World Health Organization

Guidelines on second-and third-line medicines and type of insulin for the control of blood glucose levels in non-pregnant adults with diabetes mellitus

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Contents

Abbreviations

CDC	Centers for Disease Control and Prevention
CI	confidence interval
CrI	credibility interval
COI	conflict of interest
CVD	cardiovascular disease
DOI	declaration of interest
DPP-4 inhibitors	dipeptidyl peptidase-4 inhibitors
EMA	European Medicines Agency
EML	Essential Medicines List
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HbA1c	glycated haemoglobin A1c
IDF	International Diabetes Federation
PICO	population – intervention – comparator – outcome
MET	metformin
MI	myocardial infarction
NICE	National Institute for Health and Care Excellence
NMA	network meta-analysis
NPH	neutral protamine hagedorn
OHA	oral hypoglycaemic agents
RCT	randomized controlled trial
RHI	regular human insulin
SIGN	Scottish Intercollegiate Guidelines Network
SGLT-2 inhibitor	sodium-glucose co-transporters type 2 inhibitors
SU	sulfonylureas
TZDs	thiazolidinediones (glitazones)
UHC	universal health coverage
WHO PEN	*WHO Package of Essential Non-Communicable Disease (NCD) Interventions* for primary care in low-resource settings

Glossary

Cardiovascular diseases (CVDs)
A group of disorders of the heart and blood vessels that include coronary heart disease and cerebrovascular disease.

Diabetic ketoacidosis and hyperosmolar hyperglycaemia
Life-threatening conditions characterized by fluid and electrolyte depletion, high blood glucose levels and metabolic acidosis (metabolic acidosis may be absent in hyperosmolar hyperglycaemia).

Dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors or gliptins)
Oral hypoglycaemic agents used in treating type 2 diabetes. They suppress the degradation of incretins by blocking the action of the enzyme dipeptidyl-peptidase 4. This stimulates insulin secretion and suppresses glucagon release.

HbA1c
Haemoglobin glycated by non-enzymatic attachment of glucose to haemoglobin. The concentration of HbA1c is the most commonly used measure of chronic glycaemia in clinical trials and diabetes management. It is considered to reflect the integrated mean glucose level over the previous 8–12 weeks.

Hypoglycaemia
Potentially life-threatening low concentration of blood glucose, most frequently a side-effect of pharmacological treatment. There is no universally agreed definition. In studies the definitions of hypoglycaemia are most frequently in the range <4 mmol/L to ≤ 2.8 mmol/L. Severe hypoglycaemia is most frequently defined as a symptomatic condition that requires the assistance of a third person for resuscitative actions.

Insulin analogues
Insulins different from any occurring in nature and derived from human insulin by modifying its structure to change the pharmacokinetic profile.

Metformin
A biguanide oral hypoglycemic agent used in treating type 2 diabetes. It decreases glucose production by the liver and increases the insulin sensitivity of body tissues.

Neutral Protamine Hagedorn (NPH or isophane) insulin
An intermediate-acting insulin preparation used in type 1 and type 2 diabetes. It is produced by crystallizing zinc-insulin-protamines at neutral pH. It is called neutral protamine Hagedorn for inventor Hans Christian Hagedorn.

Sodium-glucose co-transporters type 2 inhibitors (SGLT-2 inhibitors)
Oral hypoglycaemic agents used in treating type 2 diabetes. They lower blood glucose by causing the kidneys to remove glucose from the body through the urine.

Sulfonylureas
Oral hypoglycemic agents used in treating type 2 diabetes. They stimulate insulin secretion by the pancreas.

Thiazolidinediones (glitazones)
Oral hypoglycaemic agents used in treating type 2 diabetes. They work by lowering insulin resistance – a core physiologic defect in those with type 2 diabetes.

Type 1 diabetes
Diabetes caused by the destruction of pancreatic beta-cells, resulting in lack of insulin production by the pancreas and need for insulin injections for survival.

Type 2 diabetes
Diabetes characterized by various degrees of disorders of insulin action in the body and insulin secretion by the pancreas. Insulin injections are not needed for survival, but might be needed for controlling blood glucose levels.