CHOOSE · START · TITRATE

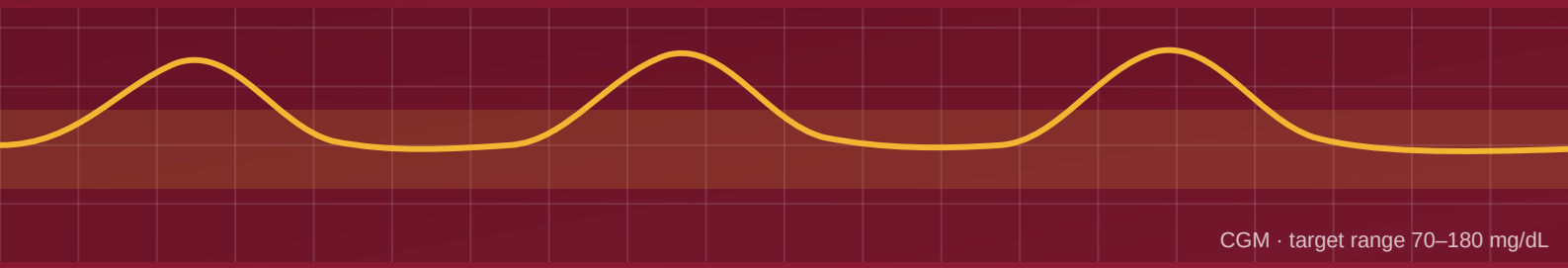
AETCM

Diabetes Drug Therapy

Oral Hypoglycaemic Agents & Insulin Therapy — for India

Every oral drug class with doses, renal adjustment and cautions; how to combine and step up; and how to start, titrate and intensify insulin — basal, premixed and basal–bolus — in the clinic, the ward and the emergency department

Metformin · Sulfonylureas · DPP-4 inhibitors · SGLT2 inhibitors · Pioglitazone · α-glucosidase inhibitors · Master OHA dose table · Fixed-dose combinations · Insulin chart & costs · Basal start & titration · Premix & basal–bolus · Dose calculations · IV insulin & DKA · Hypoglycaemia



AETCM
Academy for Emergency, Trauma & Critical care Medicine

By

Dr. Gireesh Kumar K.P.

For general practitioners, physicians, emergency doctors, postgraduates, interns, nurses and MBBS students

Diabetes Drug Therapy

Oral Hypoglycaemic Agents and Insulin Therapy — A Practical Guide for India

Drug classes · Doses and renal adjustment · Combinations and step-up · Special situations
Insulin types · Starting and titrating insulin · Intensification · Dose calculations · Hospital and emergency insulin · Hypoglycaemia



Dr. Gireesh Kumar K.P.

Academy for Emergency, Trauma & Critical care Medicine (AETCM)
First Edition · October 2026

How to use this book

If you need to…	Go to
See the whole of drug therapy on one page	Diabetes drug therapy at a glance (p. 4)
Set a target and choose the first and second drug	Chapter 1
Know how a drug class works, its benefits and its cautions	Chapters 2–6
Look up a dose, maximum dose or renal adjustment	Chapter 7 (master OHA table) and Chapter 9
Prescribe a fixed-dose combination or add the next drug	Chapter 8
Compare insulins and costs; U-40/U-100; inject and store insulin	Chapter 10
Start and titrate basal insulin	Chapter 11
Intensify — premixed, basal-plus or basal–bolus	Chapters 12–13
Treat hyperglycaemia in the ward, DKA/HHS or surgery	Chapter 14
Treat hypoglycaemia; insulin in pregnancy, CKD and the elderly	Chapter 15
Teach injection technique, storage and sick-day rules	Chapter 16

Note on doses. Doses are usual adult doses used in India and are given as a guide. Always check the current product information, adjust for renal and hepatic function, age and co-morbidity, and individualise therapy. Brand names are given only as examples of products available in India; no endorsement is implied. Recommendations follow the ADA Standards of Care in Diabetes (2025), the ADA/EASD consensus on management of hyperglycaemia in type 2 diabetes, RSSDI clinical practice recommendations and the Joint British Diabetes Societies inpatient guidance.

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Preface

India has more than one hundred million people living with diabetes, and most of them are treated by general practitioners and physicians in busy clinics. In that setting the questions are practical ones: which tablet to start, what dose, when to add the next drug, what to do when the kidney function falls — and, sooner or later, how to start insulin without fear and titrate it safely.

The choice of drugs has never been wider. Metformin and the sulfonylureas have been joined by DPP-4 inhibitors, SGLT2 inhibitors with proven heart and kidney benefits, GLP-1 receptor agonists, dual agonists and a range of analogue insulins, many now available as low-cost generics in India. With this choice comes the need for a clear, practical guide.

This book deliberately leaves out the theory of diabetes. It deals only with drug treatment: every oral drug class with its doses, renal adjustment, benefits and cautions; a master dose table; fixed-dose combinations and step-up therapy; and then insulin — the types and brands, how to start basal insulin, how to titrate it, how to intensify with premixed or basal–bolus regimens, how to calculate doses, and how to use insulin in the ward, in DKA and HHS, around surgery and in pregnancy. Tables, flow charts, worked examples and clinical pearls are used throughout so that the answer can be found in seconds.

I hope this book helps doctors, nurses and students to treat diabetes more confidently and to keep their patients safe from both hyperglycaemia and hypoglycaemia.

Dr. Gireesh Kumar K.P.
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Pages 5, 10, 15, 22 and 27 feature other books by the author.

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Diabetes Drug Therapy at a Glance

The whole book on one page — for the busy clinic.

