Guselkumab

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Approved indication: plaque psoriasis

Tremfya (Janssen-Cilag)
prefilled syringe containing 100 mg/mL solution
Australian Medicines Handbook section 8.2.1, Immunosuppressants

Interleukins are signalling molecules involved in the regulation of the immune system. Changes in interleukins can upset this regulation and cause immune-mediated diseases. Increases in interleukins 17 and 23 can lead to the abnormal proliferation of keratinocytes seen in psoriatic skin. These interleukins have therefore become the targets for treatment when systemic therapy is needed for moderate to severe psoriasis. Interleukin 17 is a target for the monoclonal antibodies ixekizumab and secukinumab, while interleukin 23 is the target of tildrakizumab and ustekinumab.

Guselkumab is another monoclonal antibody. It binds to a subunit of interleukin 23. This prevents the interleukin from binding to its receptor so cell proliferation should be reduced.

The antibody has to be given by subcutaneous injection. A maximum concentration is reached 5.5 days later and with the recommended regimen a steady state is reached at 20 weeks. The antibody is probably catabolised and has a half-life of about 18 days.

The main efficacy studies of guselkumab included two double-blind, placebo-controlled phase III trials in patients with moderate to severe psoriasis (Table).[1,2] Guselkumab 100 mg was injected at weeks 0, 4 and then every 8 weeks. Adalimumab, a tumour necrosis factor inhibitor, was given as an active comparator. The primary outcomes were improvements in the Investigator Global Assessment and the Psoriasis Area and Severity Index (PASI). Although the trials lasted for 48 weeks, the primary end points were assessed at 16 weeks.

In the first trial (VOYAGE 1) 329 patients were randomised to receive guselkumab, 334 adalimumab and 174 placebo. After 16 weeks of treatment with guselkumab the psoriasis had cleared or was minimal in 85.1% of the patients and 73.3% had achieved at least a 90% reduction in the PASI score (PASI 90). The corresponding figures were significantly lower for adalimumab (65.9% and 49.7%) and placebo (6.9% and 2.9%). Patients in the placebo group were then switched to guselkumab and by 48 weeks they had achieved similar responses to those seen in patients who took guselkumab for the whole trial. The advantage over adalimumab was also maintained at 48 weeks.[1]

The second trial (VOYAGE 2) had a similar design with 496 patients randomised to guselkumab, 248 to adalimumab and 248 to placebo, switching to guselkumab after 16 weeks. In addition, at 28 weeks patients who responded to guselkumab were re-randomised to continue it or switch to placebo. Those switched to placebo could be re-treated if the psoriasis relapsed. After 16 weeks the psoriasis was minimal or had cleared in 84.1% of the guselkumab group, 67.7% of the adalimumab group and 8.5% of the placebo group. The respective results for PASI 90 were 70%, 46.8% and 2.4%. These responses were sustained in patients who continued taking guselkumab throughout the trial. For those switched to placebo it took about 15 weeks for the benefit

Table **Sixteen-week efficacy of guselkumab in moderate to severe plaque psoriasis**

Trial	Treatment*	Number of patients	Proportion of patients achieving primary end points	
			Minimal or cleared psoriasis %	PASI 90 %
VOYAGE 1[1]	guselkumab	329	85.1	73.3
	adalimumab	334	65.9	49.7
	placebo	174	6.9	2.9
VOYAGE 2[2]	guselkumab	496	84.1	70
	adalimumab	248	67.7	46.8
	placebo	248	8.5	2.4

* Regimens given by subcutaneous injection:
- guselkumab 100 mg at weeks 0 and 4 then every 8 weeks
- adalimumab 80 mg at week 0, 40 mg at week 1 then every 2 weeks

PASI 90 Improvement of at least 90% in the Psoriasis Area and Severity Index

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(PASI 90) to be lost. At 48 weeks 36.8% of these patients still had a PASI 90 response compared with 88.6% of those who continued treatment with guselkumab.[2]

In VOYAGE 2, 112 patients who did not respond to adalimumab were switched to guselkumab at week 28. By week 48, 66% of these patients had achieved a PASI 90 response.[2]

Another trial (NAVIGATE) looked at patients who did not respond to ustekinumab. After 16 weeks of treatment with ustekinumab 133 patients with an inadequate response were randomised to continue ustekinumab while 135 switched to guselkumab. The end point of the trial was the number of visits at which the investigators assessed the psoriasis as cleared or minimal. Between 28 and 40 weeks this outcome had been achieved at a mean of 1.5 visits with guselkumab and 0.7 visits with ustekinumab. The proportions of patients with minimal or cleared psoriasis at week 52 were 36.3% with guselkumab and 17.3% with continued ustekinumab.[3]

Infections were the most frequent adverse events in the clinical trials.[1-3] These were mainly upper respiratory tract infections. Injection-site reactions were also common. Some patients develop antibodies to guselkumab and serious hypersensitivity reactions have occurred. In view of the risk of reactivation, patients should be screened for tuberculosis before starting guselkumab. Live vaccines should not be used during treatment or for 12 weeks afterwards. Guselkumab has not been studied in human pregnancy or lactation. Whether guselkumab significantly increases the risk of malignancy is uncertain.

Biological therapies can be considered when a patient with moderate to severe plaque psoriasis requires systemic therapy or phototherapy. The trials show that guselkumab has greater efficacy than placebo and adalimumab.[1,2] It can also be considered for patients who do not respond to ustekinumab.[3] As the effects of guselkumab wear off after the drug is stopped, treatment may need to be continued for a longer duration than in the trials. This will require additional monitoring of its safety.

T manufacturer provided the AusPAR and the product information

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, the European Medicines Agency and the Therapeutic Goods Administration.