Diabetes Ther (2024) 15:1491–1499
https://doi.org/10.1007/s13300-024-01600-y

COMMENTARY

Counseling for Insulin Icodec: A Proposed Practitioner's Guide

Sanjay Kalra · Saptarshi Bhattacharya · Nitin Kapoor

Received: March 11, 2024 / Accepted: April 29, 2024 / Published online: May 14, 2024

ABSTRACT

Despite insulin being a lifesaving medication, insulin distress, insulin hesitancy, and insulin inertia remain oft-repeated themes in diabetes discourse. The current model lists three issues: temperament, troublesomeness, and technicality, which contribute to insulin perceptions. Therapeutic patienteducation (TPE), value-added therapy (VAT), and medication counseling are concepts that assist in optimizing insulin perceptions. Insulin icodec is a basal insulin with a half-life of 196 h and a once-weekly or circaseptan frequency of administration. Insulin icodec reduces the frequency of basal insulin administration to one-seventh, which along with the lower requirement of glucose monitoring, reduces the burden of plastic and ancillary supply disposal. Because of its unique frequency of injection, insulin icodec usage requires appropriate counseling and education. This reader-friendly counseling guide helps practitioners offer VAT, as well as TPE while prescribing icodec and other insulins.

PLAIN LANGUAGE SUMMARY

Insulin icodec is a newly developed basal insulin that is injected once a week. Specific counseling is required in order to optimize the use of this insulin. We share a 3T model—temperament [of the person], troublesomeness [of the insulin], and technicality [of injection], that influence insulin perceptions. We then use this model to highlight the information that must accompany an insulin icodec prescription, like "value-added therapy". We suggest that as it suits a wide variety of persons living with diabetes, and as its use requires minimal troubleshooting and technical know-how, icodec can be termed a person-friendly insulin. Icodec also reduces the burden of plastic generation and disposal.

S. Kalra (✉)
Department of Endocrinology, Bharti Hospital, Karnal, India
e-mail: brideknl@gmail.com

S. Kalra
University Center for Research and Development, Chandigarh University, Mohali, India

S. Bhattacharya
Department of Endocrinology, Apollo Indraprastha Hospitals, New Delhi, India
e-mail: saptarshi515@gmail.com

N. Kapoor
Department of Endocrinology, Diabetes and Metabolism, Christian Medical College, Vellore, India
e-mail: nitin.endocrine@gmail.com

N. Kapoor
Non Communicable Disease Unit, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia

Keywords: Basal insulin; Diabetes; Insulin icodec; Medication counseling; Person-centered care; Person-friendly insulin

Key Summary Points
Insulin icodec is a novel once-weekly basal insulin, with a half-life of 196 h.
Insulin perceptions are influenced by the temperament of the person, the perceived troublesomeness of an insulin regimen or preparation, and the technicality of insulin usage.
Insulin icodec is a person-friendly insulin that is not only effective but easy to use as well.
Insulin icodec suits persons with a wide range of temperaments, as it is less intrusive or troublesome, and does not require extensive technical skills.
Insulin icodec can be used with oral glucose-lowering drugs, as well as prandial insulins.
It reduces the frequency of basal insulin administration to one-seventh, which along with the lower requirement of glucose monitoring, reduces the burden of plastic and ancillary supply disposal.
Specific counseling adds value to therapy with insulin icodec.

MAKING INSULIN PERSON-FRIENDLY

Insulin has been serving mankind for over a century now [1]. It has saved millions of people from avoidable complications and early death [2]. Yet, insulin distress, insulin hesitancy, and insulin inertia remain oft-repeated themes in diabetes discourse [3]. Persons with diabetes frequently voice reluctance to initiate insulin therapy, and dissatisfaction with ongoing treatment [4].

Many reasons have been suggested to explain the suboptimal perception of insulin. The biopsychosocial model of health has helped us understand the barriers to insulin initiation and intensification. These have been classified as biomedical, psychological, and social [5].

In this article, we list three challenges faced by persons living with diabetes – temperament, troublesomeness, and technicality – that contribute to insulin perceptions (Table 1). An understanding of these factors can help the diabetes care provider craft an appropriate strategy to mitigate distress. Developing an internal compass of health, reducing the index of intrusion of insulin, and simplifying the implementation of insulin use help address the limitation of temperament, troublesomeness, and technicality, respectively. This model of insulin motivation should be used in conjunction with toolkits and suggestions that have been published earlier [5].

