Scottish Medicines Consortium

Bemiparin, 2500 IU in 0.2 ml injection for sub-cutaneous administration (Zibor®) No. (203/05)

Amdipharm

New chemical entity, prevention of thromboembolic disease: general surgery

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 thromboembolic disease in patients undergoing general surgery.

In one small study neither bemiparin nor unfractionated heparin was associated with thromboembolic complications following abdominal surgery but major bleeding and wound haematoma were more common with unfractionated heparin. Bemiparin has not been evaluated in other general surgery settings or against other low molecular weight heparins. No evidence of the cost effectiveness of bemiparin during general surgery has been presented by the manufacturer.

Overleaf is the detailed advice on this product.

Chairman
Scottish Medicines Consortium

Bemiparin 2500 IU injection for sub-cutaneous administration (Zibor®)

Licensed indication under review

Prevention of thromboembolic disease in patients undergoing general surgery (with a moderate risk of venous thromboembolism)..

Dosing information under review

On the day of surgery, 2500 IU to be administered sub-cutaneously (sc) 2 hours before or 6 hours after surgery. On subsequent days, 2500 IU every 24 hours.

UK launch date

November 2003

Comparator medications

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

Cost per treatment period and relevant comparators

The prices given below are for a peri-operative dose and seven days' post-operative treatment with the recommended dose of low molecular weight heparins licensed for this indication. In practice, doses may be adjusted in the light of monitoring and response, and duration will vary according to patient factors and response.

Preparation	Dose	Cost
Bemiparin 2500 IU in 0.2 ml syringe	**2500 IU sc on the day of surgery then daily for seven days**	**£27**
Dalteparin 2500 IU in 0.2ml syringe	2500 IU sc on the day of surgery then daily for seven days	£15
Enoxaparin 20 mg in 0.2 ml syringe	20 mg sc on the day of surgery then daily for seven days	£25
Reviparin 1432 IU in 0.25 ml syringe	1432 IU sc on the day of surgery then daily for seven days	£29
Tinzaparin 3500 IU in 0.35 ml syringe	3500 IU sc on the day of surgery then daily for seven days	£22

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.

For peri-operative prevention of venous thromboembolism (VTE), bemiparin at a dose of 2500 IU daily sub-cutaneously (sc) has been compared to unfractionated heparin (UFH) at a dose of 5000 IU sc twice daily in 166 patients aged >40 years and undergoing elective general abdominal surgery (classified as low/moderate risk of deep vein thrombosis (DVT) requiring a general anaesthetic for >30 minutes. Both were given for 7 days, commencing 2 hours before surgery. There were no cases of VTE, DVT (either symptomatic or when investigated by ultrasound), pulmonary embolism or death during the study.

Summary of evidence on comparative safety

In the trial involving prophylaxis for general surgery no patients experienced major bleeding with bemaparin compared with 5/82 cases in the UFH group (6.1%, $p<0.05$). Bemiparin was associated with a significantly lower incidence of wound haematoma than UFH (5/84 [6.0%] vs 15/82 [18%] $p<0.05$). No patients died during the study period.

Pooled data are available from published post-marketing surveillance studies involving 10,012 patients receiving bemiparin for surgical prophylaxis of VTE of whom 83% (at high risk of VTE) were exposed to 3500 IU per day and the remainder (at low/moderate risk of VTE) were exposed to 2500 IU/day. The incidences of adverse events were as follows: major bleeding 37/1012 (0.37%); mild to moderate thrombocytopenia, not requiring treatment discontinuation 47/1012 (0.47%) and mild to moderate injection site reaction 31/1012 (0.31%). There were 49 deaths (0.49%) of which three were considered thromboembolic. No case of spinal haematoma, type II severe thrombocytopenia, general allergic reaction, cutaneous necrosis or any other rare or unexpected adverse drug reaction was reported.

Summary of clinical effectiveness issues

Bemiparin has been shown to be as effective as unfractionated heparin in preventing venous thromboembolic events in patients undergoing abdominal surgery, with a lower rate of wound haematoma formation. No evidence is presented for its use in patients undergoing other general surgical procedures or for its efficacy and safety in comparison to other low-molecular-weight heparins.

Summary of comparative health economic evidence

No evidence of the cost effectiveness of bemiparin during general surgery has been presented by the manufacturer within the submission. The cost effectiveness of bemiparin in general surgery has not been demonstrated.

Budget impact

No estimate of the budget impact from using bemiparin in general surgery 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.

Moreno González E, Fontcuberta J, de la Llama F, EMRO (Grupo Estudio Multicéntrico RO-11). Prophylaxis of thromboembolic disease with RO-11 (ROVI), during abdominal surgery. Hepato-Gastroenterology. 1996; 43:744-7.