



PBS Post-Market  
Department of Health and Ageing  
MDP 900  
GPO Box 9848  
CANBERRA ACT 2601

2<sup>nd</sup> July, 2013

To Whom It May Concern,

*Re: Post Market Review of Products Used in the Management of Diabetes: Stage Three of the Review for Medicines Used in the Treatment of Type 2 Diabetes*

Sanofi is pleased to provide the following response to Stage 3<sup>1</sup> of the Post Market Review of Products used in the Management of Diabetes (Diabetes review). Sanofi, a global and diversified healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth platforms: diabetes solutions, human vaccines, innovative drugs, rare diseases, consumer healthcare, emerging markets and animal health. Sanofi is a manufacturer of products for the management of diabetes, including Lantus<sup>®</sup> and Apidra<sup>®</sup> which are listed on the Pharmaceutical Benefits Scheme (PBS) for use in the management of Type 1 and Type 2 diabetes. Lantus was first listed on the PBS on 1 October 2006 and Apidra was first listed on 1 July 2007.<sup>2</sup>

The health, social and economic burden from Type 2 diabetes (T2DM) in Australia is not in dispute as recognised by the government determination of diabetes as National Health Priority in 2007. There are around 371 million people worldwide affected by diabetes (8.3% of the global population), with numbers expected to increase to 552 million people with diabetes by 2030 according to the International Diabetes Federation (IDF). In the AIHW Australia's Health 2012<sup>3</sup> report the age-standardised prevalence of diabetes at 4% has more than doubled to 2007–08, with 986,900 people in Australia diagnosed with diabetes according to the 2011-12 Australian Health Survey. The overwhelming majority of people with diabetes have T2DM (85.3%). Of perhaps greatest concern is research which suggests the number of Australians with diabetes is greatly underestimated, with approximately 4 cases of T2DM undiagnosed for every 5 diagnosed cases.

The burden of diabetes on Australian society is high. In 2003 diabetes in Australia accounted for 8.3% of the total burden of disease. In 2010, diabetes was the seventh highest cause of disease-related death in Australia. One out of every 25 hospitalisations in 2009-2010 was attributed to diabetes and its complications. The total cost of T2DM is estimated at \$10.3 billion, due to carer costs (\$4.4 billion), lost productivity (\$4.1 billion), health system costs (\$1.1 billion) and obesity (\$1.1 billion).<sup>4</sup>

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<sup>1</sup> Focusses on 1) addressing the utilisation and patterns of treatment of PBS listed drugs for T2DM, and compare these with PBS restrictions and if this represents expected cost effective use and 2) consolidating the clinical evidence used to support current PBS listings of diabetes medicines listed since 2002, through Terms of Reference 1 to 4.

<sup>2</sup> PBS, 2013, <http://www.pbs.gov.au/medicine/item/9039R>, <http://www.pbs.gov.au/medicine/item/1921D-9224L> Accessed 10 June 2013

<sup>3</sup> AIHW 2012. Australia's health 2012. Australia's health no. 13. Cat. no. AUS 156. Canberra: AIHW.

<sup>4</sup> diabetes: the silent pandemic and its impact on Australia. Edited by Associate Professor Jonathan Shaw and Stephanie Tanamas, Baker IDI Heart and Diabetes Institute, with input from Diabetes Australia and Juvenile Diabetes Research Foundation (JDRF). <https://www.diabetesaustralia.com.au/Documents/DA/What's%20New/12.03.14%20Diabetes%20management%20booklet%20FINAL.pdf>



The value of primary prevention and the benefits in terms of the burden of T2DM is clear. However, the role of secondary prevention, through appropriate management which aims to stop the development of diabetic complications is equally critical. The average annual healthcare cost per person with diabetes and no associated complications is \$4,025 which increases sharply to a cost of \$9,645 per person in the case of micro- and macrovascular complications of diabetes. Clearly, a reduction in the severity of T2DM through appropriate management, ranging from lifestyle to medication, will not only result in cost savings in the health budget but also increased participation and productivity in the workforce and better health outcomes and quality of life for Australians.