Temperament of the concerned individual influences one's approach towards insulin. Knowledge about diabetes and insulin's role in its therapy, and confidence in navigating the social environment impact insulin acceptance. Troublesomeness is another domain: frequency of injection, monitoring, and visits to the health care system negatively influence insulin acceptance. The third domain, technicality, is linked to the (perceived) complexity of insulin administration and titration. A person-friendly insulin would be one that is suitable for persons of diverse temperaments, has a minimal index of intrusion, and is easy to administer and monitor. We utilize this framework to optimize the usage of insulin icodec.

Insulin icodec is a newly approved once-weekly basal insulin analog, which offers a pragmatic solution to challenges of temperament, troublesomeness, and technicality. Its unique duration of action requires specific information to be shared while counseling and educating persons with diabetes regarding its usage. We share this information and highlight the physio-friendly, psycho-friendly, and praxis-friendly nature of this drug.

This article is based on previously conducted studies and does not contain any new studies

Table 1 Factors influencing insulin[a] perception

Domain	Temperament	Troublesomeness	Technicality
Pain points	Knowledge needed to use insulin	Need for frequent monitoring	Fixed timing of the day of injection
	Attitude towards diabetes care	Need for frequent injections	Injection-meal time gap
	Confidence in self-care	Need for frequent visits to the health care system	Complexity of titration
	Social embarrassment related to injection	Burden of disposal of supplies	
Focus of intervention	Strengthening one's internal compass	Minimizing the intrusion index of insulin	Simplifying implementation issues

[a]These factors influence perceptions related to all injectable therapy

with human participants or animals performed by any of the authors.

MEDICATION COUNSELING

Medication counseling is an integral part of any prescription [6]. In fact, quality counseling adds value to the patient–physician encounter and improves the effectiveness of the prescribed drugs [7]. This therapeutic patient education (TPE) [8] is also known as value-added therapy (VAT) [9]. The need for medication counseling is especially important in diabetes management, which requires a significant amount of self-care [10]. The need is even more pronounced with the use of insulin and other injectable glucose-lowering drugs, which are self-administered.

Each insulin is unique, however. There are subtle differences in the education that accompanies various insulin regimens, preparations, concentrations, and delivery devices [11]. At the same time, there are also general rules for insulin usage and hygiene, which apply to all insulin users [12].

The BLACK mnemonic serves as a reminder of the various aspects of a drug that must be discussed with the patient. These are the expected Benefits, Limitations, potential Adverse effects, Costs involved, and Knowledge necessary to use the drug safely and effectively [13]. Insulin technique is a multifaceted science, as well as art, and is guided by international evidence-based guidelines [14]. The use of physio-friendly insulins, which are perceived to be psycho-friendly and person-friendly as well, helps in enhancing acceptance of, and adherence to, prescribed therapy. This acceptance and adherence can be improved by appropriate counselling.

INSULIN ICODEC

Recent advances in insulin pharmacotherapeutics have made it much easier for people living with diabetes to use insulin. One example is icodec [15]. Insulin icodec is a person-friendly insulin. It suits most patient temperaments, as its frequency and method of administration are associated with minimal intrusion and inconvenience, as well as maximal freedom and flexibility.

This insulin, administered in circaseptan frequency, requires adequate counseling to achieve optimal outcomes. In this regard, we discuss the various aspects of insulin icodec administration training.

MOLECULAR DESIGN OF INSULIN ICODEC

Molecular engineering a once-weekly insulin requires not only a very long half-life but also a glucose-lowering effect, which is evenly distributed throughout the week. The design of insulin icodec incorporates four key features—high affinity for albumin, improved stability, low IR binding affinity, and high solubility—to

achieve this. A 20-carbon atom of icosanedioic acid is connected via a hydrophilic linker to the lysine in position B29, which facilitates a very strong, reversible albumin binding. Additionally, three amino acid substitutions (A14E, B16H, and B25H) lower the insulin receptor (IR) binding and IR-mediated clearance to prolong the half-life. A14E and B25H substitutions confer an improved solubility, facilitating a U700 formulation, thus ensuring that the dose volume is low and similar to once-daily basal insulin dosing volumes [15].

