Medtronic Response to Stage 2 of the Post Market Review on Insulin Pumps

Executive Summary

Currently used by one in 10 people with type 1 diabetes (T1D), insulin pumps are a mainstream intensive insulin regimen for achieving tight glycaemic control. The evidence suggests there is a high clinical need for insulin pump therapy as an alternative intensive insulin regimen where multiple daily injections are inappropriate, impractical or people fail to achieve glucose control targets. However, access to insulin pump therapy is currently limited.

Providing appropriate access to insulin pumps under the Government funded Insulin Pump Program is an investment in the health of Australians with T1D. Increasing this investment, including the extension of funding to adults, is required to improve short and long term clinical and patient relevant outcomes for all eligible Australian patients with T1D.

There are clinical and social benefits for the use of insulin pumps. Cost -effectiveness of the therapy continues to be evaluated and is realised in relation to the associated improved clinical and social benefits of the technology. Such benefits include the potential to improve diabetes management outcomes resulting in decreased costs associated with the healthcare and living costs associated with poor disease control. This point is amplified considering almost half of the current Australian population who receive insulin pump therapy are under 25 years of age. [18]

Further to pump technology, continuous glucose monitoring (CGM) systems used in association with the pump as an integrated diabetes management system form the basic components of an eventual automated closed loop system or 'artificial pancreas'. Known as sensor augmented pump therapy (SAPT), such a system allows for both the tracking of daily glucose patterns to inform proactive therapy adjustment, and in some devices, the reactive suspension of insulin to avoid dangerously low glucose levels (in the event that a person cannot make those adjustments themselves). This delivers both patient and taxpayer value. Further to the continuation and expansion of the current Insulin Pump Program (to also include adults), consideration should be given to Government funding of CGM technologies.

Failure to subsidise these technologies and ensure access for patients who require them to reduce the occurrence of diabetes-related complications (which increase the healthcare cost burden), risks Australians not having access to future treatment advances providing further clinical and quality of life gains. Consequently, the 'gap' between technologies available locally and globally will simply be too wide to support emerging therapies, if the Australian healthcare system fails to keep pace with the rest of the world now.

Available pump and CGM technologies delivering insulin and continuously monitoring daily glucose levels, along with insulin suspension capability, deliver both patient and taxpayer value. These technologies are also the essential components of an automated closed loop system or 'artificial pancreas'. It is critical that all of these components are subsidised, otherwise future technological advances in diabetes care providing improved clinical and quality of life benefits, will remain out of reach for adults and children with T1D.

Who is Medtronic?

We are an innovative global medical technology company with a heritage of more than 60 years researching, developing and 'pushing boundaries' to make available to patients technologies providing value in treating over 30 chronic diseases.

Driven by a passion for improving health outcomes in everything we do, diabetes management is a key focus. With almost 30 years expertise creating revolutionary diabetes technologies and, being the world leader in insulin pump therapy and continuous glucose monitoring (CGM) technologies, Medtronic has fully integrated insulin delivery, glucose monitoring and data management as three key elements in optimising glucose control.

These technologies substantially enhance the lives of children and adults who have diabetes based on feedback from patients using our therapies. Medtronic also provides direct and substantial ongoing support and education to help patients achieve and maintain glucose control.

What makes us write to this Review?

Insulin pump therapy (IPT) delivering insulin continuously 24 hours a day, is recognised as an advance on multiple daily injections (MDI) and self-monitoring blood glucose (SMBG) via finger prick tests , providing both significant clinical and quality of life (QoL) benefits in the management of T1D.[1,2,3,4,5,6,7,8,9]

Evidence-based clinical guidelines recommend that IPT should be used where MDI is inappropriate or impractical; attempts to achieve target HBA_{1c} levels with MDI have failed or led to disabling hypoglycaemia despite a high level of care; or the expected benefit is clinically significant for reducing HbA_{1c}, reducing hypoglycaemia, decreasing glucose variability and improving QoL.[1,10,11]

Insulin pump technologies available now are the basic building blocks of an eventual closed loop system or 'artificial pancreas' for T1D. Depending on the pump model and its capabilities, current technology can integrate insulin delivery, glucose monitoring, insulin adjustment and even suspension to help prevent hypoglycaemia episodes, improving both clinical and quality of life health outcomes.

