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Use of Once-Weekly Insulin Icodec in the Perioperative and Inpatient Settings

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Introduction

Hyperglycemia in hospitalized patients is associated with increased morbidity, mortality, and healthcare utilization, and effective glycemic management remains a central component of inpatient care.[1] Basal insulin therapy is a cornerstone of this management strategy, traditionally relying on once-daily long-acting insulin analogs that allow for flexible titration.[1] Insulin icodec,[2] a once-weekly basal insulin analog, represents a significant therapeutic advance by reducing injection burden and providing stable pharmacokinetics; however, it also introduces new challenges in acute care settings.

Insulin icodec exhibits reversible albumin binding and a prolonged half-life of approximately 196 hours (~8 days).[3] It reaches a steady state after 3–4 weekly injections and is associated with a relatively flat, sustained glucose-lowering profile.[3] While these properties are advantageous in the outpatient setting, they limit the ability to rapidly titrate insulin dosing in response to acute illness, fasting, or surgical stress. This reduced flexibility raises concerns regarding its safety and practicality in hospitalized and perioperative patients, where insulin requirements may change abruptly. Diabetes Canada inpatient guidance emphasizes the importance of individualized insulin regimens and the ability to adjust therapy dynamically in response to changing clinical status, principles that may be more difficult to implement with once-weekly insulin formulations.[4] This review focuses on adults with type 2 diabetes, in whom most clinical experience with insulin icodec has been accumulated.

Use of Insulin Icodec During Hospitalization

A proposed approach to the management of patients receiving once-weekly insulin icodec during hospitalization is shown in **Figure 1**. Please see **clinical vignette cases 1 and 2** for the use of icodec insulin during hospitalization. Evidence supporting inpatient use of insulin icodec is primarily derived from post hoc analyses of the Once Weekly Analogue exploring DiabeteS (ONWARDS) phase 3 clinical trials. These analyses included three trials in insulin-naïve adults living with type 2 diabetes (ONWARDS 1, 3 and 5), two in insulin-treated participants living with type 2 diabetes (ONWARDS 2 and 4), and one in people living with type 1 diabetes (ONWARDS 6).[5-10] Across these analyses, hospitalization rates were similar between patients treated with insulin icodec and those receiving daily basal insulin analogs, with no signal of increased risk of hospitalization associated with icodec.[11] Length of stay was also comparable.[11]

Glycemic control was maintained throughout hospitalization, with stability in A1C observed before, during, and after admission.[11] Among 180 hospitalizations in participants receiving icodec, 97.8% had no additional daily basal insulin documented during hospitalization. More than 90% continued icodec according to their usual schedule after discharge, and 84.9% completed the trial without permanently discontinuing treatment.[11] Few clinically significant or severe hypoglycemic events were reported during hospitalization; however, the small number of events and reliance on participant reporting preclude reliable comparisons between treatment groups. The analysis suggested that once-weekly icodec could be managed similarly to once-daily basal insulin analogs during hospitalization.[11]

Despite these reassuring findings, important limitations constrain their interpretation. The generalizability of trial results to real-world hospitalized populations is uncertain, as patients enrolled in phase 3 studies are typically healthier and more closely monitored than those encountered in routine clinical practice. This distinction is particularly relevant in inpatient settings, where patients often have greater clinical complexity, including advanced age, renal impairment, and variable nutritional intake. As a result, the safety profile observed in clinical trials may underestimate the risks in more vulnerable populations.

In addition, the outcomes reported in these analyses are relatively coarse and do not capture other clinically meaningful aspects of inpatient glycemic control. Events were participant-reported and systematic inpatient glucose or continuous glucose monitoring data were unavailable. These gaps limit confidence in extrapolating trial findings to routine inpatient care.

When Icodec Is Unavailable or Conversion Is Required

On admission, the date, time, and dose of the last icodec injection should be confirmed. Because clinically relevant icodec activity persists beyond the weekly dosing interval, once-daily basal insulin should not routinely be added during the initial hospitalization solely because icodec is unavailable on the hospital formulary. Prandial, correctional, or intravenous insulin may be used according to nutritional intake, glucose levels, and clinical status.