1 · Targets

- HbA1c <7% for most adults; <6.5% if achievable safely; <8% in frail elderly or limited life expectancy
- Fasting / pre-meal glucose 80–130 mg/dL; 1–2 h post-meal <180 mg/dL
- CGM: time in range (70–180) >70%, below 70 <4%

2 · First drug

- **Metformin** 500 mg OD–BD with meals, titrate weekly to 1–2 g/day
- ASCVD, heart failure or CKD → add **SGLT2 inhibitor** and/or **GLP-1 RA** regardless of HbA1c
- HbA1c ≥1.5% above target → start dual therapy

3 · Second and third drug

- SGLT2i · DPP-4i · sulfonylurea (gliclazide/glimepiride) · pioglitazone · GLP-1 RA
- Choose by heart/kidney benefit, weight, hypoglycaemia risk and cost
- Review every 3 months; do not wait with an HbA1c above target

4 · When to start insulin

- HbA1c >10% or glucose ≥300 mg/dL, or symptoms / weight loss / ketosis
- Not at target on 2–3 oral drugs
- Pregnancy, acute illness, surgery, severe CKD or liver failure

5 · Basal insulin

- Start 10 U/day or 0.1–0.2 U/kg (glargine any fixed time; NPH at bedtime)
- ↑ 2 U every 3 days until fasting 80–130 mg/dL
- Hypoglycaemia → ↓ 10–20%. Basal >0.5 U/kg → intensify

6 · Intensify

- **Basal-plus:** 4 U (or 10% of basal) rapid insulin before largest meal
- **Premix BD:** 2/3 before breakfast, 1/3 before dinner
- **Basal–bolus:** TDD 0.4–0.5 U/kg; 50% basal, 50% split over meals

7 · Hospital and emergencies

- Ward: basal–bolus + correction; no sliding scale alone; target 140–180 mg/dL
- DKA: fixed-rate IV insulin 0.1 U/kg/h after K^+ ≥3.5; add dextrose when glucose <250
- Stop SGLT2i 3 days before surgery

8 · Safety

- Hypoglycaemia: 15–20 g glucose, recheck in 15 min; unconscious → 25% dextrose IV or glucagon 1 mg
- Sick days: pause metformin, SGLT2i, SU; never stop basal insulin in type 1
- Teach injection technique and rotation

KEY POINT

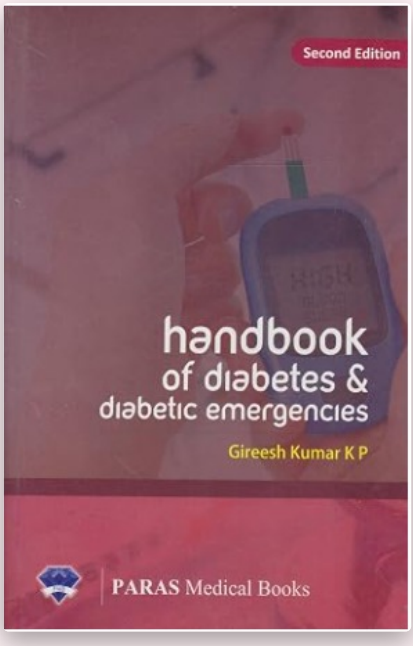
Diabetes treatment is a ladder that moves every 3 months: set a target, choose drugs that also protect the heart and kidney, add the next drug promptly, and start insulin early when it is needed — not as a last resort.

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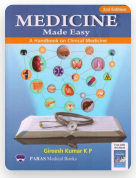
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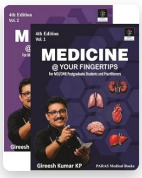
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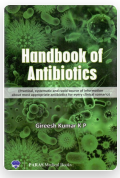
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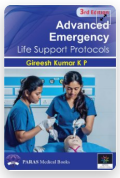
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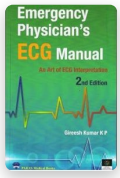
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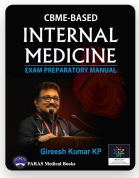
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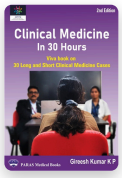
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PART I · CHAPTER 1

Treatment Targets and Choosing Therapy

Individualised goals and a stepwise, organ-protective plan for type 2 diabetes

Individualised glycaemic targets (ADA 2025)

Patient	HbA1c	Fasting / pre-meal	Post-meal (1–2 h)
Most non-pregnant adults	<7%	80–130 mg/dL	<180 mg/dL
Young, short duration, no CVD, low hypoglycaemia risk	<6.5%	80–130	<160
Elderly, frail, hypoglycaemia unawareness, advanced complications	<8%	90–150	<200
Pregnancy (pre-existing or GDM)	<6% (if no hypo)	<95	1 h <140; 2 h <120

Choosing therapy — a stepwise approach

1. **At diagnosis:** lifestyle + **metformin** (unless contraindicated). HbA1c ≥1.5% above target → start **two drugs**. HbA1c >10%, glucose ≥300 mg/dL, symptomatic or catabolic → **insulin** (± metformin).

▼

2. **Organ protection, independent of HbA1c:** established ASCVD or high risk → GLP-1 RA or SGLT2i with proven benefit · Heart failure → **SGLT2i** · CKD (eGFR ≥20 or albuminuria) → **SGLT2i**, plus GLP-1 RA if more glucose lowering needed.

▼

3. **Add the next drug by patient priority:** weight loss → GLP-1 RA / tirzepatide, SGLT2i · avoid hypoglycaemia → DPP-4i, SGLT2i, pioglitazone, GLP-1 RA · cost → sulfonylurea (gliclazide/glimepiride), pioglitazone, generic DPP-4i/SGLT2i.

▼

4. **Not at target on 2–3 drugs after 3 months:** add GLP-1 RA or **basal insulin**; then intensify insulin (Chapters 11–12).

Drug classes compared

Class	HbA1c ↓	Hypo risk	Weight	Heart failure	CKD / kidney	Cost (India)
Metformin	1–1.5%	None	Neutral / ↓	Neutral	Dose ↓ eGFR <45	Low
Sulfonylurea	1–1.5%	Yes	↑	Neutral	Caution; gliclazide/glipizide	Low
DPP-4 inhibitor	0.5–0.8%	None	Neutral	Avoid saxagliptin	Dose ↓ (except linagliptin)	Low–moderate
SGLT2 inhibitor	0.5–0.8%	None	↓	**Benefit**	**Benefit**	Low–moderate
Pioglitazone	0.7–1%	None	↑	**Avoid**	No adjustment; oedema	Low
α-glucosidase inhibitor	0.5–0.8%	None	Neutral	Neutral	Avoid eGFR <25	Low
GLP-1 RA / tirzepatide	1–2%	None	↓↓	Neutral	Benefit (semaglutide)	High
Insulin	Unlimited	Yes	↑	Neutral	Dose ↓ in CKD	Low (human)–mod.

CLINICAL PEARL

Reassess every 3 months. "Clinical inertia" — leaving a patient above target for years — is the commonest reason for poor control in India.