TYPING OF SUITABLE PERSONS

Regimen and Concomitant Therapy

Insulin icodec is a basal insulin with a half-life of 196 h and a once-weekly or circaseptan frequency of administration [15]. It can be used as a basal insulin in place of other basal insulins, in a basal-only, basal plus, or basal-bolus regimen. It may be tried as an alternative to once-daily premixed or coformulation regimens. However, it will not be a suitable alternative to prandial insulin. It may work as a safer substitute for sulfonylurea therapy.

Icodec can be used with any rapid or ultra-rapid-acting insulins and has also been studied in combination with all major oral glucose-lowering drugs. Insulin icodec is therefore suitable for any person living with diabetes who requires basal insulin for glycemic control [16–21]. More participants achieved HbA1c targets of < 7% with icodec compared to the once-daily insulins in both insulin-naïve [16, 18, 20] and insulin-experienced individuals (basal regimen) [17]. The internationally recommended continuous glucose monitoring (CGM) targets with time in range (TIR) > 70% is achieved with icodec in insulin-naïve individuals [16]. Icodec was found to be superior to once-daily glargine U100 with an additional 1 h and 4 min per day spent in TIR with insulin icodec [16].

Comorbid Illness

Insulin icodec may be used safely in persons with stable comorbid illness. Persons who are hospitalized for acute illness, and need rapid glycemic control, may benefit from intravenous insulin infusion (in critical care settings), bolus + once-daily basal insulin (in ward settings), or conventional bolus or premixed insulin regimens (in outdoor settings). Insulin icodec monotherapy may not be the best choice if rapid resolution of fasting hyperglycemia is required. However, it can be initiated in conjunction with rapid-acting insulin in sick persons.

Health Care System and Environment

The once-weekly frequency of insulin icodec allows it to be used as 'weekend therapy' or 'directly observed therapy' (DOT) [22, 23]. It can be administered by caregivers, and a ± 3 days window of flexibility is allowed. This makes the insulin easy to use in situations where the person cannot self-inject, and where the health care system or family is unable to manage frequent injections.

Insulin icodec reduces the frequency of basal insulin administration to one-seventh. This, along with the lower requirement of self-monitoring of plasma glucose (SMPG), reduces the burden of plastic and ancillary supply disposal. This supports the cause of 'green diabetology' [24] and contributes to mitigating the impact of diabetes care on global warming.

TECHNICALITIES

Initial Dosage and Titration

Initiation

Based on published literature, insulin icodec may be initiated with a weekly dose of 70 units. This is equivalent to starting a once-daily basal insulin at 10 units/day [16]. Steady state is achieved within 3–4 weeks [15]. For people who are already on once-daily degludec, detemir,

glargine U100, or neutral protamine Hagedorn insulin (NPH), the initial dose of icodec may be calculated from the current weekly dose. However, in the published studies, a 50% loading dose was used [25]. The first injection of icodec can be given at any time of the day, irrespective of the timing of the last insulin injection.

Intensification/Dose Titration

Titration may be done at once-weekly or circaseptan intervals. Increments of 20 units are advised if fasting plasma glucose is above target. Similar decrements may be prescribed if fasting plasma glucose is below target [22]. Three pre-breakfast self-measured plasma glucose values, measured on 2 days prior to and on the day of the weekly titration, should be measured. A pragmatic titration guide is shown below (Table 2).

The titration target and insulin dose adjustments to provide the optimal balance between glycemic control and hypoglycemia for insulin icodec are based on phase 2 and 3 studies of the icodec clinical development program [16–21].

Interchange from Other Basal Insulins

When switching patients from once-daily or twice-daily basal insulins, the weekly icodec dose is to be calculated as the total daily basal dose multiplied by seven. For the first injection only, a one-time additional 50% icodec dose is to be administered to prevent any transient and slight elevation in mean fasting SMPG levels that might happen during the initial weeks of transition to icodec from once-daily or twice-daily basal insulins. From week 2, patients should receive the calculated once-weekly dosage with titration on subsequent weeks, as needed.

Technique

Insulin icodec is administrated subcutaneously using a pre-filled pen injector, which contains 700 units/ml in its cartridge. The technique is the same as for other insulins. While it is important to avoid intramuscular delivery, it is uncertain if an inadvertent intramuscular injection of insulin icodec will act like a rapid-acting insulin. It must be noted that once-daily basal insulins, such as glargine, are known to work as a rapid-acting insulin, if injected intramuscularly [26].