If a prolonged admission necessitates conversion to once-daily basal insulin, an estimated daily dose may be calculated by dividing the most recent weekly icodec dose by seven. In the ONWARDS transition protocols, daily basal insulin was generally initiated two weeks after the last icodec injection, or earlier when prebreakfast glucose exceeded 10 mmol/L.[8,9] Earlier initiation should be individualized because residual icodec activity may increase the risk of hypoglycemia.

Use of Insulin Icodec Perioperatively

The perioperative period introduces additional complexity due to fasting, variable nutritional intake, and stress-induced alterations in insulin sensitivity. In this context, the prolonged duration of action of insulin icodec presents a fundamental challenge, as insulin exposure cannot be rapidly reduced or discontinued in response to changing metabolic demands. **Table 1** presents preoperative management approaches for insulin icodec.

Perioperative data remain particularly sparse, with no prospective studies specifically evaluating insulin icodec in surgical populations. Existing

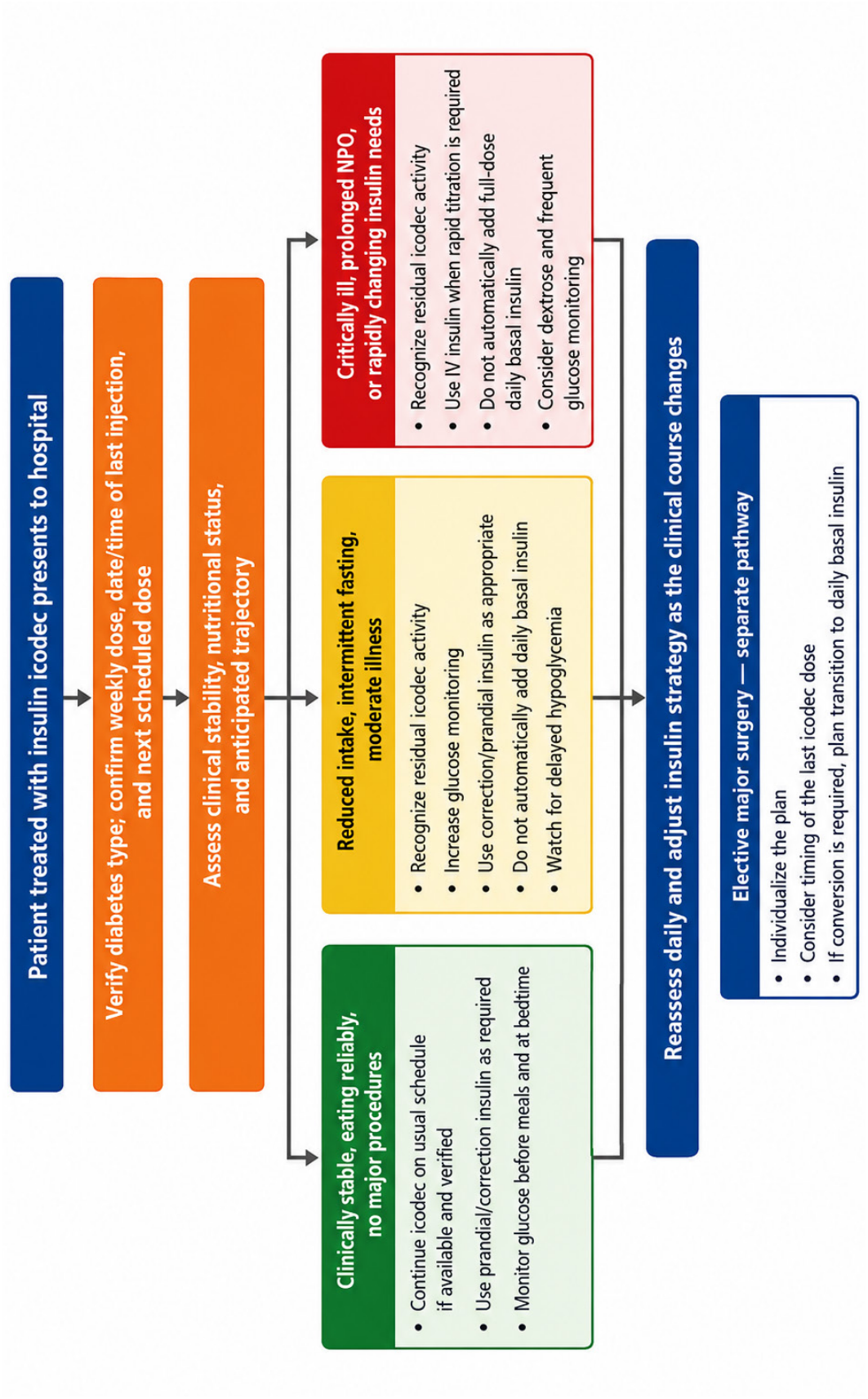

Figure 1. Proposed approach to inpatient management of patients treated with once-weekly insulin icodec; *courtesy of Robyn Houlden, MD, FRCPC.*

Case 1. Use of Icodec During Hospitalization
A 75-year-old man with type 2 diabetes was admitted with COVID-19 pneumonia. Prior to admission, his diabetes was well controlled on once-weekly insulin icodec 350 units, tirzepatide 5 mg subcutaneously weekly, and dapagliflozin 10 mg daily. His most recent dose of icodec was administered 2 days prior to admission. His medical history includes obesity, metabolic dysfunction-associated steatohepatitis (MASH), and stage 3 chronic kidney disease.
On admission, dapagliflozin was withheld due to dehydration risk, and tirzepatide was held due to concerns regarding nausea and reduced oral intake. Given the recent icodec dosing and its prolonged half-life (~8 days), it was assumed that a substantial proportion of his basal insulin requirements remained covered. Point-of-care capillary blood glucose monitoring was initiated before meals and at bedtime, and correctional insulin using a rapid-acting analog was administered at the same time points.
Over the first several days, he required frequent correction doses, with a pattern of postprandial hyperglycemia. In response, a low-dose prandial insulin regimen was initiated. Given the long half-life of icodec and the expected decline in insulin requirements with treatment of his pneumonia, close monitoring was provided for hypoglycemia with plans for de-escalation of insulin therapy.