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PART I · CHAPTER 2

Metformin

The first-line oral drug — start low, go slow, and dose by kidney function

How it works

A biguanide that reduces hepatic glucose output and improves insulin sensitivity. It does not cause hypoglycaemia on its own and is weight-neutral or causes modest weight loss.

Indications

- First-line drug in type 2 diabetes with lifestyle measures
- Prediabetes at high risk (BMI ≥35, age <60, prior GDM)
- Add-on to insulin to limit insulin dose and weight gain
- PCOS with insulin resistance; gestational diabetes (selected, see Ch. 15)

Adverse effects

- **GI upset** (nausea, diarrhoea, metallic taste) — 20–30%; reduce with meals, slow titration and XR form
- **Vitamin B12 deficiency** with long-term use — check B12 periodically, especially with neuropathy or anaemia
- **Lactic acidosis** — rare; occurs with renal failure, shock, hypoxia, sepsis, liver failure

Contraindications

- eGFR <30 mL/min/1.73 m²
- Acute illness with hypoxia, shock, sepsis, dehydration; decompensated heart failure
- Severe liver disease, alcohol excess

Dosing

Preparation	Starting dose	Titration	Usual dose	Maximum
Metformin IR 250, 500, 850, 1000 mg	500 mg OD or BD with meals	↑ 500 mg every 1–2 weeks	1000 mg BD	2550 mg/day (in 2–3 doses)
Metformin XR / SR 500, 750, 1000 mg	500 mg OD with evening meal	↑ 500 mg weekly	1500–2000 mg OD	2000 mg/day

Dose by kidney function

eGFR (mL/min/1.73 m²)	Action
≥45	Full dose; check eGFR at least yearly
30–44	Do not start; if already on it, reduce to maximum 1000 mg/day; check eGFR every 3–6 months
<30	Stop

HOLD METFORMIN

On the day of iodinated contrast in patients with eGFR 30–60, liver disease, alcoholism or heart failure, and in intra-arterial studies; restart after 48 h if renal function is stable. Hold during acute illness with vomiting, dehydration or sepsis, and on the morning of major surgery.

CLINICAL PEARL

Most "metformin intolerance" is due to starting at 1 g/day on an empty stomach. Restart at 500 mg after dinner, or switch to the XR form — most patients then tolerate 1.5–2 g/day.

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PART I · CHAPTER 3

Sulfonylureas and Meglitinides

Insulin secretagogues — effective and inexpensive, but watch for hypoglycaemia

How they work

Close K_{ATP} channels on β-cells and release insulin regardless of the glucose level — hence the risk of hypoglycaemia. Meglitinides act the same way but briefly, and are taken with meals.

Sulfonylureas — doses

Drug	Strengths	Starting dose	Maximum	Frequency	Comments
Gliclazide	40, 80 mg	40–80 mg	320 mg/day	OD–BD before meals	Lower hypoglycaemia risk; preferred in elderly and CKD
Gliclazide MR	30, 60 mg	30 mg	120 mg	OD with breakfast	Once daily; 30 mg MR ≈ 80 mg IR
Glimepiride	0.5, 1, 2, 3, 4 mg	0.5–1 mg	8 mg (usually ≤4 mg)	OD before breakfast	Widely used in India; in many FDCs
Glipizide	2.5, 5 mg	2.5–5 mg	20 mg/day	OD–BD, 30 min before meals	Hepatic metabolism; usable in CKD
Glibenclamide (glyburide)	2.5, 5 mg	2.5 mg	15 mg/day	OD–BD	**Avoid in elderly and CKD** — prolonged hypoglycaemia

Meglitinides — doses

Drug	Dose	Maximum	When to take	Comments
Repaglinide	0.5–1 mg with each main meal	4 mg/dose; 16 mg/day	0–30 min before meals; skip meal → skip dose	Irregular meals; usable in CKD (start 0.5 mg)
Nateglinide	60–120 mg with each main meal	120 mg TDS	1–30 min before meals	Weaker; mainly post-meal glucose

Adverse effects

- **Hypoglycaemia** — commonest with glibenclamide, in the elderly, CKD, missed meals, alcohol
- Weight gain (2–3 kg)
- Rashes; rarely haemolysis in G6PD deficiency
- Secondary failure after several years as β-cell function declines

Contraindications and cautions

- Type 1 diabetes, DKA, pregnancy (switch to insulin)
- eGFR <30: avoid glimepiride and glibenclamide; gliclazide or glipizide at low dose
- Severe liver disease
- Interactions: fluconazole, clarithromycin, cotrimoxazole, alcohol ↑ hypoglycaemia

SULFONYLUREA HYPOGLYCAEMIA

Can be prolonged and recurrent for 24–72 h. Admit, give dextrose infusion and monitor glucose 1–2 hourly; octreotide 50–100 µg SC 6–12 hourly helps refractory cases. Do not send the patient home after a single glucose bolus.

CLINICAL PEARL

When basal insulin is started, continue the sulfonylurea at a lower dose; when prandial insulin is added, stop it.

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PART I · CHAPTER 4

DPP-4 Inhibitors (Gliptins)

Well-tolerated, weight-neutral and low hypoglycaemia risk — the most prescribed add-on in India

How they work

Inhibit dipeptidyl peptidase-4 and raise endogenous GLP-1 and GIP, increasing glucose-dependent insulin release and lowering glucagon. They lower HbA1c by about 0.5–0.8%, do not cause hypoglycaemia on their own and are weight-neutral. Most need dose reduction in CKD — linagliptin does not.

