

Efalizumab

recommended for approval by the European Medicines Agency (EMA)

The first in a new class of biological treatments for psoriasis has been recommended for approval by the European Medicines Agency (EMA). Efalizumab is self administered treatment indicated for psoriasis via once a week injection. Trials for the use of efalizumab in psoriatic arthritis were stopped earlier this year because of lack of efficacy.

Efalizumab is not the only biological therapy on or near the market, at least in the US. There, alefacept, another T cell-targeting therapy that acts by destroying the lymphocytes associated with the disease.

Meanwhile, etanercept was also recommended for approval in psoriasis earlier this year, and is on course to be the first anti-TNF drug cleared for this indication. Alefacept was turned down by the EMA last year, despite being cleared in the US. The agency is demanding head-to-head trials with approved therapies - such as cyclosporine, methotrexate or oral retinoids - before it will back the drug.

Biologics have emerged as alternatives to systemic therapy that offer not only much more convenient treatment - a single weekly injection in the case of efalizumab - but also improved efficacy and fewer side effects.

Competitive position

But despite its promise, efalizumab and other biologics cannot help every patient. For example, around 25 per cent of patients in the CLEAR study had no response at all to efalizumab, and manufacturer Serono now has a pharmacogenetic programme ongoing trying to determine the genetic profile of responders versus non-responders.

It is estimated that at least six genes are involved in the disease, with the disease occurring once a patient is immunologically primed and a trigger event - such as an infection - takes place. Once it emerges, patients have psoriasis for life.

Looking further back in the pipeline, Serono is continuing to conduct basic research in psoriasis, and one focus is on the use of agents that bind DNA and switch off the disease.

Finally, there is the difficult issue of cost. In the US, efalizumab is priced at around \$14,000 a year, so its use is likely to be reserved for those patients whose lives

are significantly and severely impacted by the disease. A study published last year by Steven Feldman, a professor of dermatology at Wake Forest University School of Medicine, found that methotrexate costs about \$1,600 a year and phototherapy from \$3,600 to \$4,600, with cyclosporine coming in a little higher. In contrast, biologics range from \$16,000 to \$33,000 a year.

This has been reflected in the sales of the drug in the US. At one point tipped as a potential billion dollar drug, analysts have scaled back their expectations to the \$300-\$500 million range, at least in the short-term, as they believe it is likely to be used after the more established therapies. This pattern is likely to be the same for all biologics.

Efalizumab has seen somewhat slow take-up in the US - expected as doctors get accustomed to using the new drug - but it still brought in revenues of just under \$20 million in the first half of the year in the US alone.

How does it work?

Efalizumab works by blocking the activation of certain immune cells, called "T cells," and the migration of those cells into the skin. T cells are a type of white blood cell in the body that normally help us ward off foreign invaders and fight infection. In psoriasis, however, these T cells are mistakenly activated and there are too many of them in the skin. This triggers other immune responses that fuel the development of psoriasis lesions. By blocking T-cell activation and the movement of these cells into the skin, efalizumab interrupts the cycle of psoriasis, this can lead to improvement in signs and symptoms. In clinical trials efalizumab has not shown any significant improvement in psoriatic arthritis

Who can get it?

It is prescribed for adults with moderate to severe plaque psoriasis. The exclusions are people taking vaccines or with active serious infections. Caution is advised for the elderly, due to the already increased risk of infection for this age group. There is no data regarding use in pregnant woman or nursing mothers. Doctors will make a decision on clinical need. It is not licensed for use in children.

How is it used?

Patients take efalizumab at home once per week by giving themselves an injection

under the skin, similar to diabetes patients who give themselves insulin injections. Dosing is determined by body weight; a smaller dose is given for the first injection to help the body become accustomed to the medication. The course of treatment will be determined by your doctor (usually 12 weeks).

What are the side effects?

The most frequent side effects reported in clinical studies were:

- headache
- infections (usually upper respiratory infections)
- chills
- nausea
- flu syndrome
- fever
- back pain
- acne

These events happened most often after the first dose of efalizumab and may decrease after additional doses. These side effects are generally mild and did not cause most patients to stop taking efalizumab.

Efalizumab does suppress the immune system, which means it has the potential to increase the risk of infection. The most serious side effects were very rare, but included psoriasis relapse, serious infections and thrombocytopenia (low platelet counts).

Patient assessment of platelet counts is recommended. It is unknown at this time whether long-term use of efalizumab will result in an increased chance of developing malignancies. All patients should be given detailed information before they start to use efalizumab.

How do I get efalizumab?

Efalizumab is only prescribed by hospital doctors (Dermatologist). Certain criteria will need to be met in order to qualify, this may include failure or lack of efficacy of other treatments or therapies. The cost of efalizumab may have an impact on how efalizumab is prescribed.

Efalizumab is known commercially as Raptiva and is marketed in the UK by Serono.

This information has been prepared by the Psoriatic Arthropathy Alliance and should not be used as a replacement for advice from your doctor.

Always consult your doctor.