As his clinical status improved, his insulin requirements decreased. By the time of discharge 5 days later, his glucose levels had stabilized, and he no longer required scheduled prandial or correctional insulin. Tirzepatide and dapagliflozin were restarted once oral intake, hydration, renal function and clinical stability were satisfactory. He was instructed to administer his next dose of insulin icodec 7 days after his last injection, coinciding with the day of discharge.
Practice Point: If insulin icodec is not available on the hospital formulary, arrangements should be made for the patient to bring their home supply. If a dose is missed, administer it as soon as feasible. The original weekly dosing day may be retained provided there will be at least four days between consecutive injections; otherwise, continue weekly dosing from the new administration day. Increase glucose monitoring during the transition.

Clinical Vignette: Case 1. Use of Icodec During Hospitalization

recommendations are therefore derived largely from expert opinion and pharmacologic principles rather than empirical evidence.[12,13] This represents a critical gap, given the dynamic and often unpredictable metabolic changes that characterize the perioperative period.

The prolonged half-life of insulin icodec represents an inherent limitation that is not easily mitigated. Unlike daily basal insulin analogs, its pharmacokinetic profile precludes rapid titration or withdrawal, which may increase the risk of hypoglycemia in the setting of reduced oral intake or, conversely, hyperglycemia when insulin requirements increase abruptly. These constraints are intrinsic to the molecule and limit its adaptability in acute care environments.

Current expert guidance suggests that continuation of insulin icodec may be appropriate for minor procedures in which reduced caloric intake is expected for less than 24 hours and no prolonged preoperative liquid diet is required. In this setting, capillary blood glucose should be monitored every 2–4 hours, with hyperglycemia managed with correctional doses of a rapid-acting insulin analog. Hypoglycemia should be managed according to standard protocols. Emergency surgery should not be delayed because of recent icodec administration. The dose and timing of the last injection should be established, residual icodec activity should be recognized, and glucose should be monitored frequently. Intravenous insulin, with dextrose when required, should be used when rapid titration is necessary.