Doses and renal adjustment

Drug	Usual dose	eGFR 30–49	eGFR <30 / dialysis	Comments
Sitagliptin	100 mg OD	50 mg OD (eGFR 30–44)	25 mg OD	Neutral in heart failure (TECOS)
Vildagliptin	50 mg BD	50 mg OD	50 mg OD	Check LFT at baseline; avoid in liver disease
Saxagliptin	5 mg OD	2.5 mg OD (eGFR ≤45)	2.5 mg OD	**Avoid in heart failure** (SAVOR)
Linagliptin	5 mg OD	5 mg OD	5 mg OD	No renal adjustment — biliary excretion
Alogliptin	25 mg OD	12.5 mg OD	6.25 mg OD	Caution in heart failure
Teneligliptin	20 mg OD	20 mg OD	20 mg OD	Max 40 mg; low-cost in India; caution with QT prolongation
Evogliptin	5 mg OD	5 mg OD	Limited data	Available in India
Gemigliptin	50 mg OD	50 mg OD	50 mg OD	Available in India

Adverse effects

- Nasopharyngitis, headache
- Acute pancreatitis (rare) — stop if severe abdominal pain
- Bullous pemphigoid — stop if blisters appear
- Severe arthralgia (rare)
- Hypoglycaemia only when combined with SU or insulin

Best used

- Elderly patients and those at risk of hypoglycaemia
- CKD (linagliptin, no dose change)
- Combined with metformin as a single pill (Chapter 8)
- With basal insulin, to improve post-meal glucose

Do not combine

- DPP-4i with a GLP-1 RA or tirzepatide — no added benefit

CLINICAL PEARL

Gliptins are glucose-dependent and weight-neutral but have no proven heart or kidney protection. In a patient with heart failure or CKD, an SGLT2 inhibitor should come before a gliptin.

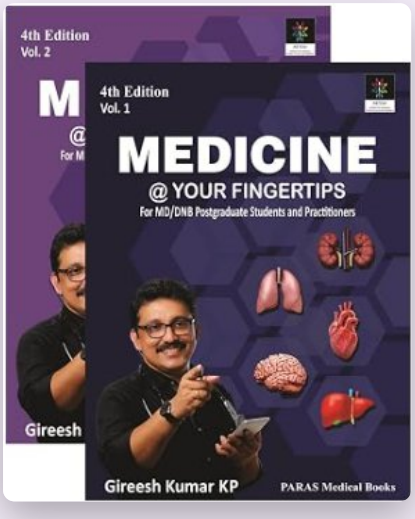
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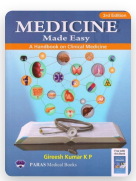
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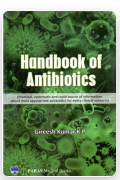
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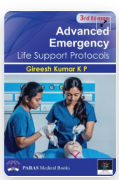
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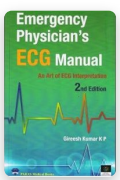
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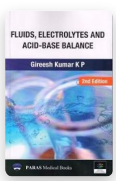
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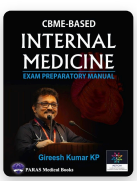
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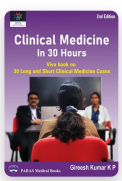
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PART I · CHAPTER 5

SGLT2 Inhibitors (Gliflozins)

Glucose lowering with proven heart and kidney protection

How they work

Block sodium–glucose co-transporter-2 in the proximal tubule, causing glycosuria (60–80 g/day), osmotic diuresis, natriuresis and weight loss (2–3 kg). HbA1c falls by 0.5–0.8%; glucose lowering is less when eGFR is below 45, but the heart and kidney benefits persist down to an eGFR of about 20.

Doses

Drug	Starting dose	Maximum	Start for heart/kidney if eGFR ≥	Proven outcome benefit
Empagliflozin	10 mg OD	25 mg OD	20	CV death (EMPA-REG), HF (EMPEROR), CKD (EMPA-KIDNEY)
Dapagliflozin	10 mg OD	10 mg OD	25	HF (DAPA-HF, DELIVER), CKD (DAPA-CKD)
Canagliflozin	100 mg OD	300 mg OD	30	CV events (CANVAS), diabetic kidney disease (CREDENCE)
Ertugliflozin	5 mg OD	15 mg OD	45 (glycaemic use)	HF hospitalisation (VERTIS-CV)
Remogliflozin	100 mg BD	100 mg BD	Glycaemic use only	Available in India

Adverse effects

- **Genital mycotic infections** (5–10%) — advise genital hygiene; treat with topical antifungal
- Urinary tract infection; rarely Fournier's gangrene
- Volume depletion, postural hypotension — reduce diuretic dose in the elderly
- Initial eGFR dip of 3–5 mL/min — expected; do not stop
- **Euglycaemic DKA** — ketoacidosis with glucose <250 mg/dL

Contraindications and cautions

- Type 1 diabetes (not licensed for glycaemia in India)
- History of DKA; ketogenic or very-low-carbohydrate diets
- Recurrent genital or urinary infections
- Dialysis — stop
- Pregnancy and lactation

EUGLYCAEMIC DKA — PREVENTION

Stop SGLT2 inhibitors **3 days before planned surgery** (ertugliflozin 4 days) and during acute illness, prolonged fasting, vomiting or dehydration. In any unwell patient on an SGLT2i with nausea, vomiting, abdominal pain or breathlessness, check blood ketones and a blood gas even if glucose is normal.

CLINICAL PEARL

In a patient with type 2 diabetes and heart failure (reduced or preserved EF) or CKD with albuminuria, start an SGLT2 inhibitor whatever the HbA1c — it is cardio-renal therapy that also lowers glucose. Generic dapagliflozin and empagliflozin have made this affordable in India.

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PART I · CHAPTER 6

Pioglitazone, α-Glucosidase Inhibitors and Other Agents

Useful add-ons when chosen for the right patient

Pioglitazone (thiazolidinedione)

A PPAR-γ agonist that improves insulin sensitivity in muscle, liver and fat. HbA1c ↓ 0.7–1%, durable effect, no hypoglycaemia, inexpensive; benefits fatty liver (MASLD/NASH) and reduced recurrent stroke (IRIS).

Dose	Maximum	Renal
7.5–15 mg OD	45 mg OD (usual ≤30 mg)	No adjustment

Cautions

- **Contraindicated in heart failure** (NYHA III–IV) — fluid retention, oedema
- Weight gain; distal fractures in women
- Avoid with active or past bladder cancer, unexplained haematuria
- Check LFT; avoid if ALT >2.5 × ULN
- Oedema worse with insulin — use the lowest dose

α-Glucosidase inhibitors

Drug	Starting dose	Maximum	How to take
Acarbose	25 mg TDS	100 mg TDS (50 mg TDS if <60 kg)	With the first bite of each main meal
Voglibose	0.2 mg TDS	0.3 mg TDS	Just before meals
Miglitol	25 mg TDS	100 mg TDS	With the first bite of each main meal

They delay carbohydrate digestion and lower **post-meal glucose** — useful in Indian carbohydrate-rich diets. Flatulence, bloating and diarrhoea are common; start low and titrate. Avoid in inflammatory bowel disease, bowel obstruction, eGFR <25 and cirrhosis.