### **Management of T2DM**

The primary target of diabetes therapy is to control blood glucose levels in order to minimise the occurrence of secondary complications. In the clinical setting, measurement of HbA1c assesses longer-term glycemic control. The general HbA1c target in people with type 2 diabetes is  $\leq 7\%$ .<sup>5</sup> More stringent goals, HbA1c ( $<6.5\%$ ), may be appropriate for selected individual patients, if this can be achieved without significant hypoglycaemia or other adverse effects of treatment. Appropriate patients might include those with short duration of diabetes, long life expectancy, and no significant cardiovascular disease (CVD). Less-stringent goals, HbA1c ( $<8\%$ ), may be appropriate for patients with a history of severe hypoglycaemia, limited life expectancy, advanced microvascular and macrovascular complications, extensive comorbid conditions, and those with longstanding diabetes in whom the general goal is difficult to attain despite previous interventions.

The landmark Diabetes Control and Complications Trial and the United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that achieving normal HbA1c levels can reduce the incidence and progression of microvascular complications, CV morbidity and importantly mortality. With every 1% reduction in HbA1c, a corresponding decrease of 37%, 43%, 21%, and 14% occurs in microvascular complications, amputation or mortality from peripheral vascular disease, mortality related to diabetes, and incidence of myocardial Infarction, respectively.<sup>6</sup>

Even with the development of newer medications to manage diabetes the increasing burden of disease is clear. These challenges need to be confronted in diabetes management and the range of therapies, existing and new, must be available to patients and clinicians. Advances in disease management including both oral and injectable therapies will be critical to our overall response to this epidemic.

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<sup>5</sup> Colagiuri S, Dickinson S, Girgis S, Colagiuri R. National Evidence Based Guideline for Blood Glucose Control in Type 2 Diabetes. Diabetes Australia and the NHMRC, Canberra 2009, Inzucchi SE, Bergenstal RM, Buse JB, et al. 2012. Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 35(6): 1364-1379); IDF Clinical Guidelines Task Force. Global Guideline for Type 2 Diabetes. Brussels, International Diabetes Federation, 2012.

<sup>6</sup> Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000; 321:405–12;



## The role of insulin in the management of diabetes

The challenge of effectively treating patients with T2DM continues to evolve with the development of newer treatment options and in an ideal world treatment practice guidelines would reflect each new development. However, the critical role of insulin in the management of diabetes, both T1DM and T2DM, has been undisputed over time as evidenced in the local and international treatment guidelines.<sup>5</sup>

In T1DM there is effectively no endogenous production of insulin therefore patients rely on insulin replacement therapy to normalise blood glucose levels. T2DM is a progressive disease where the function of beta cells diminishes over time which results in declining levels of endogenous insulin, similar to T1DM. Ultimately, the majority of patients with T2DM will require insulin therapy alone or in combination with other agents to maintain a normal glycaemic profile.<sup>5, 7</sup>

Although there are a multitude of therapies available for the management of diabetes there is evidence that HbA1c targets are not being met in Australian patients. The Changing Diabetes Map, which provides an overview of HbA1c values across a large sample of the Australian population with diabetes, demonstrates that in 2010 almost half (47%) of people with diabetes have an HbA1c greater than 7%. Evidence over the 4 years from 2004 to 2010 indicates the percentage of patients who have not reached target is consistent, ranging from 45% to 49%.<sup>8</sup> This is compounded by the fact patients are initially asymptomatic leading to delays in diagnosis, with epidemiological studies suggesting the onset of T2DM often occurs 5–10 years before clinical diagnosis. Early detection is critical as almost half of T2DM cases in Australia may remain undiagnosed even though patients are already experiencing complications.<sup>9</sup>

The long-term consequences of not achieving tight glycaemic control, which leads to greater complications, reduced life expectancy and compromised quality of life, are irrefutable.<sup>10</sup> Despite this, the commencement of insulin treatment is often delayed with many patients having significant periods of poorly managed diabetes before insulin treatment commences.<sup>11</sup> Even with the availability of newer medicines the most recent guidelines state insulin is likely to be the most effective agent in the 2<sup>nd</sup> and 3<sup>rd</sup> line setting.<sup>12</sup>