Case 2. Use of Icodec with Steroid-Induced Hyperglycemia During Hospitalization
A 65-year-old man with type 2 diabetes was admitted for an exacerbation of chronic obstructive pulmonary disease and pneumonia. Prior to admission, his diabetes was well controlled with once-weekly insulin icodec 350 units, semaglutide 2 mg subcutaneously weekly, and metformin 1000 mg twice daily. His last dose of icodec was administered 4 days prior to admission. His medical history was significant for obesity, hypertension, obstructive sleep apnea, and cigarette smoking.
On admission, he was treated with short-acting bronchodilators, supplemental oxygen, and amoxicillin-clavulanate. Prednisone was started with a planned tapering regimen. Metformin was held initially and resumed once clinical stability was achieved. Semaglutide was held due to concerns about nausea and reduced oral intake. Given the recent administration of insulin icodec and its prolonged half-life (~8 days), it was assumed that a substantial proportion of his basal insulin requirements remained covered.
Point-of-care capillary blood glucose monitoring was initiated before meals and at bedtime, with correctional insulin using a rapid-acting analog administered at the same time points. Within 24–48 hours of starting prednisone, he developed marked hyperglycemia, predominantly in the afternoon and evening, with frequent need for correction insulin. In response, scheduled prandial insulin was initiated and titrated. Given the pattern of steroid-induced hyperglycemia, additional daytime insulin coverage was required despite recent icodec dosing. As hyperglycemia persisted, further intensification was required with escalation of prandial insulin doses. Consideration was given to adding intermediate-acting insulin timed to steroid administration; however, glycemic management was achieved with adjustment of prandial insulin alone. His regularly scheduled icodec dose became due on hospital day 3 and was administered at his usual dose. Glucose was monitored closely because prednisone treatment and acute illness had temporarily increased his prandial insulin requirements.
As his clinical status improved and a 5-day course of prednisone was completed, his insulin requirements declined rapidly. Prandial and correctional insulin were progressively reduced and ultimately discontinued to avoid hypoglycemia, recognizing the continued presence of long-acting basal insulin from prior icodec dosing. By the time of discharge 7 days later, his glucose levels had stabilized. Semaglutide was restarted. He was instructed to administer his next dose of insulin icodec seven days after the dose administered in hospital.
Practice Point: In patients receiving insulin icodec, glucocorticoid therapy may produce substantial daytime and postprandial hyperglycemia that is not adequately addressed by existing basal insulin coverage. Morning prednisone typically produces glucose excursions that peak in the afternoon and evening. Management generally requires glucose-guided titration of scheduled prandial and correctional insulin and, in selected patients, addition of intermediate-acting insulin timed to prednisone administration. Dexamethasone produces more sustained hyperglycemia and may require scheduled prandial and correctional insulin, intermediate-acting insulin in divided doses, or intravenous insulin in clinically unstable patients. Because icodec provides prolonged and relatively fixed basal insulin exposure, routine addition of another long-acting basal insulin should be avoided. Supplemental insulin should be reduced proactively as glucocorticoids are tapered or discontinued to minimize the risk of hypoglycemia.

Clinical Vignette: Case 2. Use of Icodec with Steroid-Induced Hyperglycemia During Hospitalization

