Ixekizumab

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Approved indication: psoriasis

Taltz (Eli Lilly)
1 mL single-dose prefilled pen
Australian Medicines Handbook section 8.2.1

Ixekizumab is indicated for moderate–severe plaque psoriasis. Like secukinumab,[1] it is a monoclonal antibody that targets interleukin 17A. This cytokine is involved in the activation and proliferation of keratinocytes so blocking its action aims to reduce the severity of psoriasis.

This drug has been investigated in three main trials – UNCOVER-1, -2 and -3.[2,3] In total, 3866 people requiring systemic treatment or phototherapy for their psoriasis were enrolled in the studies. Subcutaneous ixekizumab 80 mg (every 2 or 4 weeks) was compared to placebo in the UNCOVER-1 trial[2] and to placebo and subcutaneous etanercept 50 mg (twice a week) in the UNCOVER-2 and -3 trials.[3] The primary outcome of the trials was at least a 75% reduction in patients' Psoriasis Area and Severity Index (PASI75) score and a score of 0 (clear) or 1 (minimal psoriasis) on the six-point static Physician Global Assessment (sPGA) after 12 weeks of treatment.

At baseline, the patients had psoriasis on 25–29% of their skin. After 12 weeks, over 80% of the people who received fortnightly ixekizumab responded and reached the primary endpoint (see Table).[2,3] Both 2- and 4-week regimens of the drug were significantly better than placebo and etanercept. Differences in the efficacy of ixekizumab over etanercept were apparent within the first two weeks of treatment. In the UNCOVER-2 and -3 trials, around 30–40% of patients given ixekizumab had a complete resolution of their psoriatic plaques compared with 0.6% (1 of 168 patients) and 0% in the placebo groups and 5.3% and 7.3% in the etanercept groups.[3]

In two of the trials (UNCOVER-1 and -2), patients who had responded to ixekizumab treatment in the first 12 weeks (sPGA 0, 1) were randomised to ixekizumab or placebo for a further 48 weeks. At the end of these extension studies, 74.6% of the 181 patients who had originally responded to fortnightly ixekizumab injections continued to respond to ixekizumab given every four weeks. This compared with only 7.4% of the 203 patients who were switched to placebo.

The most common adverse events with ixekizumab were mild–moderate injection-site reactions which occurred in 16.8% of those receiving fortnightly treatment. This was followed by upper respiratory

Table **Efficacy of ixekizumab in moderate–severe plaque psoriasis**

Trial	No. of patients	Treatment arm*	Efficacy endpoints†	
			PASI75	sPGA (0, 1)
UNCOVER-1	433	ixekizumab every 2 weeks	89.1%	81.8%
	432	ixekizumab every 4 weeks	82.6%	76.4%
	431	placebo	3.9%	3.2%
UNCOVER-2	351	ixekizumab every 2 weeks	89.7%	83.2%
	347	ixekizumab every 4 weeks	77.5%	72.9%
	168	placebo	2.4%	2.4%
	358	etanercept	41.6%	36%
UNCOVER-3	385	ixekizumab every 2 weeks	87.3%	80.5%
	386	ixekizumab every 4 weeks	84.2%	75.4%
	193	placebo	7.3%	6.7%
	382	etanercept	53.4%	41.6%

* Patients were given subcutaneous injections of an active treatment or placebo for 12 weeks. Those in the ixekizumab arm received a 160 mg loading dose followed by 80 mg doses every 2 or 4 weeks. Etanercept 50 mg was given twice weekly.

† Proportion of patients who had at least a 75% reduction in their Psoriasis Area and Severity Index score (PASI75) from baseline to week 12 and a score of 0 (clear) or 1 (minimal psoriasis) on the static Physician Global Assessment (sPGA) after 12 weeks of treatment. sPGA is a 6 category scale from 0 (clear) to 5 (very severe) of plaque thickness, erythema and scaling.

Source: References 2, 3

tract infection (14%), nausea (2%), oropharyngeal pain (1.4%) and tinea infection (1.5%). Oral and vaginal candidiasis were also reported, as was neutropenia. As there is an increased risk of infection, caution is urged if ixekizumab is given to people with chronic or active infection. Patients should be tested for tuberculosis before treatment and live vaccines are not recommended.

Patients can have hypersensitivity reactions to ixekizumab, and 9–17% of patients developed antibodies to treatment. However, most of these cases were not associated with reduced efficacy.

Crohn's disease and ulcerative colitis, including exacerbations, were more common with ixekizumab than with placebo (0.1–0.2% vs 0%). People with inflammatory bowel disease should therefore be monitored closely.

There have been no drug interaction studies with ixekizumab and it has not been assessed in pregnant or breastfeeding women. In studies on monkeys, the drug crossed the placenta but did not appear to be toxic to the fetus. It was also excreted at low levels in the breastmilk of lactating monkeys. It is not known if ixekizumab affects fertility.

The recommended regimen for ixekizumab is a 160 mg loading dose as two subcutaneous injections. This should be followed by a single 80 mg injection every two weeks until week 12, then every four weeks.

Ixekizumab seems to be very effective for people with moderate–severe plaque psoriasis in the short term. It also appeared to be relatively safe but, because of its effects on the immune system, patients need to be monitored for infections. As ixekizumab probably needs to be continued indefinitely, it will be important to find out what the long-term safety of this drug is and how it compares to other biological drugs for psoriasis such as secukinumab, ustekinumab, adalimumab and infliximab. Ixekizumab has also shown efficacy in psoriatic arthritis.[4]

[X] manufacturer did not respond to request for data

REFERENCES

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, and the European Medicines Agency.