Idrabiotaparinux for the treatment of DVT and/or PE and secondary prevention of venous thromboembolism

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Idrabiotaparinux for the treatment of DVT and/or PE and secondary prevention of venous thromboembolism

Target group
- Symptomatic deep vein thrombosis (DVT) and/or pulmonary embolism (PE) – treatment and secondary prevention of recurrent venous thromboembolism (VTE).

Technology description
Idrabiotaparinux (biotinylated idraparinux, SSR-126517, SSR-126517E) is a long-acting selective pentasaccharide indirect factor Xa coagulation inhibitor, administered by once weekly subcutaneous (SC) injection at a dose of 3mg in patients without severe renal insufficiency and, after an initial dose of 3mg, at 1.8mg in those with renal insufficiency. Idrabiotaparinux is intended as a substitute for current long-term oral anticoagulation (e.g. with warfarin) and has no known food or drug interactions, no need for overlapping with other anticoagulants or for laboratory blood monitoring.

Idrabiotaparinux has superseded the development and marketing of the non-biotinylated idraparinux. Idrabiotaparinux is also in phase III clinical trials for the prevention of stroke in patients with atrial fibrillation (AF).

Innovation and/or advantages
Idrabiotaparinux will be the first once a week anticoagulant for the treatment of patients with VTE. It is intended to provide a predictable response with fixed dosing, no interactions with food, no requirement for overlapping with other therapy and no routine laboratory monitoring.

Developer
Sanofi-aventis.

Availability, launch or marketing dates, and licensing plans:
The company anticipate a licensing application for the treatment of DVT and/or PE and long-term prevention of VTE in 2009.

NHS or Government priority area:
This topic is relevant to:

Relevant guidance
NICE technology appraisals in development:
- Rivaroxaban for the prevention of VTE after elective orthopaedic surgery of the lower limb. Expected issue June 2009\(^1\).
- Dabigatran for the prevention of VTE after hip or knee replacement surgery in adults. Issue date to be confirmed\(^2\).
NICE clinical guidelines and service guidance:
- The prevention of venous thromboembolism in patients admitted to hospital. Expected issue Sept 2009³.
- Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in in-patients undergoing surgery. 2007⁴.
- Commissioning Guides: Anticoagulation therapy service. 2006⁵.
- British Committee for Standards in Haematology:
  - British safety indicators for inpatient and outpatient oral anticoagulant care. 2007⁷.
  - Care Guideline. Procedures for the outpatient management of patients with deep venous thrombosis. 2005⁹.
  - Care Guideline. Management of deep vein thrombosis (DVT) as an out-patient. 2003¹⁰.

Clinical need and burden of disease
There is a lack of reliable information on the incidence or prevalence of DVT and PE in the UK but it is estimated that around 5-10% of people with untreated DVT die from PE¹². In 2005 over 25,000 people in England died from VTE contracted in hospital following surgery¹³. Following an initial episode of VTE, the risk of recurrence within eight years is approximately 30%¹⁴,¹⁵.

It is estimated that around 500,000 people are currently prescribed oral anticoagulants in the UK¹⁶, of which the majority are on warfarin (around 470,000 in 2001)¹⁷. The use of warfarin is also associated with a relatively high incidence of medication errors, with 480 cases of harm or near harm and 92 deaths reported in the UK during 1990-2002¹⁷.

Existing comparators and treatments
The initial treatment of VTE is with intravenous heparin or subcutaneous (SC) low molecular weight heparin (LMWH) such as enoxaparin, bemiparin, dalteparin or tinzaparin, administered once or twice daily. An oral vitamin K antagonist (VKA, usually warfarin) is started at the same time and titrated using the International Normalised Ratio (INR). Warfarin is administered once daily for 3-6 months or longer with frequent INR monitoring and dose adjustment. Aacenocoumarol or phenindione can be used for patients allergic or resistant to warfarin.

Efficacy and safety
A 2008 review¹⁸ of idraparinux (the earlier non-biotinylated formulation) concluded that in patients with DVT, the efficacy and safety profile of idraparinux for 3 or 6 months was similar to that of heparin(s) plus VKA. Idraparinux was, however, less effective than standard therapy in patients with PE. Trials of idraparinux or placebo for 6 months following initial therapy for 6 months with either idraparinux or a VKA found that idraparinux reduced the recurrent rate of VTE from 3.7% to 1.0%¹⁹.

<table>
<thead>
<tr>
<th>Trial code, name, phase</th>
<th>EQUINOX (NCT00311090)²⁰; DVT; idrabiotaparinux vs. idraparinux; phase III</th>
<th>CASSIOPEA (NCT00345618)²¹; PE; idrabiotaparinux vs. vitamin K antagonist; phase III</th>
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<tr>
<td>Sponsor</td>
<td>Sanofi-aventis</td>
<td>Sanofi-aventis</td>
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<tr>
<td>Status</td>
<td>Ongoing: recruitment complete.</td>
<td>Ongoing: 1/3 of patients recruited.</td>
</tr>
</tbody>
</table>
Location USA, Canada, Europe, New Zealand, Australia, South Africa, Latin America, Turkey, Russia.

Design Randomised, double-blind, active control.

Participants in trial n=700; adults; acute symptomatic DVT of the lower limbs. Randomised to idrabiotaparinux 3.0mg or idraparinux 2.5mg (equimolar doses) SC once-weekly for 6 months.

Follow-up 3 and 6 months.

Primary outcome Bioequivalence; avidin neutralisation, pharmacokinetics; antithrombotic (anti-Xa) activity.

Secondary outcomes Symptomatic recurrent DVT/PE (fatal or not) <6 months; time to steady anti-Xa activity; safety - bleeding and deaths <6 months.

Expected reporting Expected reporting end 2008 or Q1 2009.

Expected reporting end 2010.

Estimated cost and cost impact
The cost of idrabiotaparinux is not yet known. A typical maintenance dose of warfarin (3-9mg daily) costs £1.20 - £1.38 per 28 days\(^a\).

Potential or intended impact – speculative

Patients
☑ Reduced morbidity ☐ Reduced mortality ☑ Improved quality of life for patients and/or carers: reduced need for regular monitoring
☐ Quicker, earlier or more accurate diagnosis or identification of disease ☐ Other: SC administration may be difficult for some patients; training required ☐ None identified

Services
☑ Increased use: SC injection replacing oral therapy ☐ Service reorganisation required ☐ Staff or training required
☐ Decreased use: reduced need for laboratory blood monitoring ☐ Other: ☐ None identified

Costs
☐ Increased unit cost compared to alternative ☐ Increased costs: more patients coming for treatment ☑ Increased costs: capital investment needed
☑ New costs: SC injection ☑ Savings: laboratory costs ☐ Other:

References


\(^a\) British National Formulary No. 55, March 2008.


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The views expressed in this publication are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health