# Continuous subcutaneous insulin infusion therapy

## *for treating type 1 diabetes*

**Technology Guidance from the MOH Medical Technology Advisory Committee**

## Guidance recommendations

The Ministry of Health Medical Technology Advisory Committee has recommended:

- ✓ Continuous subcutaneous insulin infusion therapy (CSII) and its consumables as a treatment option for adults and children with type 1 diabetes mellitus:
  - who use multiple daily injections of insulin (MDI) to achieve target HbA1c but result in the person experiencing disabling hypoglycaemia, where disabling hypoglycaemia is defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on quality of life (QoL); or
  - who have unacceptably high HbA1c (i.e. at 8.5% or above) on MDI despite a high level of care, where a high level of care refers to patient adherence to structured education programmes provided by a multidisciplinary team at specialist outpatient clinics in the public healthcare sector, which comprise an endocrinologist with a special interest in CSII, a diabetes nurse educator, and a dietician; or
  - where MDI is not clinically suitable and acceptable for children younger than age 12 years, and where careful consideration is made jointly by the multidisciplinary healthcare team, the children, and their caregivers who are responsible for supervising them in using CSII instead of MDI.

- ✓ CSII should be discontinued if it does not result in a sustained improvement in glycaemic control as evidenced by a fall in HbA1c levels or an increase in time-in-range blood glucose readings, or a sustained improvement in disabling hypoglycaemia, or a sustained improvement in QoL.

### Subsidy status

CSII subsidies for the abovementioned indications apply only to the CSII device and its consumables listed in the Annex.

*Published on 23 March 2020*

# Factors considered to inform the recommendations for subsidy

## Technology evaluation

1.1 The MOH MTAC ("the Committee") considered evidence presented for the evaluation of continuous subcutaneous insulin infusion therapy (CSII) for the treatment of people with type 1 diabetes mellitus (T1DM). The evaluation was conducted in consultation with clinical experts from the public healthcare institutions. Available clinical and economic evidence for CSII was considered in line with the HSA registered indications.

1.2 The evidence was used to inform the Committee's deliberations around five core decision-making criteria:

- Clinical need of patients and nature of the condition
- Clinical effectiveness and safety of the technology
- Cost-effectiveness (value for money) – the incremental benefit and cost of the technology when compared with existing alternatives
- Estimated annual technology cost and the number of patients likely to benefit from the technology
- Organisational feasibility, which covers the potential impact of adopting technology, especially barriers for mainstream subsidy across PHIs

1.3 Additional considerations, such as ethical or social issues related to adoption of the technology, may also be part of the Committee's deliberations.

## Clinical need

2.1 T1DM is a chronic metabolic disorder caused by autoimmune β-cell destruction that leads to insulin deficiency. The Committee acknowledged multiple daily injections of insulin analogues (MDI) are currently the main treatment option for local population with T1DM. The MDI regimen uses the basal-bolus approach, which combines basal injections of long-acting insulin with pre-prandial bolus injection of rapid-acting insulin. Insulin pens of rapid-acting and long-acting insulin analogues are currently subsidised.

2.2 The Committee noted that MDI do not allow basal rates of insulin to be readily adjustable once it is administered. With CSII, the infusion rates can be instantaneously adjusted, and a smaller unit of insulin can be administered. The flexible and precise adjustment of insulin doses closely mimics normal insulin secretion patterns to avert hyperglycaemia and hypoglycaemia, and may contribute to prevention of diabetic complications.

2.3 The Committee also considered the impracticalities of administering small insulin doses to very young children and midday doses of insulin to young school children.

## Clinical effectiveness and safety

3.1 In line with local clinical practice, the main comparator used in the evaluation was MDI. The Committee noted that randomised controlled trials (RCTs) which compared CSII with MDI demonstrated no significant difference in the incidence of severe hypoglycaemia (SHG) and HbA1c reduction. The RCTs reported that CSII reduced HbA1c greater than MDI, but the reduction was not statistically or clinically significant. In adults using CSII, greater improvements in quality of life (QoL) and treatment satisfaction were observed, compared with MDI. Observational studies showed more favourable outcomes to CSII in reduction in HbA1c (-0.2 to -1.4%) and rate of SHG, and improvement in QoL. The HbA1c lowering effect was more pronounced in patients with high baseline HbAa1c of approximately 9%, compared to those with baseline HbA1c 7-8%.

3.2 The Committee acknowledged that none of the studies looked at long-term benefits of HbA1c reduction associated with CSII, such as prevention of microvascular and macrovascular complications. The Committee also noted that some primary studies included in systematic reviews used a conventional insulin such as neutral protamine hagedorn (NPH) insulin as a basal insulin, which may overestimate the incremental benefits of CSII.

## Cost-effectiveness

4.1 The Committee considered the costs-effectiveness of CSII compared with MDI for adults and children with T1DM. The Committee noted that there was no local economic evaluation available. Published economic analyses reported inconsistent results majorly due to different assumptions used for glycaemic outcomes. An economic analysis which adopted data from RCT showed higher ICER, compared with the other which used an HbA1c reduction of 0.9% from a clinical database, and assumed 50% reduction of SHG episodes.

## Estimated annual technology cost

5.1 The Committee estimated the annual cost to the Government of subsidising the use of CSII was less than $1 million, based on a projection of about 640 adults and children with T1DM in Singapore who could benefit from Government subsidy for CSII.

## Organisational feasibility

6.1 The Committee acknowledged that structured patient education and continuous reinforcement on self-management are essential to achieve successful outcomes with CSII. All people who initiate CSII should be competent in carbohydrate counting, flexible insulin dosing, self-monitoring of blood glucose, sick day management, and troubleshooting issues that patients commonly encounter during the use of CSII. Such training would require additional resources for both the providers (e.g. skills, time, and space), and patients and their caregivers.

## Recommendation

7.1 The Committee recommended to subsidise CSII and its consumables as a treatment option for adults and children with T1DM:

- who use multiple daily injections of insulin (MDI) to achieve target HbA1c but result in the person experiencing disabling hypoglycaemia, where disabling hypoglycaemia is defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on QoL; or
- who have unacceptably high HbA1c (i.e. at 8.5% or above) on MDI despite a high level of care, where a high level of care refers to patient adherence to structured education programmes provided by a multidisciplinary team at specialist outpatient clinics in the public healthcare sector, which comprise an endocrinologist with a special interest in CSII, a diabetes nurse educator, and a dietician; or
- where MDI is not clinically suitable and acceptable for children aged younger than 12 years, and where careful consideration is made jointly by the multidisciplinary healthcare team, the children, and their caregivers who are responsible for supervising them in using CSII instead of MDI.

7.2 The Committee recommends to subsidise CSII and its consumables listed in Annex.

7.3 In addition, CSII should be discontinued if it does not result in a sustained improvement in glycaemic control as evidenced by a fall in HbA1c levels or an increase in time-in-range blood glucose readings, or a sustained improvement in disabling hypoglycaemia, or a sustained improvement in QoL.

**About the Agency**

The Agency for Care Effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health. It conducts evaluations to inform the subsidy of treatments, and produces guidance on the appropriate use of treatments for public hospitals and institutions in Singapore. The guidance is based on the evidence available to the Committee as at 22 March 2019. This guidance is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

*Find out more about ACE at www.ace-hta.gov.sg/about*



Principal Head (Evaluation)
Agency for Care Effectiveness
Email: ACE_HTA@moh.gov.sg

In citation, please credit the "Ministry of Health", when you extract and use the information or data from the publication.