Scottish Medicines Consortium

Bemiparin, 2500 IU in 0.2 ml and 3500 IU in 0.2 ml, injection for sub-cutaneous administration (Zibor®) No. (205/05)

Amdipharm

New chemical entity: prevention of clotting in the extracorporeal circuit during haemodialysis

9 September 2005

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission

Bemiparin (Zibor®) is not recommended for use within NHS Scotland for the prevention of clotting in the extracorporeal circuit during haemodialysis.

It showed similar efficacy to unfractionated heparin in preventing coagulation in the extracorporeal circuit but has not been compared with other low molecular weight heparins. No evidence of the cost effectiveness of bemiparin during haemodialysis has been presented by the manufacturer.

Overleaf is the detailed advice on this product.

Chairman
Scottish Medicines Consortium

Bemiparin, strength, injection for sub-cutaneous administration (Zibor®)

Licensed indication under review

Prevention of clotting in the extracorporeal circuit during haemodialysis.

Dosing information under review

For patients requiring repeated haemodialysis of no longer than 4 hours in duration and with no risk of bleeding, inject a single dose in the form of a bolus into the arterial line at the beginning of the dialysis session. For patients weighing less than 60 kg, the dose will be 2500 IU. For those over 60 kg, it will be 3500 IU.

UK launch date

November 2003

Comparator medications

Unfractionated heparin Low molecular weight heparins: dalteparin sodium (Fragmin®), enoxaparin sodium (Clexane®), tinzaparin sodium (Innohep®).

Cost per treatment period and relevant comparators

For comparative purposes, prices given below are for a single dialysis session (patients on long term dialysis) lasting 6 hours at the recommended dose of low molecular weight heparins licensed for this indication. Where dosage recommendations are based on body weight, a weight of 70 kg has been assumed. Dosing may differ in different circumstances e.g. for short-term dialysis, dialysis in acute renal failure and according to the patient risk factors.

Preparation	**Dose**	**Cost per session**
Bemiparin 3500 IU in 0.35 ml syringe	**3500 IU sc for patients >60 kg**	**£4.50**
Dalteparin 10 000 IU in 1.0ml or 4.0 ml vial	30-40 IU/kg followed by 10-15 IU/kg/hour	£5.12
Enoxaparin 120 mg in 0.8 ml or 150 mg in 1.0 ml syringe	1 mg/kg followed by 0.5 to 1.0 mg/kg	£9.77 to £11.10
Tinzaparin 3500 IU in 0.35 ml syringe	2500 IU followed by 750 IU/hour	£5.54

Summary of evidence on comparative efficacy

Heparin binds to antithrombin (AT) and inhibits a number of clotting factors, including factors IIa (thrombin) and Xa. Low molecular weight heparins (LMWH) are obtained by chemical depolymerisation and fractionation. Amongst other differences, this increases their ability to inhibit Factor Xa but decreases their ability to bind to AT and inhibit IIa. It is thought that a high Xa/IIa ratio may lead to greater antithrombotic activity without increasing the risk of bleeding. Compared with other LMWH, bemiparin has a particularly high Xa/IIa ratio. It also alters the pharmacokinetic profile, allowing less frequent dosing.

An open, cross-over, randomised clinical trial was performed to compare the efficacy and safety of bemiparin and unfractionated heparin (UFH) for the prevention of clotting in the extracorporeal circuit during haemodialysis in patients with severe chronic renal failure. Bemiparin was administered as a single dose bolus injection into the arterial line of the extracorporeal circuit at the beginning of each haemodialysis session. After an initial dose adjustment phase to achieve a mean plasma anti-Xa activity between 0.5-0.8 IU/ml, the bemiparin dose to be used in the second phase was 2500 IU in patients below 60 kg and 3500 IU in those above 60 kg. During the period on UFH, an initial 1000 IU bolus was administered into the arterial line of the extracorporeal circuit, followed by a maintenance dose of 1,000 IU/h. A total of 2815 haemodialysis sessions in 67 patients were assessed, of which 1426 were performed with bemiparin and 1389 with UFH. The mean duration of the haemodialysis sessions was 3.9 hours. The percentage of haemodialysis sessions in which some degree of coagulation occurred in the extracorporeal circuit, as quantified by a visual scale graded from 0 (no clots) to 4 (total obstruction), was similar with bemiparin and UFH (3.5% vs 4.1%). Anti-Xa levels were significantly higher during the haemodialysis sessions performed with bemiparin (0.5 vs 0.2 IU/ml; $p < 0.001$).

Summary of evidence on comparative safety

There were no major bleeding events during this study and the rates of bleeding of the arteriovenous fistula were similar in both groups.

Summary of clinical effectiveness issues

Bemiparin showed similar efficacy and safety to UFH in preventing coagulation in the extracorporeal circuit during haemodialysis in patients with chronic renal failure. No comparative data with other low molecular weight heparins (LMWHs) are presented.

Summary of comparative health economic evidence

No evidence of the cost effectiveness of bemiparin during haemodialysis has been presented by the manufacturer in the submission.

The cost effectiveness of bemiparin in haemodialysis has not been demonstrated.

Budget impact

No estimate of the budget impact from using bemiparin in haemodialysis has been presented by the manufacturer.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

This assessment is based on data submitted by the applicant company up to and including 14 July 2005.

Drug prices are those available at the time the papers were issued to SMC for consideration.

The undernoted references were supplied with the submission.

Planes A. Review on bemiparin sodium – a new second generation low-molecular-weight heparin – and its applications in venous thromboembolism. Expert Opin Pharmacother. 2003;4:1551-1561.