The National Diabetes Strategy<sup>9</sup> highlights the need for further action, significant commitment and investment which is required for the effective management of diabetes. One of the goals in the Strategy highlights the need to *Develop and implement national structured self-management education and support programs for type 1 and type 2 diabetes with particular focus on: Insulin commencement and ongoing therapy support* as part of the goal to prevent complications through optimal management and earlier diagnosis. As we see from Diabetes Australia the role of education is critical in ensuring patients with diabetes receive the most appropriate care and support which in turn maximises the chance of successful disease management, leading to healthier and more productive lives.

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<sup>7</sup> Nelson S & Palumbo P. 2006. Addition of Insulin to Oral Therapy in Patients with Type 2 Diabetes. *American Journal of Medical Sciences*; 331(5):257-263.

<sup>8</sup> The Mapping Glycaemic Control Across Australia (MGCAA) project, 2007. <http://www.glycomate.com/changingdiabetes/>

<sup>9</sup> Diabetes Australia, A National Diabetes Strategy and Action Plan, 2013.

<http://www.diabetesaustralia.com.au/PageFiles/3/National%20Diabetes%20Strategy%20and%20Action%20Plan.pdf>

<sup>10</sup> Goodall G, et al. 2009. The consequences of delaying insulin initiation in UK type 2 diabetes patients failing oral hyperglycaemic agents: a modelling study. *BMC Endocr Disord*. Oct 5;9:19.

<sup>11</sup> Davis T, Davis W, Bruce D. 2006. Glycaemic levels triggering intensification of therapy in type 2 diabetes in the community: the Fremantle Diabetes Study. *MJA*. 184 (7): 325-328.

<sup>12</sup> ADA/EASD joint position statement 2012, Inzucchi SE, Bergenstal RM, Buse JB et al. 2012. Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 35(6): 1364-1379



The need to consider the role of *prescriber education, amending restrictions, telephone authorities...* in ensuring the appropriate use of diabetes management options was flagged by the PBAC, at the April 2013 Special meeting.

The information provided in the Diabetes review indicates insulin is not part of Stage 3<sup>13</sup>, which is appropriate given the role of insulin in the effective long-term of management diabetes is undisputed. Indeed, evidence from the February 2013 DUSC review indicates that *DUSC further examined the utilisation of medicines for type 2 diabetes in a prevalent population of patients. ....and DUSC considered that the PBS restrictions do not align with recent clinical guidelines and the perceived place of newer medicines for type 2 diabetes in practice.*<sup>14</sup>

Our response reflects the primary focus of Stage 3 of the Diabetes review, that is, the newer anti-diabetic agents. Regardless of the focus of Stage 3 It is important to emphasise the timeframe for preparation of submission, six weeks from the opening of Stage 3, is insufficient to provide a comprehensive review of the anti-diabetic medicines to the standards required for applications for listing new medicines on the PBS. Coupled with this is the lack of clarity and consistency in advice to sponsors on the scope of the review across the diabetes management options. We believe joint stakeholder engagement in the early stages of determining the scope of this review would have benefited all parties and should be adopted as part of the process for the establishment of future reviews.

As the focus of Stage 3 of the Diabetes review is the newer medications for the management of T2DM Sanofi retains the right to respond should the outcomes of this stage of the Diabetes review recommend any changes to the circumstance of use of our products which have not been the focus of this stage of the review. Should the Committee require any additional information or would like to discuss our submission further we would welcome the opportunity.

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<sup>13</sup> Correspondence: Pharmaceutical Policy Branch, Attachment B: Notice of upcoming public call for submissions: stage three of the post-market review of products used for the treatment of diabetes; Department of Health and Ageing, 3 May 2013.

<sup>14</sup> Post-Market Review of Products Used in the Management of Diabetes, 2013. <http://www.pbs.gov.au/info/reviews/diabetes>