The insulin can be injected weekly at any time of the day of the week with a flexibility of ± 3 days, without regard to the timing of meals, exercise, or sleep [16]. This provides flexibility, convenience, and freedom of lifestyle.

Glucose Monitoring

Frequent glucose testing is not required to monitor the effect of insulin icodec. Weekly glucose estimation suffices. However, the frequency of SMPG will depend upon the other insulin or oral antidiabetic drugs being used by an individual. This advice is similar to that suggested for once-weekly glucagon-like peptide 1 receptor agonist (GLP-1 RA) monitoring [27].

Table 2 Dose titration scheme for insulin icodec

Pre-breakfast self-monitored plasma glucose (SMPG)		**Icodec dose adjustment (U/week)**
Up-titration	Mean of SMPG values (> 130 mg/dl)	+ 20 U
Target	Mean of SMPG values (80–130 mg/dl)	0 U
Down-titration	Lowest SMPG value (< 80 mg/dl)	− 20 U

TROUBLE SHOOTING

Local Site Reactions

Local site reactions (LSR), such as bruising, bleeding, pain, or lipohypertrophy may occur with insulin icodec, as with any other insulin. The neutral pH of icodec reduces the risk of pain, while the lower frequency of administration reduces the risk of other LSR. LSR should be managed as per the standard of care [12].

Hypoglycemia

The risk of hypoglycemia is minimal with insulin icodec [15]. The albumin binding, which leads to a protracted duration of action, also acts as a buffer against sudden release of insulin and protects against sudden drop in glucose levels [15]. The administered dose enters as an inactive albumin-bound form, which leads to a slow and steady glucose-lowering effect. The strong albumin binding and low IR affinity ensure that, despite the weekly dose, there is no immediate large glucose-lowering effect.

Overall observed rates of combined clinically significant or severe hypoglycemia have been reported to be less than one event per patient year exposure (PYE) with icodec in insulin-naïve individuals [16, 18, 20] as well as insulin-experienced individuals (basal regimen) [17]. The time below range (TBR) level 1 & level 2 has remained well below the internationally recommended CGM targets of 4% and 1%, respectively across various time periods in both insulin-naïve [16] and insulin-experienced individuals [17, 19]. More participants achieved HbA1c targets of less than 7% without clinically significant or severe hypoglycemia with icodec compared to the once-daily insulins in both insulin-naïve [16, 18, 20] and insulin-experienced individuals (basal regimen) [17]. Furthermore, the CGM-derived duration of hypoglycemia was also found to be ≤ 40 min, which was found to be comparable with the once-daily basal insulins, glargine U100 and degludec [28]. There was no apparent clustering of episodes of hypoglycemia reported during any time periods in participants taking icodec. The data on safety of icodec is reassuring.

Optimal glycemic control in diabetes is limited by episodes of hypoglycemia, which in turn is counterbalanced by intact symptomatic and hormonal responses. For any newly developed basal insulin like icodec, it is therefore important to investigate whether hypoglycemia induced by that insulin elicits a robust symptomatic and counterregulatory response, which was evaluated by double and triple doses of once-weekly icodec compared to once-daily glargine U100 in type 2 diabetes [29]. The study reassured that double and triple doses of once-weekly icodec do not lead to an increased risk of hypoglycemia compared with once-daily glargine U100, and that the time to develop hypoglycemia and recovery from hypoglycemia were comparable for icodec and glargine U100. The symptomatic and counterregulatory responses for icodec were at least as robust as those seen for glargine U100, to support restoration of euglycemia.

Overdosage of Insulin Icodec

The above results may not only be applicable to scenarios where an unintentionally high insulin dose is administered, due to miscalculated dose or taking two weekly doses close to each other by mistake. It can also be applied to instances where the usually administered insulin dose is too high to match the insulin needs, due to reduced insulin requirement, like during and after exercise, during intercurrent illness, or during hospitalization that often implies fasting prior to medical testing or operative procedures. The observations provide further reassurance about the safety of insulin icodec.

In routine practice, if hypoglycemia does occur, it will usually be due to the concomitant glucose-lowering medications such as bolus insulin or sulfonylurea, rather than insulin icodec. The doses and dose frequencies of these drugs may be modified until recovery occurs.

Sick-Day Rules

An individual on insulin icodec treatment who falls ill should be managed as per standard of care. Short-acting insulins and/or oral glucose-lowering drugs should be adjusted as per requirement. Good clinical sense should prevail in such situations. Persons requiring critical care facilities should be started on intravenous insulin. Those who need non-critical care hospitalization may be managed with subcutaneous rapid-acting insulin.

