

# The role of animal-sourced insulin in the treatment of type 1 diabetes and its availability

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### Abstract

As a result of a number of factors, the treatment of insulin-dependent diabetes has moved away from using insulin of beef or pork origin to using recombinant (biosynthetic) insulin preparations. However, some people with type 1 diabetes can manage their diabetes better using animal-sourced insulin. Despite dwindling options and decreased production, animal-sourced insulin—and pork insulin in particular—is still available on the Canadian market.

This communication describes the actions taken by Health Canada with respect to the availability of animal insulin.

**Keywords:** *insulin, pork insulin, beef insulin, recombinant insulin, biosynthetic insulin, type 1 diabetes*

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### Introduction

The discovery that insulin controls blood sugar was a vital contribution to the treatment of diabetes mellitus. Insulin has not only saved lives, it has also allowed most people with diabetes to live a relatively normal life. In its early days, insulin was extracted from bovine and porcine pancreases. However, a number of complex factors have resulted in a decline in the use of animal-sourced insulin. These factors include the development of recombinant (biosynthetic or rDNA-derived) insulin preparations with various lengths of activity; the emergence of prion diseases, most notably Bovine Spongiform Encephalopathy or “mad cow disease” in cattle, and the dwindling of beef insulin production and supply as a consequence; constant threats of a short-fall of animal pancreases used to produce an adequate supply of insulin; and other less clear factors.

### Current situation

Biosynthetic (recombinant) insulin, which is structurally similar to endogenously secreted insulin, was developed with the expectation that an insulin very similar to human endogenous insulin would neither cause immunological phenomena or elevate serum IgG levels, specifically in people with type 1 diabetes. However, over the past decade, some of those who contacted Health Canada reported that they experienced frequent and severe hypoglycemic episodes when undergoing treatment with biosynthetic insulin. In addition, these patients’ glycemic control was more even and consistent and they generally felt better and healthier while on insulin of animal origin. Health Canada also noted that some people reported that their level of antibodies in response to the biosynthetic insulin was higher than that to pork insulin and, more particularly, to beef insulin. Let’s recall that the immuno-

genicity of biosynthetic insulin is similar to that of highly purified pork insulin, to which it is considered clinically equivalent.

Hypoglycemia is the most common adverse effect of all insulin products, regardless of their type or origin. In certain cases—long duration of diabetes mellitus, the presence of diabetic neuropathy, the very strict control of diabetes mellitus, recurrent exposure to severe hypoglycemia or the age of the patients—the nature and intensity of the early warning signs of hypoglycemia (pallor, sweating, anxiety, headache, tachycardia and hunger) may be less pronounced. Hypoglycemia may also occur without recognizable symptoms and lead to confusion, loss of consciousness and/or convulsions.<sup>1</sup>

Impaired awareness of hypoglycemia, which may develop regardless of whether animal or biosynthetic insulin is used,<sup>2</sup> affects approximately 25% of people with type 1 diabetes.<sup>3</sup> Rates of severe hypoglycemia that require external assistance, that is, the administration of glucagon to raise blood glucose levels, are 5.1 times higher in those with impaired hypoglycemia awareness and 9.6 times higher in those with hypoglycemia unawareness.<sup>4,5</sup>

A systematic review conducted in 2005 and updated in 2009 “to assess the effects of different insulin species by evaluating their efficacy (in particular glycaemic control) and adverse effects profile (mainly hypoglycaemia)” showed no rele-

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vant clinical differences in either efficacy or adverse reactions between the different insulin preparations. However, high quality randomized clinical trials examining outcomes such as health-related quality of life or diabetic complications were never conducted.<sup>6,7</sup>

An Expert Advisory Panel on Insulin was convened to help Health Canada learn about the benefits of animal-sourced versus biosynthetic insulin as well as about labelling the insulin preparations.<sup>8</sup> One of the Panel's recommendations was to improve communications about the insulins of diverse origins. In addition, the Panel recommended that Health Canada continue to make animal-sourced insulins available for those patients with type 1 diabetes mellitus who achieve better metabolic control with this type of insulin; doing so is in keeping with the International Diabetes Federation's 2005 position statement on animal, biosynthetic and analogue insulins, which notes that no single insulin type will suit every person, and that maintaining a variety of insulins from which to select one that suits each patient best is ideal.<sup>9</sup> At the same time, the Panel noted that further research may be needed to elucidate the differences seen in/by certain patients when they use insulin of animal origin as opposed to biosynthetic/recombinant forms of insulin.