For these reasons, it is imperative that Australian children and adults with T1D for whom multiple daily injections (MDI) are considered a suboptimal approach to improving glycaemic control and quality of life receive timely subsidised access to current and future insulin pump technologies.

It is within this context that Medtronic as a healthcare organisation with current and new diabetes technologies to bring to Australians, appreciates the opportunity to provide input to Stage 2 of this Review.

1. Body of Evidence Supports Clinical and Quality of Life Benefits of Insulin Pump Therapy

There is a sound body of evidence showing that use of IPT and sensor augmented pump therapy (SAPT) , which combines insulin pump therapy with continuous glucose monitoring (CGM), is associated with improved clinical outcomes and quality of life benefits in patients with T1D. This includes evidence-based clinical guidelines,[10,11] numerous systematic reviews and meta-analyses of randomised controlled trials, which represent the highest level of evidence,[3,4,5,7,8,9] as well as many published observational studies .

1.1 Clinical Outcomes –Glycaemic Control, Hypoglycaemia

- Lowering HbA_{1c} to target levels and preventing diabetes related complications via intensive insulin therapy without increasing the risk of hypoglycaemia is a major challenge in managing T1D.
- Hypoglycaemia is considered the greatest barrier to achieving and maintaining glycaemic control.[2]

A recent meta-analysis of 22 randomised controlled trials and before/after studies of at least six months duration of IPT and totalling 1,414 T1D patients with a history of severe hypoglycaemia occurring > 10 episodes/100 patient years on MDI found a fourfold higher incidence of severe for MDI compared with IPT (rate ratio 4.19; 95%CI 2.86-6.13).[3] The greatest reduction was seen in patients who had the highest number of initial severe hypoglycaemia episodes while on MDI (p<0.001). Among these individuals, the severe hypoglycaemia rate was higher by a factor of about 30 with MDI than with IPT.[2,3]

Other recent systematic reviews and meta-analyses of IPT, SAPT and CGM report these key findings:

- A Cochrane review of 23 studies totalling 976 patients with T1D found a statistically significant difference in HBA_{1c} favouring IPT versus MDI, being -0.3% (95%CI: -0.1 to -0.4), as well as reduced severe hypoglycaemia with IPT and preference over MDI based on quality of life outcomes [7]
- Sensor-augmented pump therapy is associated with a significantly greater reduction in HbA_{1c} of -0.68% (95%CI: -0.81% to -0.54%]) than MDI used with SMBG in individuals with T1D without increasing the risk of hypoglycaemia [5]
- Real-time CGM is superior to SMBG for glycaemic control in T1D without increasing the risk of severe hypoglycaemia.[5,8] The meta-analysis of six randomised studies involving 449 patients on CGM and 443 using SMBG with pump therapy or MDI also found exposure to hypoglycaemia was reduced with CGM.[8]

1.2 Quality of Life

A major challenge with T1D is ensuring quality of life while maintaining glycaemic control within targets. T1D management is arduous, imposing daily demands that are difficult and frustrating, particularly for children. IPT and SAPT allow individuals flexibility in their daily activities, while SAPT in particular provides insights on glucose fluctuations, unpredictable variability not otherwise available via other test methods, which can inform timely insulin adjustment.

There is evidence from randomised controlled trials and observational studies showing significantly improved quality of life outcomes for IPT compared with MDI, in particular quality of life gains from increased flexibility in activities of daily living, reduced fear of hypoglycaemia and greater treatment satisfaction.[1,12,13,14] Insulin pump therapy can also improve thinking, mood and well-being:[1,15,16] For example, Australian research showed children with T1D who switched to pump therapy experience improved perceptive reasoning, selective attention and working memory with fewer mood related symptoms and fewer behavioural problems.[1,15] Other research showed lower parental stress, hypoglycaemia worry and overall diabetes burden. [1,16]