HYPOGLYCAEMIA ON AN AGI

When combined with an SU or insulin, treat hypoglycaemia with **glucose (dextrose)**, not table sugar — sucrose absorption is blocked.

Other oral agents

Drug	Dose	Use and comments
Oral semaglutide (GLP-1 RA)	3 mg OD × 30 days → 7 mg → 14 mg OD	Take on waking with ≤120 mL water, 30 min before food or other drugs. Weight loss; GI side effects. Higher-dose formulations are available in some countries
Saroglitazar (PPAR-α/γ)	4 mg OD	Approved in India for diabetic dyslipidaemia (high triglycerides) and MASLD/NASH; modest HbA1c effect
Bromocriptine-QR	0.8 mg on waking, ↑ weekly to 1.6–4.8 mg	Within 2 h of waking with food; nausea, dizziness; rarely used
Colesevelam	3.75 g/day	Bile acid sequestrant; small HbA1c and LDL fall; constipation; limited availability

CLINICAL PEARL

Pioglitazone 15 mg with metformin is an inexpensive, hypoglycaemia-free combination for an insulin-resistant patient with fatty liver and no heart failure — check for ankle oedema at every visit.

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PART I · CHAPTER 7

Master Table of Oral Hypoglycaemic Agents

Class, drug, starting dose, maximum dose, frequency and key cautions — adult doses

Start at the lower dose in the elderly and in CKD. Adjust for eGFR as shown in Chapter 9. Check current product information.

Drug	Starting dose	Maximum dose	Frequency	Key cautions
BIGUANIDE — first line				
Metformin IR	500 mg	2550 mg/day	BD–TDS, with meals	GI upset, B12 ↓; stop eGFR <30; hold for contrast/acute illness
Metformin XR	500 mg	2000 mg/day	OD with dinner	Better GI tolerance
SULFONYLUREAS				
Gliclazide / MR	40–80 mg / 30 mg	320 mg / 120 mg	OD–BD / OD	Preferred SU in elderly and CKD
Glimepiride	0.5–1 mg	8 mg	OD	Hypoglycaemia, weight gain; avoid eGFR <30
Glipizide	2.5–5 mg	20 mg	OD–BD	Usable in CKD at low dose
Glibenclamide	2.5 mg	15 mg	OD–BD	Avoid in elderly and CKD
MEGLITINIDES				
Repaglinide	0.5–1 mg	4 mg/dose; 16 mg/day	With meals	Skip dose if meal skipped
Nateglinide	60 mg	120 mg TDS	With meals	Weak; post-meal effect
DPP-4 INHIBITORS				
Sitagliptin	100 mg	100 mg	OD	50 mg eGFR 30–44; 25 mg <30
Vildagliptin	50 mg	100 mg/day	BD	50 mg OD if eGFR <50; LFT
Saxagliptin	5 mg	5 mg	OD	2.5 mg eGFR ≤45; avoid in HF
Linagliptin	5 mg	5 mg	OD	No renal adjustment
Teneligliptin	20 mg	40 mg	OD	Caution with QT prolongation
Alogliptin	25 mg	25 mg	OD	12.5 mg eGFR 30–59; 6.25 mg <30
SGLT2 INHIBITORS				
Empagliflozin	10 mg	25 mg	OD	Genital infection, volume depletion, euglycaemic DKA
Dapagliflozin	10 mg	10 mg	OD	Stop 3 days before surgery
Canagliflozin	100 mg	300 mg	OD before breakfast	100 mg if eGFR <60
Ertugliflozin	5 mg	15 mg	OD	Stop 4 days before surgery
Remogliflozin	100 mg	200 mg/day	BD	Glycaemic use
THIAZOLIDINEDIONE · α-GLUCOSIDASE INHIBITORS · OTHERS				
Pioglitazone	7.5–15 mg	45 mg	OD	Avoid in HF; oedema, weight gain, fractures
Acarbose	25 mg	100 mg TDS	TDS, first bite	Flatulence; treat hypo with glucose
Voglibose	0.2 mg	0.3 mg TDS	TDS before meals	Flatulence
Miglitol	25 mg	100 mg TDS	TDS, first bite	Avoid eGFR <25
Oral semaglutide	3 mg	14 mg	OD, fasting	30 min before food; nausea
Saroglitazar	4 mg	4 mg	OD	Diabetic dyslipidaemia, MASLD

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PART I · CHAPTER 8

Combinations, Step-Up Therapy and Non-Insulin Injectables

Rational fixed-dose combinations, how to add the next drug, and GLP-1-based therapy

Rational combinations

Combination	Why it works	Watch for
Metformin + SGLT2i	Complementary; weight loss; heart and kidney protection	Genital infections, volume depletion
Metformin + DPP-4i	Low hypoglycaemia risk; well tolerated	Avoid saxagliptin in HF
Metformin + sulfonylurea	Potent, inexpensive	Hypoglycaemia, weight gain
SGLT2i + DPP-4i (± metformin)	Additive; no hypoglycaemia; single-pill options	Cost
Metformin + pioglitazone	Insulin resistance, fatty liver	Oedema, weight gain
Basal insulin + metformin ± SGLT2i/DPP-4i	Less insulin, less weight gain	Stop SU when prandial insulin added

AVOID THESE COMBINATIONS

Two drugs of the same class (two SUs, two gliptins) · DPP-4i with GLP-1 RA or tirzepatide · sulfonylurea with meglitinide · pioglitazone with insulin in heart failure.

Common fixed-dose combinations in India (strengths in mg)

Combination	Common strengths	Combination	Common strengths
Glimepiride + metformin	1/500, 2/500, 1/1000, 2/1000	Dapagliflozin + metformin XR	5/500, 10/500, 10/1000
Gliclazide + metformin	80/500; MR 30/500, 60/500	Empagliflozin + metformin	12.5/500, 12.5/1000
Sitagliptin + metformin	50/500, 50/1000	Empagliflozin + linagliptin	10/5, 25/5
Vildagliptin + metformin	50/500, 50/850, 50/1000	Dapagliflozin + sitagliptin	10/100
Teneligliptin + metformin	20/500, 20/1000	Pioglitazone + metformin	15/500
Linagliptin + metformin	2.5/500, 2.5/1000	Glimepiride + metformin + voglibose	1/500/0.2, 2/500/0.3

Use FDCs once the individual doses are known to be tolerated; prescribe only CDSCO-approved combinations.