The patients' current regimen, including the last date of icodec administration, should be shared with the treating health care team. There is no need to add a once-daily basal insulin or premixed insulin in a person on icodec therapy.

CONCLUSIONS

Insulin icodec is a person-friendly basal insulin that makes insulin usage more convenient, less intrusive, and easier for the person living with diabetes. It suits most temperaments, is not troublesome, and does not need much technical knowhow to use safely. The reader-friendly counseling guide that we have shared helps practitioners offer VAT as well as TPE, while prescribing insulin icodec.

Medical Writing/Editorial Assistance. No medical writing/editorial assistance was received for this study or publication of this article.

Author Contributions. Sanjay Kalra conceptualized the topic and wrote the first draft. Saptarshi Bhattacharya and Nitin Kapoor shared insights and refined the draft.

Funding. No funding or sponsorship was received for this study or publication of this article.

Declarations

Conflict of Interest. Sanjay Kalra is an Editorial Board member of Diabetes Therapy. Sanjay Kalra was neither involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Sanjay Kalra and Saptarshi Bhattacharya have received speaker fees from Novo Nordisk. Nitin Kapoor has nothing to disclose.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

REFERENCES

1. Vecchio I, Tornali C, Bragazzi NL, Martini M. The discovery of insulin: an important milestone in the history of medicine. Front Endocrinol. 2018;9:613.

2. Falcetta P, Aragona M, Bertolotto A, Bianchi C, Campi F, Garofolo M, et al. Insulin discovery: a pivotal point in medical history. Metabolism. 2022;127: 154941.

3. Liu C, De Roza J, Ooi CW, Mathew BK, Elya, Tang WE. Impact of patients' beliefs about insulin on acceptance andadherence to insulin therapy: a qualitative study in primary care. BMC Prim Care. 2022;23(1):15. https://doi.org/10.1186/s12875-022-01627-9.

4. Brod M, Kongsø JH, Lessard S, Christensen TL. Psychological insulin resistance: patient beliefs and implications for diabetes management. Qual Life Res. 2009;18:23–32.

5. Kalra S, Bajaj S, Sharma SK, Priya G, Baruah MP, Sanyal D, et al. A practitioner's toolkit for insulin motivation in adults with type 1 and type 2 diabetes mellitus: evidence-based recommendations from an international expert panel. Diabetes Ther. 2020;11:585–606.

6. Hämeen-Anttila K, Mikkola H. Is there a need for standardization of medication counseling in community pharmacies. Res Soc Admin Pharm. 2024;20(5):547–52.

7. Neumann M, Edelhäuser F, Kreps GL, Scheffer C, Lutz G, Tauschel D, et al. Can patient–provider interaction increases the effectiveness of medical treatment or even substitute it?—an exploration on why and how to study the specific effect of the provider. Patient Educ Couns. 2010;80(3):307–14.

8. Correia JC, Waqas A, Aujoulat I, Davies MJ, Assal JP, Golay A, et al. Evolution of therapeutic patient education: a systematic scoping review and scientometric analysis. Int J Environ Res Public Health. 2022;19(10):6128.

9. Kalra S, Gupta Y, Baruah MP. Insulin and value-added therapy. J Soc Health Diabetes. 2014;2(2):59–61.

10. Shrivastava SR, Shrivastava PS, Ramasamy J. Role of self-care in management of diabetes mellitus. J Diabetes Metab Disord. 2013;12(1):1–5.

11. Buse JB, Davies MJ, Frier BM, Philistsimikas A. 100 years on: the impact of the discovery of insulin on clinical outcomes. BMJ Open Diabet Res Care. 2021;9(1): e002373.

12. Bahendeka S, Kaushik R, Swai AB, Otieno F, Bajaj S, Kalra S, et al. EADSG guidelines: insulin storage and optimisation of injection technique in diabetes management. Diabetes Ther. 2019;10:341–66.

13. Kalra S, Aggarwal S, Kumar A. Counseling for growth hormone therapy. Turk Archiv Pediatr. 2021;56(5):411.

14. "9. Pharmacologic approaches to glycemic treatment: standards of care in diabetes—2024". Diabetes Care 47(Supplement 1): S158–78; 2024.