2. Evidence Based Clinical Guidelines Provide Appropriate Eligibility Criteria

The NHMRC approved comprehensive Australian clinical guidelines for managing T1D in children, adolescents and adults - endorsed by healthcare professional bodies and patient support organisations - clearly outline clinical and other criteria identifying those patients likely to benefit from IPT or SAPT. [10]

Among these criteria are individuals with micro-vascular complications of diabetes; hypoglycaemia unawareness or reduced hypoglycaemia awareness; recurrent severe hypoglycaemia or suspected nocturnal hypoglycaemia; some children and adolescents including infants and young children; pregnant women (ideally preconception); individuals (or their supervising adults) with desirable motivational factors such as those seeking to improve blood glucose control, as well as those exhibiting various desirable pump treatment-related behaviours.[10]

The above criteria are consistent with current eligibility criteria for accessing NDSS subsidised insulin pump consumables for T1D.[17] The NDSS criteria are very specific and include the use of IPT/SAPT across all age groups, in pregnancy (including gestational diabetes) and in adults who have been on a MDI regimen for at least three months, yet show at least one suboptimal outcome, namely, $HbA_{1c} > 7$; recurring hypoglycaemia; repeated "dawn phenomenon occurrence" with overnight fasting blood sugars frequently over 9mmol/L; or a history of severe glycaemic excursions.

Importantly, the NDSS criteria require individuals with T1D (or their carers) to have completed a comprehensive diabetes education program provided by a diabetes team; to have demonstrated competence in insulin pump function, operation and insulin adjustment; and to be regularly reviewed by their diabetes team, including a review within six months of pump therapy initiation.[17]

Both Australian clinical guidelines recommendations and the NDSS criteria are in keeping with the NICE guidance criteria for IPT/SAPT. These are based on a comprehensive health technology assessment of effectiveness and cost-effectiveness of IPT/SAPT, which found advantages over MDI for both children and adults with T1D.[11]

The NDSS criteria assessing eligibility for subsidised access to insulin pump consumables are appropriate, unambiguous and work well for pumps covered by private health insurance. These same criteria should be applied to assess eligibility for accessing insulin pumps available under the Government Insulin Pump Program for T1D. Furthermore, the Program should be expanded to include adults, providing full coverage as do private health funds, particularly given the advantages of IPT and especially SAPT compared with MDI have been shown in randomised controlled studies.

3. Subsidising Insulin Pumps is an Investment in the Health of Australians With T1D

The Insulin Pump Program, which subsidises insulin pump therapy - an intensive insulin treatment to achieve superior glycaemic control and reduce risk of serious diabetes complications - *is an investment in the health of Australians with T1D, and not a mere cost.*

Given evidence-based guidelines and the large body of evidence showing improved clinical and quality of life outcomes in adults and children using IPT/SAPT, which can lead to cost savings elsewhere in the healthcare system (e.g. less hospitalisation from fewer severe hypoglycaemia events) and in the broader community (e.g. less missed work days - data on file), there is a compelling case for expanding the Insulin Pump Program to include adults with T1D.

Managing T1D effectively so those with the condition can lead 'normal' lives is a challenge that requires more than a 'one size fits all' approach whereby only MDI is available to all age groups as a Government subsidised general benefit on the PBS. Yet insulin pump therapy today is a mainstream treatment option

for intensive diabetes management, such that one in ten Australians with T1D currently use a pump, almost half of whom are under 25 years of age.[18] Eighty-five percent of this use is fully reimbursed by private health insurance for patients who can afford PHI, while less than 3% is subsidised by the Government funded Insulin Pump Program.[18]

Adults and children in need of IPT or SAPT to manage their T1D in accordance with Australian clinical guidelines recommendations [10] and NDSS criteria for pump consumables[17] should not be denied access to these therapies if they cannot afford private health insurance. Their only alternative is MDI, which would be a suboptimal approach for these individuals.

Investment in the future is also relevant, whereby current insulin pump and CGM sensor technologies, as advances on multiple daily insulin injections and finger prick tests for glucose control, are the basic building blocks of an eventual 'closed loop' system or 'artificial pancreas' for T1D that would function like a normal pancreas. Reimbursement mechanisms should therefore evolve to subsidise available technology advances, starting now, if Australians are to access future therapies such as the automated 'closed loop' system for delivering insulin, monitoring glucose levels and adjusting insulin requirements accordingly.