GLP-1 receptor agonists and dual agonist (injectables)

Drug	Start	Titrate to	Frequency	Notes
Liraglutide	0.6 mg	1.2–1.8 mg	SC daily	↑ weekly; CV benefit (LEADER)
Dulaglutide	0.75 mg	1.5 mg (up to 4.5 mg)	SC weekly	CV benefit (REWIND)
Semaglutide	0.25 mg × 4 wk	0.5 → 1 mg (2 mg)	SC weekly	CV and kidney benefit (SUSTAIN-6, FLOW)
Tirzepatide (GIP/GLP-1)	2.5 mg × 4 wk	↑ 2.5 mg every 4 wk to 5–15 mg	SC weekly	Largest HbA1c and weight fall

Nausea, vomiting and diarrhoea are common — titrate slowly and advise small meals. Avoid with past pancreatitis and personal/family history of medullary thyroid carcinoma or MEN 2. Delayed gastric emptying: inform the anaesthetist before surgery or endoscopy.

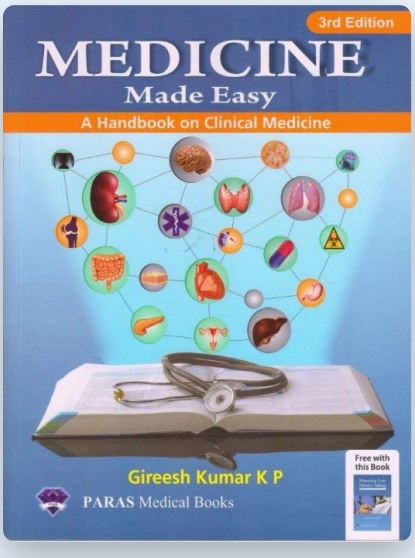
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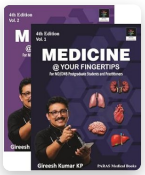
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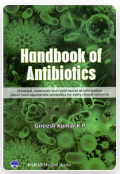
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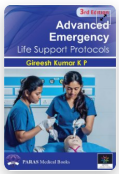
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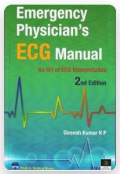
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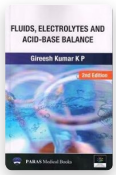
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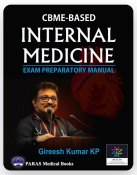
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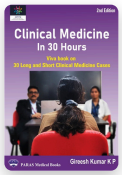
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PART I · CHAPTER 9

OHAs in Kidney Disease, Liver Disease and Special Situations

What to use, reduce or stop — at a glance

Dose adjustment by eGFR (mL/min/1.73 m²)

Drug	≥60	45–59	30–44	15–29	<15 / dialysis
Metformin	Full	Full; monitor	Max 1 g/day; do not start	Stop	
Gliclazide / glipizide	Full	Full	Low dose	Low dose, caution	Avoid / insulin
Glimepiride	Full	Low dose	Low dose	Avoid	
Glibenclamide	Avoid in CKD	Avoid			
Sitagliptin	100 mg	100 mg	50 mg	25 mg	
Linagliptin	5 mg at all levels				
Vildagliptin	50 mg BD	50 mg BD (OD if <50)	50 mg OD		
SGLT2i (empa/dapa)	Full	Full	Continue for heart/kidney	Start if ≥20 (empa) / ≥25 (dapa)	Stop on dialysis
Pioglitazone	No adjustment — watch fluid retention				
Acarbose	Full	Full	Full	Avoid (<25)	
Repaglinide	Full	Full	Full	Start 0.5 mg; titrate carefully	
GLP-1 RA	No adjustment (liraglutide, dulaglutide, semaglutide)				Limited data

Liver disease

- Fatty liver (MASLD): pioglitazone, GLP-1 RA, SGLT2i preferred
- Cirrhosis: avoid metformin if decompensated; avoid SU (hypoglycaemia); avoid acarbose; insulin is safest
- Vildagliptin: avoid if ALT >3 × ULN

Elderly and frail

- Target HbA1c <7.5–8%; avoid hypoglycaemia above all
- Prefer DPP-4i, low-dose metformin, SGLT2i (watch volume), basal insulin once daily
- Avoid glibenclamide and complex insulin regimens

Fasting (Ramadan, religious fasts)

- Metformin: 2/3 dose at the evening meal, 1/3 at pre-dawn meal
- SU: switch to gliclazide; give at the evening meal, reduce dose
- DPP-4i: no change. SGLT2i: give at evening meal; ensure hydration
- Basal insulin: reduce by 20–40%; break the fast if glucose <70 or >300 mg/dL

Pregnancy and planning pregnancy

- Insulin is the drug of choice; stop other OHAs before conception where possible
- Metformin may be continued or used in GDM in selected cases (crosses the placenta)
- Stop SGLT2i, DPP-4i, GLP-1 RA, pioglitazone and SU

KEY POINT

As kidney function falls, three things change: metformin dose falls and stops at eGFR <30; most gliptins need a lower dose (except linagliptin); and insulin requirement falls — reduce insulin by 25–50% in advanced CKD.

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PART II · CHAPTER 10

Insulin Comparison Chart, Injection and Storage

Every insulin available in India by its time–action profile and approximate cost in rupees