Clinical Scenario	Suggested Management Approach	Rationale
Minor procedure with minimal fasting and expected return to usual intake within 24 hours	Continue icodec at the usual dose and weekly schedule. Monitor glucose every 2–4 hours while fasting and use rapid-acting correction insulin as required.	The existing icodec dose provides basal coverage throughout the procedure. Brief fasting generally does not require conversion to another basal insulin.
Short-term fasting, reduced intake, or moderate acute illness	Recognize that residual icodec activity remains present. Increase glucose monitoring and use scheduled prandial insulin when eating and correction insulin as required. Do not automatically add once-daily basal insulin. Monitor for delayed hypoglycemia as illness resolves or intake decreases.	The prolonged action of icodec limits down-titration. Flexible short-acting insulin can address temporary hyperglycemia without creating prolonged basal-insulin overlap.
Emergency procedure or surgery	Do not delay the procedure because of recent icodec administration. Confirm the dose and timing of the last injection, account for residual icodec activity, and monitor glucose frequently. Use intravenous insulin, with dextrose when required, if rapid titration is necessary.	The administered icodec dose cannot be withdrawn. Intravenous insulin and dextrose permit rapid adjustment around changing operative and nutritional requirements.
Elective major surgery with anticipated fasting or reduced caloric intake for more than 24 hours, or a preoperative liquid diet lasting at least 2 days	Consider a planned transition to once-daily basal insulin. Administer the final icodec dose approximately 4 weeks before surgery. Estimate the daily basal requirement by dividing the weekly icodec dose by seven and generally initiate daily basal insulin approximately 2 weeks after the last icodec dose, or earlier if fasting glucose exceeds 10 mmol/L. Titrate according to fasting glucose.	Daily basal insulin provides greater perioperative flexibility. Delaying its initiation reduces the risk of excessive overlap with residual icodec activity.
High-risk patient, including frailty, renal impairment, recurrent hypoglycemia, or unpredictable nutritional intake	Develop an individualized plan before surgery and consider transition to once-daily basal insulin when time permits. Use more conservative dosing and more frequent glucose monitoring. Consider endocrinology consultation.	Reduced insulin clearance and changing nutritional intake may increase hypoglycemia risk, while daily insulin permits more responsive dose adjustment.
Critical illness or intensive care	Account for residual icodec activity. Use intravenous insulin when rapid titration is required; do not automatically add full-dose once-daily basal insulin. Provide dextrose when clinically indicated and monitor glucose frequently.	Icodec continues to provide basal insulin exposure during critical illness. Intravenous therapy allows rapid adjustment while avoiding unrecognized overlap with another basal insulin.
Postoperative period while residual icodec remains active	Monitor glucose frequently and use prandial, correctional, or intravenous insulin according to clinical status and nutritional intake. Reduce supplemental insulin proactively as stress hyperglycemia resolves or intake declines.	Persistent icodec activity may not match rapidly changing postoperative insulin requirements, increasing the risk of both hyperglycemia and delayed hypoglycemia.
Restarting icodec after temporary treatment with once-daily basal insulin	Once the patient is clinically stable and eating reliably, calculate the weekly icodec dose by multiplying the current daily basal requirement by seven. Administer the first icodec dose on the day following the final daily basal dose. Individualize—and consider omitting—the optional one-time additional dose when postoperative insulin requirements are reduced or unstable.	Using the current daily basal requirement reflects postoperative insulin needs and reduces the risk of excessive overlap or return to an inappropriate preoperative dose.

Table 1. Practical Perioperative Management of Insulin Icodec; *courtesy of Robyn Houlden, MD, FRCPC*

