AWMSG Secretariat Assessment Report – Limited submission

Evolocumab (Repatha®▼) 140 mg solution for injection in prefilled pen or syringe

Company: Amgen Limited

Licensed indication under consideration:

Evolocumab (Repatha®▼) for the treatment of adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.

Marketing authorisation date: 17 July 2015

Limited submission details

A full submission was originally requested by AWTTC as evolocumab is a new medicine licensed for a new therapeutic indication.

However a National Institute for Health and Care Excellence (NICE) single technology appraisal (STA) is currently in progress for primary hypercholesterolaemia (heterozygous familial and non-familial) and mixed dyslipidaemia and a Final Appraisal Determination (FAD) has been published which recommends evolocumab as an option for treating primary hypercholesterolaemia or mixed dyslipidaemia.

In view of the NICE positive FAD being published and pending the publication of NICE positive guidance AWTTC have decided to proceed with the licensed indication for homozygous familial hypercholesterolaemia as it is considered a minor licence extension with minimal budgetary impact.

Comparator(s)

- The company has suggested that evolocumab will be used in conjunction with existing treatments for homozygous familial hypercholesterolaemia (HoFH) and therefore no comparator applies. A clinical expert contacted by AWTTC suggested that evolocumab was likely to be used alongside apheresis in the majority of cases.

Clinical effectiveness

- The Committee for Medicinal Products for Human Use (CHMP) recognise that although there are a number of conventional treatment strategies available to achieve low-density lipoprotein cholesterol (LDL-C) control, these may not result in adequate control in patients with HoFH to be sufficiently effective or their use may be limited by toxicity. CHMP highlighted that there was an undisputed medical need for new effective and well tolerated treatments of lipid disorders. AWTTC sought clinical opinion suggests that there is an unmet clinical need for suitable treatment options for patients in Wales.
- The company submission included two phase II/III studies (TESLA Part B and

TAUSSIG) to demonstrate the safety, tolerability and efficacy of evolocumab in subjects with HoFH.

- TESLA Part B was a 12-week, double blind, randomised (2:1), placebo-controlled, multi-centre phase III study in patients (n = 49) ≥ 12 years of age. Results demonstrated that when added to stable lipid lowering therapy; at 12 weeks evolocumab resulted in a 23.1% reduction in LDL-C levels from baseline (95% confidence interval [CI] −30.7, −15.4; p < 0.0001). The study excluded patients who had received lipoprotein apheresis within eight weeks before screening.
- TAUSSIG is an on-going, open-label phase II/III study enrolling subjects (≥ 12 years) who completed TESLA as well as de novo subjects with severe familial hypercholesterolaemia, including HoFH (n = 100). Results were similar to the TESLA part B study; 20.9% and 23.4% of HoFH subjects had a reduction in LDL-C from baseline by week 12 (n = 94) and week 24 (n = 67), respectively. At week 48 (n = 30) there was an 18.6% reduction observed in LDL-C levels.
- Patients receiving apheresis observed slightly lower reductions in LDL-C at all time points between 12 and 36 weeks (10–20% in HoFH patients on apheresis compared to 20–30% in HoFH patients not on apheresis). The company state that the additional LDL-C reduction experienced with evolocumab in patients already receiving apheresis may allow patients to receive apheresis less frequently. It is unclear whether this will occur in clinical practice.
- Treatment-emergent adverse events across both studies with evolocumab were similar to those with placebo, and the overall safety profile was similar to that in the overall clinical trial programme for evolocumab. No subjects tested positive for neutralising antibodies
- Long term efficacy data in HoFH patients was based on a limited number of patients, which is to be expected considering the rarity of the disease.
- The rates of early-onset and premature coronary heart disease events in patients with HoFH are high. Although the reduction in LDL-C observed with statin therapy is considered an established surrogate marker for cardiovascular risk reduction, this has not yet been demonstrated for newer therapies such as evolocumab treatment.

Budget impact

- The company estimates that three patients in Wales with HoFH would be eligible for treatment with evolocumab, based on an estimated annual prevalence of one person per million. A clinical expert confirmed that that this estimate was reasonable for the Welsh population.
- [commercial in confidence text removed]

Additional information

AWTTC is of the opinion that, if recommended, evolocumab (Repatha®▼) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

Evidence search

Date of evidence search: 3 March 2016
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. evolocumab (Repatha®▼) 40 mg solution for injection in prefilled pen or syringe. Reference number: 2866. May 2016