It is imperative the Government invests in IPT/SAPT and new generation technologies via the Insulin Pump Program and other subsidy schemes to meet both the current and future healthcare needs of children and adults living with T1D, particularly where MDI with SMBG is considered unsuitable or fails to provide adequate glycaemic control. *Such investment would represent value for money to the Australian taxpayer dollar* since failure to control glucose levels often results in serious longer term complications such as blindness, kidney failure requiring dialysis, cardiovascular events (e.g. myocardial infarctions) and amputations. The healthcare costs per person with T1D who has diabetes-related complications are also more than *five times* higher than those for a person without complications.[19]

Poorly controlled glucose levels can also lead to acute complications including hypoglycaemia, which if severe may result in seizure, coma and death.

Of note are acute diabetic complications, unnatural deaths and sudden unexplained deaths as the predominant causes of death among Australians with T1D under 40 years of age.[20] Compared with a control population of young Australians without diabetes, sudden unexplained death represents a significantly higher proportion of deaths among those with T1D (5% vs 22%; $p<0.001$). At least some of this difference is likely to relate to diabetes-specific causes of the well-recognised "dead-in-bed syndrome" for which acute hypoglycaemia is thought to play a role.[20]

Importantly, hypoglycaemia unawareness and night time hypoglycaemia, which increase the risk of severe episodes, are particular complications that sensor augmented pump therapy offering real time continuous glucose monitoring combined with low glucose insulin suspension functionality can effectively address to prevent or minimise the occurrence of serious consequences.

A sensor augmented pump with insulin suspension capabilities is currently the closest therapy to a closed loop 'artificial pancreas' available among various types of insulin pump that would mimic the human pancreas. It is critical that all components of this current therapy are subsidised so patients with a clinical need can access their benefits now. This would also help to optimise the introduction of future technologies which are steps toward an artificial pancreas.

*4. **Insulin Pump Program Should Provide Equitable Access and Expand to Adults***

The premise of our healthcare system is that Australian residents should have access to healthcare, regardless of their ability to pay. This ensures equitable access and should reduce disparities in health outcomes.

4.1 Insulin Pump vs MDI Funding

A capped budget of $692,000 for the Insulin Pump Program was allocated to June 2012 (data on file) – a program restricted to individuals ≤18 years of age, income means tested, subsidising up to 80% of the pump value to a maximum of $6,400 and which has been without available funds for most of financial year 2012-13. *This is not in keeping with the underlying premise of affordable and equitable access to healthcare for Australians.*

There is no evidence base for the difference in funding arrangements between MDI and insulin pumps, which are both key mainstream intensive insulin regimens. Insulin pumps not only deliver insulin but, depending on type, also have continuous glucose monitoring and insulin suspension capabilities to prevent hypoglycaemia episodes, thus there should be adequate funding to support subsidised use.

The different funding arrangements create an inequity of access issue for Australians with T1D, which is at odds with diabetes being one of six top National Health Priority Areas by the Government .[21]

4.2 Australia Lags Behind

Many countries around the world provide subsidised access to insulin pump therapy for both children and adults with T1D, based upon well-defined eligibility criteria reflecting clinical indications. These criteria do not contain age restrictions or income means testing for patients requiring a pump, which is fully reimbursed by Government in countries with comparable healthcare systems to that in Australia such as the UK (data on file).

Australia lags behind other developed countries in providing adults and children with T1D affordable access to insulin pump therapy whereby under current arrangements there is no subsidy for:

- adults with T1D aged 19 years and over who do not have private health insurance cover
- children with T1D previously supported under the Insulin Pump Program, who on turning 19 years of age cannot access a pump unless covered by private health insurance.
- Children ≤18 years who are eligible since there are no funds left for the year ending June 2013.

This has the effect of a two tiered healthcare system for people with T1D, i.e. individuals who can afford private health insurance coverage *and* have the right level of cover for an insulin pump to be fully funded compared with those who cannot afford private health insurance and do not qualify subsidy under the Insulin Pump Program.

