Weekly Basal Insulin: A Phase II Randomized Controlled Trial Initial Dosing and Titration

INSULIN EFSITORA ALFA

INITIAL VISIT: Week 0, Visit 3 (Randomization Visit)

Initial dose[a]: Obtain BW and median FBG in week prior to V3 and consult table below.

Median FBG, mg/dL	BIF Dose for BW ≤ 80kg, mg	BIF Dose for BW 80.1-100 kg, mg	BIF Dose for BW 100.1-120 kg, mg	BIF Dose for BW ≥ 120.1 kg, mg
≤140	3	4.5	6	7.5
141-180	6	7.5	10.5	12
181-220	9	10.5	12	13.5
>220	12	13.5	15	16.5

Loading dose strategy found to be safe and effective in reducing transient hyperglycemia

TITRATION

Week 1, Visit 4:

Calculate total weekly dose BIF mg from dose administered at V3 (1/3 the dose administered at V3).

Visit 5: Use the table below.

Median FBG (mg/dL)[b]	Week 1 (V4) Second Dose, mg	Week 2 (V5) Third Dose, mg	Subsequent Dose ≤ 5 mg, mg	Week Dose > 5 mg, mg
<80 mg/dL or any nocturnal hypoglycemia or multiple episodes of hypoglycemia[e]	D^c -1.5	D^c -1.5	D^d -1.5	D^d -2
80-100	D^c -1	D^c - 0.5	No change	No change
101-140	No change	No change	D^d + 0.25	D^d + 0.5
141-180	D^c + 3	D^c + 1.5	D^d + 0.5	D^d + 1
>180	D^c + 5	D^c + 3	D^d + 0.75	D^d + 1.5

Once-weekly basal insulin formulations are not currently approved by the FDA.

BIF, basal insulin efsitora alpha; BW, body weight; FGB, fasting blood glucose; SMBG, self-monitoring blood glucose; V, visit; wk, week.

[a] The initial dose of BIF reflects the 3-fold increase needed to reduce the time to target glycemic response and should only be administered once at Visit 3.

[a] Based on median fasting glucose (MFG) from ≥3 FG from previous wk.

[a] Dose for wk 1 (V4) was 1/3 of the initial dose. Dose for wk 2 (V5) was week 1 (V4) dose.

[d] BIF dose adjustment starting at wk 3 (V6) depended on whether previous (wk 2) dose was ≤5 mg or >5 mg and was adjusted weekly up to wk 12 (V15) then at wk 16 (V17) wk 20 (visit 18), and wk 24 (V19).

[e] The BIF dose was not increased in any SMBG reading was documented at ≤70 mg/dL at any time in the preceding wk. If multiple episodes of hypoglycemia with SMBG ≤70 mg/dL were recorded, guidance for dose reduction according to the applicable visit number followed. Dose decreases of 1 mg were made when severe hypoglycemia (requiring assistance) occurred, or if any SMBG was documented at ≤54 mg/dL in the preceding wk.

Bue-Valleskey JM, et al. *Diabetes*. 2023;72(suppl1):811-P.

Weekly Basal Insulin: A Phase IIIa Randomized, Open Label Trial Initial Dosing and Titration

INSULIN ICODEC

Prior Basal Insulin Status	ICODEC INITIAL DOSING		
	WEEK 1	WEEK 2	WEEK 3
Insulin naïve	70 units	70 units + titration as needed	Ongoing titration as needed
Prior basal insulin	10.5× daily basal dose	7× daily basal dose	4× daily basal dose + titration as needed

Pre-Breakfast SMBG		Icodec Weekly Dose Adjustment
Up-titration	Mean of SMBG values >7.2 mmol/L (>130 mg/dL)	+20 units
Target	Mean of SMBG values 4.4-7.2 mmol/L (80-130 mg/dL)	0 units
Down-titration	Lowest SMBG value <4.4 mmol/L (<80 mg/dL)	-20 units

One unit of icodec has a comparable glucose-lowering effect to one unit of comparator basal insulin; therefore, at randomization, the once-weekly dose of icodec corresponds to 7× the once-daily dose of comparator basal insulin

50%

In patients switching from once- or twice-daily basal insulin, the dose will be increased by 50% for the first injection only

Once-weekly basal insulin formulations are not currently approved by the FDA.

Philis-Tsimikas A, et al. *Lancet Diabetes Endocrinol.* 2023; 11(6):414-425. Erratum in: *Lancet Diabetes Endocrinol.* 2023 Jul;11(7):e9; Bajaj HS, et al. *touchREV Endocrinol.* 2023;19:4-6.

SMBG, self-monitoring blood glucose.