Managing the discontinuation of bovine insulin

Bovine insulin will no longer be available from the end of this year. **Professor Nick Oliver**, Professor of Metabolism, Imperial College, London, and **Dr Shivani Misra**, Consultant in Metabolic Medicine, Imperial College Healthcare NHS Trust, present Diabetes UK’s recommendations for healthcare professionals whose patients will need to transition to an alternative insulin.

Bovine insulin preparations will be withdrawn from the end of 2017 owing to limited availability of the active ingredient. The predicted stock depletion is as follows:

<table>
<thead>
<tr>
<th>Description</th>
<th>Form</th>
<th>Predicted depletion date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypurin® Bovine Isophane</td>
<td>3ml Cartridges</td>
<td>December 2017 (product expiry)</td>
</tr>
<tr>
<td>Hypurin® Bovine Neutral</td>
<td>3ml Cartridges</td>
<td>June 2018</td>
</tr>
<tr>
<td>Hypurin® Bovine Neutral</td>
<td>10ml Vial</td>
<td>July 2018</td>
</tr>
<tr>
<td>Hypurin® Bovine Isophane</td>
<td>10ml Vial</td>
<td>December 2018</td>
</tr>
<tr>
<td>Hypurin® Bovine Lente (LZS)</td>
<td>10ml Vial</td>
<td>May 2019 (product expiry)</td>
</tr>
<tr>
<td>Hypurin® Bovine PZI</td>
<td>10ml Vial</td>
<td>August 2019</td>
</tr>
</tbody>
</table>

People with insulin-treated diabetes using bovine insulin preparations will continue to require insulin treatment, so will need to be changed to alternative, acceptable insulin preparations. Those using bovine insulins are likely to be an older population, with longer duration of diabetes, and may, therefore, have absolute insulin deficiency. These individuals will be at risk of impaired awareness of hypoglycaemia, predisposing to severe hypoglycaemia.

Use of bovine insulin has been associated with the presence of insulin auto-antibodies, which may impair the action of insulin. Porcine or human insulin analogues are likely to lower glucose levels more than the same dose of bovine insulins, and insulin dose titration may be difficult and unpredictable.

People with bovine insulin-treated diabetes are therefore a high-risk group and caution in the transition to a new insulin is paramount.

**Recommendations**

1. Transition from bovine insulin to a safe, acceptable alternative should be undertaken with diabetes specialist multidisciplinary team supervision.
2. Alternatives to bovine insulin include porcine insulin, human insulin and analogue insulin. Choice of insulin should be made with the patient and with particular consideration of the risk of hypoglycaemia. To ensure sustainability and minimise the risk of a second insulin change while optimising glucose levels, transition to human or analogue insulins may be preferred.
3. When selecting an appropriate alternative insulin, consider the duration of action, time to peak, and device.
4. Before changing to a different insulin, provide hypoglycaemia education to all patients, and their families and carers. Provide appropriate oral glucose preparations and intramuscular glucagon kits before transition, with training for all relevant people.
5. For people with a history of severe hypoglycaemia, insulin pump therapy may be considered, in line with NICE TA151.
6. Agree personalised treatment targets with the patient before transition, with an emphasis on safety and avoidance of hypoglycaemia.
7. Support people to self-monitor blood glucose frequently during transition. If there is history of severe hypoglycaemia, or impaired awareness of hypoglycaemia, consider continuous glucose monitoring in line with NICE NG17.
8. An insulin dose reduction of 10 per cent should be considered with initiation of the chosen replacement insulin preparation.
9. Specialists may consider measurement of insulin auto-antibodies prior to transition.
   a. Where the anti-insulin antibody titre is detectable, a further dose reduction (eg between 10 to 15 per cent) may be appropriate at transition.
   b. Where the anti-insulin antibody titre is very high, a greater initial dose reduction (>20 per cent) should be considered.
   c. The use of a small test dose of the new insulin, in a supervised environment, with frequent monitoring (for example on a metabolic day ward) may be considered where there are patient or healthcare professional concerns around detectable anti-insulin antibodies.

**Summary**

Bovine insulins are being withdrawn and all patients still using these insulins will need to change to different insulins. They are a vulnerable group and the change is likely to be challenging, with a high risk of hypoglycaemia and glucose instability. The change will require considerable education of patients, families and carers, and careful follow-up. Diabetes specialist multidisciplinary team supervision of this transition is essential.

These guidelines can also be found at [www.diabetes.org.uk/diagnosis-management-monitoring](http://www.diabetes.org.uk/diagnosis-management-monitoring)