Insulin (generic name)	Looks	Onset	Peak	Duration	How and when to use	Approx. MRP (₹)	₹ per 100 U
HUMAN INSULINS — lowest cost · U-40 vials and U-100 vials, cartridges and pens							
Regular (soluble) human	Clear	30–60 min	2–4 h	6–8 h	30 min before meals; the only insulin for IV infusion; mix with NPH — clear drawn first	U-40, 10 mL vial ≈ 150 U-100, 10 mL vial ≈ 450–700 3 mL cartridge/pen ≈ 300–500	38–170
NPH (isophane)	Cloudy	1–2 h	4–8 h	12–16 h	Bedtime or BD; roll and tip before use; peak may cause night hypos		
Premixed human 30/70, 50/50	Cloudy	30 min	Dual	12–16 h	30 min before breakfast and dinner; fixed meal times		
RAPID- AND ULTRA-RAPID-ACTING ANALOGUES — prandial (bolus)							
Lispro · Aspart · Glulisine	Clear	10–15 min	1–2 h	3–5 h	0–15 min before meals; pumps; fewer late hypos than regular	3 mL cartridge/pen ≈ 350–700	120–235
Faster aspart (ultra-rapid lispro*)	Clear	2–5 min	1–1.5 h	3–5 h	0–2 min before, or within 20 min of starting the meal	3 mL ≈ 650–750	215–250
LONG-ACTING BASAL ANALOGUES — once daily							
Glargine U-100 (incl. biosimilars)	Clear	1–2 h	Peakless	~24 h	Once daily, same time; never mix; clear — do not confuse with rapid insulin	3 mL pen/cartridge ≈ 550–1,000	180–330
Glargine U-300	Clear	2–6 h	Peakless	Up to 36 h	Once daily; **pen only**; needs ~10–18% more units than U-100	1.5 mL pen (450 U) ≈ 2,200	~490
Detemir	Clear	1–2 h	Flat	16–24 h	OD–BD; being withdrawn worldwide — switch to glargine/degludec	Limited supply	—
Degludec	Clear	30–90 min	Peakless	>42 h	Once daily, any time (8–40 h apart); least nocturnal hypoglycaemia	3 mL ≈ 1,300–2,000	430–670
ONCE-WEEKLY BASAL INSULIN							
Icodec (700 U/mL)	Clear	Steady state 2–4 wk	Peakless	1 week	Weekly, same day; **pen only** (10-U steps). Insulin-naive type 2: 70 U/week; from daily basal: 7 × daily dose (optional 1.5× first dose only)	1 mL (700 U) ≈ 2,611 3 mL (2,100 U) ≈ 7,833	~373
PREMIXED AND CO-FORMULATED ANALOGUES							
Biphasic aspart 30/70; lispro 25/75, 50/50	Cloudy	10–15 min	Dual	12–24 h	0–15 min before meals, BD or TDS; resuspend before use	3 mL ≈ 500–900	165–300
Degludec/aspart 70/30	Clear	10–15 min	1–2 h (aspart)	>24 h (basal)	OD–BD with the main meal(s); clear, no resuspension	3 mL ≈ 1,450–1,700	480–570
INHALED INSULIN — the only needle-free insulin							
Inhaled human insulin (4, 8, 12 U cartridges)	Powder	~12 min	35–55 min	1.5–3 h	First bite of each meal; adults; spirometry at start, 6 months, then yearly; avoid in asthma, COPD, smokers	30 cartridges ≈ 4,000–5,450	1,500–3,300†

Onset, peak and duration are approximate and vary with dose, site and person. Costs are approximate Indian MRPs (October 2026) for orientation only; Jan Aushadhi, hospital and online prices are often lower. Human insulin U-40 vials are price-controlled (≈ ₹15 per mL). *Ultra-rapid lispro: limited availability. †Inhaled cartridge units are not equivalent to injected units.

NASAL INSULIN SPRAY — NOT AVAILABLE

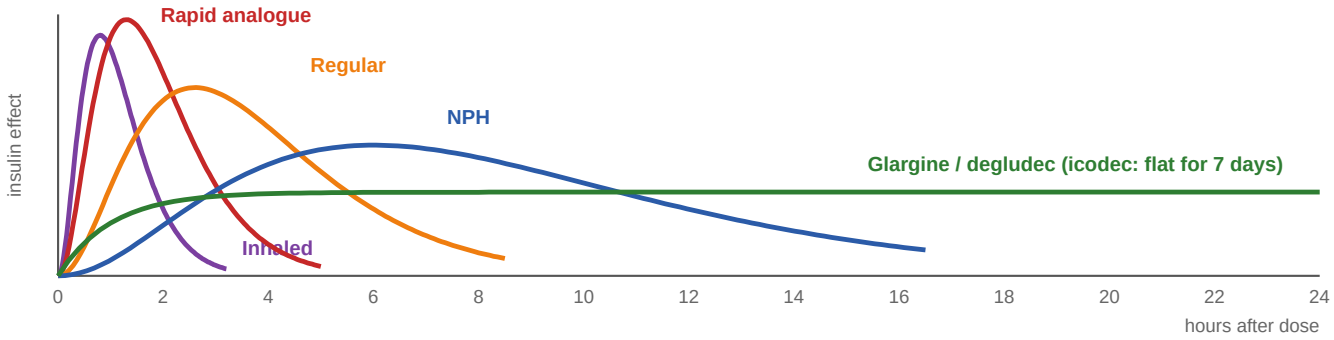
No intranasal insulin is approved for diabetes in India or elsewhere; it remains a research product. Do not confuse it with **inhaled insulin** (taken into the lungs, above) or with **nasal glucagon 3 mg**, which treats severe hypoglycaemia.

CLINICAL PEARL

Human insulins cost a fraction of analogues and remain excellent choices. A second weekly basal insulin, efsitora alfa, was approved in the USA in September 2026 but is not yet available in India.

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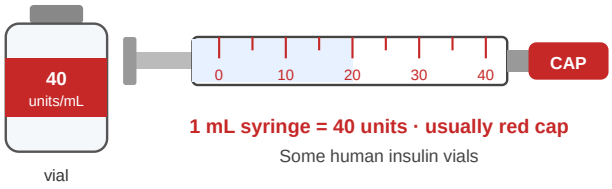
Time–action profiles at a glance



⚠ U-40 and U-100 — the commonest insulin mistake made by patients

Insulin comes in two common strengths. **U-40 = 40 units in 1 mL** (some human insulin vials). **U-100 = 100 units in 1 mL** (other vials and **all** cartridges and pens). Syringes are made for one strength only and are marked in units of *that* strength. When the vial and the syringe do not match, the number the patient reads on the syringe is not the dose the patient receives.