## Actions by Health Canada

Health Canada has undertaken a number of the activities recommended by the Expert Panel on communicating with the public and health professionals about animal-origin insulin, although the majority fall outside the direct responsibility and mandate of its regulatory arm. Health Canada has updated the product monographs for all marketed insulin products and, with the Public Health Agency of Canada, updated existing fact sheets on insulin and diabetes so as to include information about animal-sourced insulin.<sup>10</sup>

Health Canada acknowledges that pharmaceuticals are a shared responsibility between the federal, provincial and territorial governments. From the regulatory perspective Health Canada will continue

to communicate on the subject of animal insulin as needed, while respecting that drug coverage and the listing of treatments on formularies for reimbursement is a provincial and territorial responsibility. In addition, Health Canada has informed relevant stakeholders of the Panel's recommendations and is encouraging the adoption of these, including continued research to address the data gaps identified by the Panel.

Physicians can continue to prescribe Hypurin® Pork Regular and Neutral Protamine Hagedorn (NPH) insulin preparations, manufactured by Wockhardt UK Ltd., which continue to be marketed in Canada. Federal, provincial and territorial drug plans have processes to evaluate requests for compassionate access to animal-sourced insulin.

Beef insulin may also be obtained from Wockhardt UK, subject to availability, via Health Canada's Special Access Programme. Laboratorios Beta S.A. in Argentina produces some beef and pork insulin but they have neither obtained market authorization nor made their supply available in Canada.

## Conclusion

Despite the shift towards biosynthetic insulin in the treatment of type 1 diabetes in Canada, the need for animal-sourced insulin remains. There is some evidence to suggest that some patients have better metabolic and symptomatic control when receiving animal-sourced insulin and can therefore manage their diabetes more effectively. As a result, animal-sourced insulin remains available in Canada as a treatment option for health care professionals and patients. Given the need for animal-sourced insulin, Health Canada will continue to monitor the situation and work with stakeholders and manufacturers on the place in therapy and the availability of animal-sourced insulin in Canada.

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## References

1. Balodimos M, Root H. Hypoglycemic insulin reactions without warning symptoms. *J Am Med Assoc.* 1959;171(3):261-6.
2. MacLeod KM, Gold AE, Frier BM. Frequency, severity and symptomatology of hypoglycaemia: a comparative trial of human and porcine insulins in type 1 diabetic patients. *Diabet Med.* 1995 Feb;12(2):134-41.
3. Frier BM. How hypoglycaemia can affect the life of a person. *Diabetes Metab Res Rev.* 2008;24:87-92.
4. Gold AE, MacLeod KM, Frier BM. Frequency of severe hypoglycemia in patients with type I diabetes with impaired awareness of hypoglycemia. *Diabetes Care.* 1994;17(7):697-703.
5. Pedersen-Bjergaard U, Pramming S, Thorsteinsson B. Recall of severe hypoglycaemia and self-estimated state of awareness in type 1 diabetes. *Diabetes Metab Res Rev.* 2003;9(3):232-40.
6. Richter B, Neises G. 'Human' insulin versus animal insulin in people with diabetes mellitus. *Cochrane Database Syst Rev.* 2005 Jan 25;(1):CD003816.
7. Richter B, Neises G. 'Human' insulin versus animal insulin in people with diabetes mellitus (Review). *Cochrane Database Syst Rev.* 2009;(1).
8. Expert Advisory Panel on Insulin [Internet]. Ottawa (ON): Health Canada; March 2010 [cited 2010 August, archived by Health Canada 2013 June].
9. IDF Position Statement Animal, Human and Analogue Insulins [Internet]. Brussels (BE): International Diabetes Federation; March 2005 [cited 2010 Aug 11]. Available from: [http://www.modernes-tierisches-insulin.de/Downloads/patienten/idf\\_position\\_statement.pdf](http://www.modernes-tierisches-insulin.de/Downloads/patienten/idf_position_statement.pdf)
10. It's Your Health: Insulin Products [Internet]. Ottawa (ON): Health Canada; 2010 Jun [cited 2010 Aug 11]. Available from: <http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/med/insul-eng.php>