

ITEM S1. Detailed description of Class I and II safety events

Class I Events	Responding "yes" to "In the past 12 months, have you had any of the following problems":
Hypoglycemia ¹	"Nervousness, sweating, trembling, weakness, palpitations, and/or confusion with a blood sugar less than 70 (mg/dL) by finger stick or blood test, that improved with glucose tablets, juice, or other substance with sugar in it"
Hyperkalemia requiring a change ²	"High potassium blood level requiring a change in medication, change in diet, and/or required you to take a prescription of kayexelate or polystyrene (dark brown fluid prescribed to decrease potassium)"
Falling/Severe Dizziness ³	"Falling" or "Dizziness when standing up to the point that you might fall"
Bleeding ⁴	"Bleeding"
Angioedema ⁵	"Facial, tongue, and/or throat swelling"
Confusion or unable to think clearly ⁶	"Confusion or unable to think clearly"
Nausea, vomiting and/or diarrhea ⁷	"Nausea, vomiting, and/or diarrhea"
New or worsening ankle swelling (edema) ⁸	"New or worsening ankle swelling"
Muscle weakness or muscle cramps ⁹	"Muscle weakness or muscle cramps"
Skin rash ¹⁰	"Skin rash"
Class II Events	Clinical measurements
Hyperkalemia ¹¹	Potassium > 5.5 mEq/L
Hypokalemia ¹²	Potassium < 3.5 mEq/L
Hyperglycemia ¹³	Glucose > 250 mg/dL
Hypoglycemia ¹⁴	Glucose < 70 mg/dL
Low Hemoglobin ¹⁵	Hemoglobin < 8.5 g/dL
High Hemoglobin ¹⁶	Hemoglobin > 13.5 g/dL
Low Pulse ¹⁷	Pulse < 50 bpm
Low Systolic Blood Pressure (SBP) ¹⁸	SBP < 90 mmHg
Change in SBP ¹⁹	Change between sitting and standing SBP > 20 mmHg

¹antidiabetic insulin, antidiabetic non-insulin inj, antidiabetic non-insulin oral

²raas-blocker, diuretic k-sparing, NSAID

³raas-blocker, beta-blocker, diuretic non k-sparing, diuretic k-sparing, ca-channel blocker, central antihypertensive, antianginal, other antihypertensive

⁴salicylate, warfarin

⁵ACE inhibitors

⁶analgesic opiate, tramadol

⁷NSAID, colchicine, ferrous sulfate, ferrous gluconate

⁸ca-channel blocker, pioglitazone, other antihypertensive

⁹cholesterol statin

¹⁰any drug

¹¹raas-blocker, diuretic k-sparing, NSAID

¹²diuretic non k-sparing

¹³none

¹⁴antidiabetic insulin, antidiabetic non-insulin inj, antidiabetic non-insulin oral

¹⁵not on hematopoietic

¹⁶hematopoietic

¹⁷beta-blocker

¹⁸other antihypertensive, raas-blocker, beta-blocker, diuretic non k-sparing, diuretic k-sparing, ca-channel blocker, central antihypertensive, antianginal

¹⁹other antihypertensive, raas-blocker, beta-blocker, diuretic non k-sparing, diuretic k-sparing, ca-channel blocker, central antihypertensive, antianginal