsider treatment of patients with psoriasis in the future and to consider the early introduction of etanercept and other biological therapies that have been shown to be less toxic than other drugs traditionally used in the treatment of psoriasis. This will mean that prescribers will need to become familiar with this new generation of drugs and not be reluctant to use them. The safety and efficacy of these agents are supported by multiple clinical studies in psoriasis and other conditions. This is in contrast with the situation pertaining to conventional anti-psoriasis therapies, which are often used on the basis of personal clinical experience and in the absence of results obtained from rigorous scientific studies.

Acknowledgements

Dr Sánchez Carazo has received two grants from Wyeth in relation to symposia on the use of etanercept for psoriasis, has been a member of consultative committees for Wyeth, and has conducted clinical studies for Wyeth. Dr Mahiques Santos and Dr Oliver Martinez have no conflicts of interest directly relevant to the content of this review. No sources of funding were used in the preparation of this review. The authors would like to thank Wyeth for providing assistance in locating some bibliographic material used in the writing of this review.

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