NEW DRUGS

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Emicizumab

Approved indication: haemophilia A

Hemlibra (Roche)
Vials containing 105 mg/0.7 mL
Australian Medicines Handbook Appendix A

Patients with haemophilia A lack coagulation factor VIII. In the coagulation cascade this factor interacts with factor IX to activate factor X. A deficiency of factor VIII puts the patient at risk of prolonged bleeding. This can be addressed by infusions of factor VIII, however they can cause the development of antibodies which then inhibit factor VIII. One approach to this problem has been to treat the patient with factor VIII inhibitor bypassing fraction. A new approach is using emicizumab. This genetically engineered monoclonal antibody overcomes the lack of factor VIII by bridging factors IX and X to restore haemostasis.

Emicizumab is given by subcutaneous injection. There is some variation in bioavailability according to the injection site, but injections can be rotated around the abdomen, thighs and upper outer arms. The drug has an absorption half-life of 1.7 days and an elimination half-life of 28 days. It is probably catabolised. Age and the presence of factor VIII inhibitors have no clinically important effects on the pharmacokinetics of emicizumab. As the drug alters coagulation it will affect tests based on intrinsic clotting, such as the activated partial thromboplastin time.

The main trial of emicizumab in patients with factor VIII inhibitors enrolled patients aged 12 years and above. Those randomised to receive prophylaxis with emicizumab were injected with a weekly dose of 3 mg/kg for four weeks followed by 1.5 mg/kg every week. The main outcome of this open-label trial was assessed in patients who had previously had episodic treatment, rather than prophylaxis, with bypassing products. After 24 weeks the annualised rate of bleeds requiring treatment was 2.9 events in 35 patients receiving emicizumab prophylaxis. This was significantly lower than the rate of 23.3 events in a control group of 18 patients. There was no bleeding at all in 63% of the emicizumab group. In another group of 24 patients who had previously used bypassing products for prophylaxis, the bleeding rate fell from 15.7 events/year to 3.3 events/year with emicizumab prophylaxis.[1]

The full results of an open-label, paediatric trial have not yet been published. An interim efficacy analysis included 57 children younger than 12 years. In 23 children who had prophylaxis with emicizumab for at least 12 weeks the annualised bleeding rate was 2.9. There were no bleeds in 64.9% of the children.[2]

Emicizumab has also been studied as prophylaxis for patients who have haemophilia A but no factor VIII inhibitors. The trial focused on patients who had previously been managed with episodic factor VIII, given when required. After the loading doses, patients who had been randomised to receive prophylaxis with emicizumab were given either 1.5 mg/kg every week or 3 mg/kg every two weeks. After a study period of at least 24 weeks, the annualised rate of bleeds requiring treatment was 1.5 in the 36 patients given weekly injections and 1.3 in the 35 patients given fortnightly injections. The rate was 38.2 in a group of 18 patients who received no prophylaxis. There was no bleeding at all in 50% of those treated weekly and 40% of those treated fortnightly.[3]

In the main trial of patients with inhibitors the most frequent adverse effect of emicizumab was injection-site reactions. Other common reactions included headache, fatigue and arthralgia.[1] As emicizumab acts on the clotting system there is a risk of thrombotic adverse effects. In the trial these included thrombotic microangiopathy, thrombophlebitis and cavernous sinus thrombosis. The thrombotic microangiopathy could be related to the patients also being treated with activated prothrombin complex.[1] Patients can develop antibodies against emicizumab.

Although data are currently limited, emicizumab appears to be an advance. As it can be given once a week it has an advantage over other prophylactic regimens. Less frequent dosing is being studied in children.

T T manufacturer provided additional useful information

REFERENCES

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3. Mahlangu J, Oldenburg J, Paz-Priel I, Negrier C, Niggli M, Mancuso E, et al. Emicizumab prophylaxis in patients who have hemophilia A without inhibitors. N Engl J Med 2018;379:811-22. https://doi.org/10.1056/NEJMoa1803550

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.