Case 3. Perioperative Management of Icodec for Major Surgery
A 70-year-old woman with a 15-year history of type 2 diabetes was scheduled for elective coronary artery bypass grafting. Her medical history included hypertension, hyperlipidemia, and stage 2 chronic kidney disease. Her outpatient diabetes regimen consisted of once-weekly insulin icodec 420 units, metformin, empagliflozin, and semaglutide. Her most recent A1C was 7.4%.
Because major surgery and a postoperative intensive care stay were anticipated, a planned transition from icodec to once-daily basal insulin was initiated four weeks before surgery. Her final 420-unit dose of icodec was administered at that time. Fasting glucose was measured daily. Two weeks after the last icodec injection, insulin glargine was started at 60 units daily, calculated by dividing the weekly icodec dose by seven. Earlier initiation would have been considered if fasting glucose had risen above 10 mmol/L. The glargine dose was subsequently reviewed every 2–3 days and adjusted according to fasting glucose and hypoglycemia. Before surgery, fasting glucose was generally 6.5–7.5 mmol/L without hypoglycemia.
Empagliflozin was discontinued three days before surgery to reduce the risk of perioperative euglycemic diabetic ketoacidosis. Metformin was withheld on the day of surgery. Semaglutide was managed according to institutional anesthesia guidance and the patient's gastrointestinal symptoms and aspiration risk. On the evening before surgery, she received 30 units of insulin glargine, representing 50% of her usual daily basal dose.
An intravenous insulin infusion was initiated on the morning of surgery and titrated according to the institutional cardiac-surgery protocol, targeting glucose between 6 and 10 mmol/L. Glucose was monitored hourly intraoperatively and while the infusion was being actively adjusted.
Postoperatively, intravenous insulin was continued in the intensive care unit. Once she was hemodynamically stable and eating reliably, she was transitioned to a subcutaneous basal–bolus regimen. Insulin glargine was administered before discontinuation of the intravenous insulin infusion according to institutional transition procedures. Her insulin requirements declined during recovery, and her final daily glargine requirement before discharge was 50 units.
At discharge, she was transitioned back to insulin icodec. Her new weekly dose was calculated from her current daily basal requirement: 50 units multiplied by seven, giving 350 units once weekly. The first 350-unit dose of icodec was administered on the day following her final glargine dose. The optional one-time additional icodec dose was omitted because her postoperative insulin requirements remained potentially unstable and her risk of hypoglycemia was increased. She was instructed to monitor fasting and premeal glucose closely and was contacted by the diabetes team within one week to review glucose levels and determine whether further dose adjustment was required. Resumption of her non-insulin glucose-lowering medications was individualized according to oral intake, renal function, hydration, and postoperative clinical status.
Practice Point: For planned major surgery, conversion from icodec to once-daily basal insulin should be managed as a glucose-guided transition. Dividing the weekly icodec dose by seven provides an initial estimate of the daily basal requirement, but daily basal insulin is generally not started until approximately two weeks after the last icodec injection, or earlier if fasting hyperglycemia develops. When restarting icodec, calculate the weekly dose from the patient's current daily basal requirement and administer the first weekly dose on the day following the final daily basal dose. The optional one-time additional dose should be individualized and may be omitted when postoperative insulin requirements are reduced or unstable.

Clinical Vignette: Case 3. Perioperative Management of Icodec for Major Surgery

For major surgery—particularly when reduced caloric intake is anticipated for more than 24 hours postoperatively or when a preoperative liquid diet of at least 2 days is planned—insulin icodec should be discontinued in advance due to its prolonged half-life. The final dose should be administered approximately 4 weeks prior to surgery or before initiation of the liquid diet. Transition to a daily basal insulin regimen should generally occur approximately 2 weeks after the last icodec dose, or sooner if fasting hyperglycemia develops. **Clinical vignette case 3** describes the use of icodec insulin during surgery.

A practical starting dose for daily basal insulin is one-seventh of the prior weekly icodec dose, with subsequent titration based on glycemic response and clinical judgment. During periods of reduced caloric intake, such as a preoperative liquid diet, the basal insulin dose should typically be reduced (e.g., by 50%), depending on the individual's risk of hypoglycemia.[12] Fifty percent of the usual daily basal insulin dose should be administered the night before or the morning of the procedure, or reduced according to an institution's usual practice.[12]

Perioperative glycemic control, including the management of hypo- and hyperglycemia, should align with established institutional practices. When restarting icodec after temporary treatment with daily basal insulin, administer the first icodec dose on the day following the last daily basal dose.[3] Calculate the maintenance weekly dose from the current daily basal requirement rather than automatically returning to the preoperative icodec dose. The one-time additional dose should be individualized, recognizing that postoperative insulin requirements may remain reduced or unstable.

Conclusion

Insulin icodec represents an important advancement in basal insulin therapy, offering simplified dosing and stable glycemic control in outpatient settings. Available evidence suggests that it can be continued in selected clinically stable hospitalized patients, although inpatient evidence remains limited. However, its prolonged pharmacokinetic profile introduces important limitations in the inpatient and perioperative setting, particularly when rapid titration is required. Given the limitations of the current evidence base, including reliance on post hoc analyses and the absence of prospective perioperative studies, clinical use of insulin icodec in hospital should be individualized. Further research is needed to define optimal management strategies, particularly in higher-risk populations and surgical settings, and to incorporate more detailed glycemic outcomes such as continuous glucose monitoring metrics.

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