4.3 Why the Program Should Expand to Adults

Both adults and children are well represented in the large body of clinical evidence supporting clinical and quality of life advantages of insulin pump therapy. This includes systematic reviews and clinical trials comparing insulin pumps and MDI in both general and specific populations with T1D addressing a specific clinical need for which the benefit observed favouring pump is often greater in adults than children. For example, the significant reduction in severe hypoglycaemia event rate reported for insulin pump therapy versus MDI in a population with a history of severe hypoglycaemia was larger for adults than children since the former has a longer duration of T1D, therefore experience more frequent hypoglycaemia, and are more hypoglycaemia unaware [2,3] *Based on the evidence, there is no clinical basis for excluding individuals with T1D over 18 years of age from the Insulin Pump Program.*

Particular consideration for expanding the program to adults should include individuals who were eligible and received an insulin pump as a child/adolescent and who still need a pump as a young adult. Changing to MDI would be a suboptimal approach for managing their diabetes, increasing the risk of adverse outcomes since IPT /SAPT would have previously been identified as the most appropriate treatment option for them based on clinical need and quality of life considerations.

In fact, a recent report on how young Australians with diabetes aged up to 30 years manage their condition found that only those with T1D using insulin pumps bought enough blood glucose test strips to meet recommended daily monitoring levels in clinical guidelines.[22] The report also found young people with diabetes have difficulty transitioning from paediatric to adult health services and consequently may experience poor health outcomes.[22]

5. Benefit and Cost Assessment of Different Insulin Pumps Completed

A comprehensive review of the Australian Government Prostheses List insulin pump groups and benefits was recently completed as part of the Health Technology Assessment (HTA) Review in 2012. The insulin pump product groups and benefits were assessed by the Department of Health and Ageing and a Panel of Clinical Experts and subsequently reviewed and endorsed by both the HTA Consultative Committee and the Prostheses List Advisory Committee.

The value offering of Medtronic IPT/SAPT products includes extensive ongoing patient and healthcare professional education and support, starting before pump user initiation. These elements are provided at no additional cost to the Government or community yet contribute to the value of insulin pump therapy in optimising Australian health outcomes.

5.1 Health Technology Assessment

Both benefits and costs of the different insulin pumps available were considered in the review, resulting in the current Prostheses List of insulin pumps which supports different price structures, depending on the functionality of each type of pump. The Prostheses List shows varying capabilities of each pump model, ranging from insulin delivery only through to various SAPT models combining insulin delivery and CGM.

5.2 Sensor Augmented Pump Therapy With Automatic Insulin Suspension

CGM is the only test method that can track glucose patterns continuously, every day, for up to 6 days at a time, highlighting the frequency, size and duration of daily glucose high/low 'excursions'. This predictability allows people with diabetes to tailor individual insulin, dietary and exercise requirements to their daily living activities, thus addressing glucose level extremes not otherwise identified by alternative methods that would be unknown to the patient, thus avoiding an adverse event. *This capability is relevant in considering cost-effectiveness since it has impact on hypoglycaemia and hyperglycaemia events avoided and their sequelae.*

Among the SAPT models listed is a pump in its own category as it has capability to automatically adjust insulin delivery based on real time CGM readings. For example, patients can choose to be alerted before glucose levels fall 'too low' or rise 'too high', enabling immediate action to avoid unacceptably high and low glucose levels. The unique low glucose suspend (LGS) feature only available on this pump leads to an interruption in insulin supply for up to two hours. After two hours of insulin suspension, insulin delivery automatically resumes for four hours. This on/off insulin delivery cycle is to prevent the occurrence of diabetic ketoacidosis after LGS events.[23] No other available insulin pump in Australia has this functionality.

The benefit of combining SAPT and LGS is a reduction of hypoglycaemia events without compromising safety.[23] This is particularly important during sleep to prevent or minimise nocturnal hypoglycaemia and to address hypoglycaemia unawareness that is a significant problem in T1D, occurring in 20-37% of people and associated with severe hypoglycaemia.[24]

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