15. Nishimura E, Pridal L, Glendorf T, Hansen BF, Hubálek F, Kjeldsen T, et al. Molecular and pharmacological characterization of insulin icodec: a new basal insulin analog designed for once-weekly dosing. BMJ Open Diabetes Res Care. 2021;9(1): e002301.

16. Rosenstock J, Bain SC, Gowda A, Jódar E, Liang B, Lingvay I, et al. Weekly icodec versus daily glargine U100 in type 2 diabetes without previous insulin. N Engl J Med. 2023;389(4):297–308.

17. Philis-Tsimikas A, Asong M, Franek E, Jia T, Rosenstock J, Stachlewska K, et al. Switching to once-weekly insulin icodec versus once-daily insulin degludec in individuals with basal insulin-treated type 2 diabetes (ONWARDS 2): a phase 3a, randomised, open label, multicentre, treat-to-target trial. Lancet Diabetes Endocrinol. 2023;11(6):414–25.

18. Lingvay I, Asong M, Desouza C, Gourdy P, Kar S, Vianna A, et al. Once-weekly insulin icodec vs once-daily insulin degludec in adults with insulin-naive type 2 diabetes: the ONWARDS 3 randomized clinical trial. JAMA. 2023;330(3):228.

19. Mathieu C, Ásbjörnsdóttir B, Bajaj HS, Lane W, Matos AL, Murthy S, et al. Switching to once-weekly insulin icodec versus once-daily insulin glargine U100 in individuals with basal-bolus insulin-treated type 2 diabetes (ONWARDS 4): a phase 3a, randomised, open-label, multicentre, treat-to-target, non-inferiority trial. Lancet. 2023;401:1929–40.

20. Bajaj HS, Aberle J, Davies M, Donatsky AM, Frederiksen M, Yavuz DG, et al. Once-weekly insulin icodec with dosing guide app versus once-daily basal insulin analogues in insulin-naive type 2 diabetes (ONWARDS 5) a randomized trial. Ann Intern Med. 2023;176(11):1476–85.

21. Russell-Jones D, Babazono T, Cailleteau R, Engberg S, Irace C, Kjaersgaard MI, et al. Once-weekly insulin icodec versus once-daily insulin degludec as part of a basal-bolus regimen in individuals with type 1 diabetes (ONWARDS 6): a phase 3a, randomised, open-label, treat-to-target trial. Lancet. 2023;402(10413):1636–47.

22. Kalra S, Gupta Y. Weekend therapy in diabetes. J Pak Med Assoc. 2016;66(5):627–8.

23. Kalra S, Gupta Y. DOT (directly observed therapy) in diabetes: current thought, future reality. Aust J Rural Health. 2014;4(22):206.

24. Kalra S, Girdhar R, Sahay R. Green diabetology. Indian J Endocrinol Metab. 2015;19(6):698.

25. Philis-Tsimikas A, Bajaj HS, Begtrup K, Cailleteau R, Gowda A, Lingvay I, et al. Rationale and design of the phase 3a development programme (ONWARDS 1–6 trials) investigating once-weekly insulin icodec in diabetes. Diabetes Obes Metab. 2023;25(2):331–41.

26. Karges B, Boehm BO, Karges W. Early hypoglycaemia after accidental intramuscular injection of insulin glargine. Diabet Med. 2005;22(10):1444–5.

27. Kalra S, Ganapathi M, Mithal A. Glycemic monitoring with once-weekly glucagon-like peptide 1 receptor agonist (GLP1RA) use. Indian J Endocrinol Metab. 2015;19(2):193–5.

28. Bajaj HS, Ásbjörnsdóttir B, Carstensen L, Laugesen C, Mathieu C, Philis-Tsimikas A, Battelino T. Continuous glucose monitoring-based metrics and hypoglycemia duration in insulin-experienced individuals with long-standing type 2 diabetes switched from a daily basal insulin to once-weekly insulin icodec: post hoc analysis of ONWARDS 2 and ONWARDS 4. Diabetes Care. 2024;47:729–38.

29. Pieber TR, Arfelt KN, Cailleteau R, Hart M, Kar S, Mursic I, Svehlikova E, Urschitz M, Haahr H. Hypoglycaemia frequency and physiological response after double or triple doses of once-weekly insulin icodec vs once-daily insulin glargine U100 in type 2 diabetes: a randomised crossover trial. Diabetologia. 2023;66(8):1413–30.