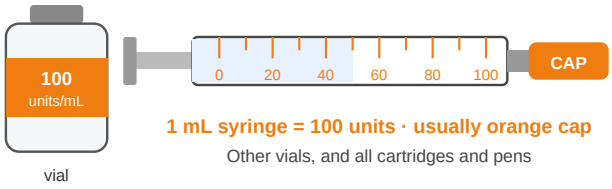
U-40 INSULIN → U-40 SYRINGE ONLY



1 mL syringe = 40 units · usually red cap

Some human insulin vials

U-100 INSULIN → U-100 SYRINGE ONLY



1 mL syringe = 100 units · usually orange cap

Other vials, and all cartridges and pens

Mismatch	Patient draws to the "20" mark	Dose actually received	Result
U-40 insulin in a U-100 syringe	0.2 mL × 40 units/mL	**8 units** (40% of dose)	Persistent hyperglycaemia; doses keep being raised; risk of DKA or HHS
U-100 insulin in a U-40 syringe	0.5 mL × 100 units/mL	**50 units** (2.5 × dose)	Severe, possibly fatal hypoglycaemia

MATCH THE NUMBER — EVERY TIME

- **Vial strength = syringe strength.** U-40 syringes usually have a red cap and U-100 an orange cap — but always read the printed label.
- Write the strength on the prescription: "human insulin **U-100** 10 mL vial + **U-100** insulin syringes".
- Ask the patient to show the vial and syringe at every visit; the pharmacy may change brand or strength at a refill.
- Do not convert doses at home with the wrong syringe — get the correct syringe.

PENS AND CONCENTRATED INSULINS

- A pen dial shows **units**, whatever the strength — no conversion is needed.
- U-200, U-300, U-500 and weekly 700 U/mL insulins are for their own pen **only**; never draw them into a syringe.
- Never draw insulin out of a cartridge or pen with a U-40 syringe.
- Prefer U-100 for every new prescription; re-teach whenever the patient changes from vial to pen or back.

When to inject — timing by insulin

Insulin	Timing	Note
Regular human; premixed human 30/70, 50/50	30 min before the meal	Injecting just before eating causes post-meal highs and late hypos
Lispro, aspart, glulisine; analogue premixes	0–15 min before the meal	Can be given just after the meal if intake is uncertain
Faster aspart	0–2 min before, or within 20 min of starting	Useful for children and erratic eaters
NPH	Bedtime (≈10 pm) or twice daily	Not with the evening meal — peaks at 2–3 am
Glargine U-100 / U-300; degludec	Same time every day; degludec any time	Not linked to meals
Icodec (weekly)	Same day every week	Missed dose: take within 3 days, then keep the usual day
Inhaled insulin	At the first bite of the meal	Short-acting — covers only that meal

How to take insulin

A · Vial and syringe

1. Wash hands. Check name, strength (U-40/U-100), expiry and date opened.
2. Cloudy insulin: roll 10 times and tip 10 times until evenly milky — never shake.
3. Wipe the rubber top. Draw air equal to the dose and push it into the vial.
4. Invert, draw the dose, tap out bubbles. Mixing: **clear (regular) first, then cloudy (NPH)**.
5. Lift a skin fold (6 mm needle), inject at 90°, push slowly, wait 5 s, release fold, withdraw.

B · Insulin pen

1. Check the insulin; resuspend if cloudy. Screw on a **new 4 mm needle**.
2. Prime: dial 2 U, point up, press until a drop appears (repeat if not).
3. Dial the dose. Inject at 90° — no skin fold needed with 4 mm in most adults.
4. Press the button fully and **count 10 seconds** before withdrawing.
5. Unscrew the needle with its outer cap at once; never store the pen with a needle on.

C · Sites and rotation

- **Abdomen** (two fingers from the navel) — fastest; best for prandial insulin
- **Thigh** (front and outer) and **buttock** — slower; good for NPH and basal
- **Back of upper arm** — when another person injects
- Rotate within a site 1 cm apart; change quadrant every week
- Never inject into lumps, scars or through clothes

Storing insulin in India

Insulin	Use within, once opened (below 30 °C)
Human vials, cartridges, pens; rapid analogues; glargine U-100; premixes	28 days (some labels longer)
Glargine U-300	6–8 weeks (as per label)
Degludec; degludec/aspart	8 weeks
Icodec (weekly)	12 weeks
Inhaled cartridges	Sealed strip 10 days; opened strip 3 days

- **Unopened:** refrigerator 2–8 °C — door or vegetable tray; never in or near the freezer. Use until the expiry date.
- **In use:** room temperature below 30 °C; write the date opened on the vial or pen.

Indian heat, power cuts and travel

- Summer rooms often exceed 30 °C — keep in-use insulin in the fridge too, and let it warm for a few minutes before injecting (cold insulin stings).
- No fridge or power cut: a **clay pot (matka)** with water, insulin in a sealed plastic pouch, or an evaporative cooling wallet.
- Never on a window-sill, top of the fridge or TV, near the stove, or in a parked car or two-wheeler box.
- Travel: carry insulin in hand luggage in a cool pouch — never in checked baggage (it may freeze); carry the prescription and spare needles.

DISCARD THE INSULIN IF

It has frozen or been exposed to heat · clear insulin turns cloudy · cloudy insulin has clumps or frosting · it is discoloured · the in-use period is over.

When to change the needle, syringe and pen

Item	Recommended	In Indian practice
Pen needle	**New needle for every injection.** After one use the tip bends and blunts.	Reuse to save cost is common. If unavoidable: same patient only, recap carefully, remove from the pen after each dose, and never beyond one day. Change at once if bent, blunt, painful or dropped.
Insulin syringe	Single use.	Same rules as pen needles. Discard if the markings fade or the plunger sticks. Never share.
Disposable (prefilled) pen	Discard when empty **or** when the in-use period is over — whichever comes first.	Do not keep a half-used pen beyond its in-use days to "save" insulin.
Cartridge in a reusable pen	Change when empty or the in-use period is over.	Use only cartridges made for that pen. If the remaining units are less than the dose, take the rest from a new cartridge.
Reusable pen device	Usually lasts 2–3 years (as per manufacturer).	Replace earlier if cracked, dropped, the dial sticks or does not return to zero. Never share a pen, even with a new needle.

Why reused needles harm: pain, bleeding, broken or blocked needles, infection, and above all **lipohypertrophy**. A needle left on the pen lets insulin leak and air enter the cartridge, so doses become inaccurate.

SHARPS DISPOSAL

Collect used needles, syringes and lancets in a thick plastic bottle with a screw cap, labelled "sharps", and return it to the hospital or clinic for biomedical-waste disposal — never into the household dustbin.

CLINICAL PEARL

Feel the injection sites at every visit. Lipohypertrophy from needle reuse and poor rotation is a leading cause of erratic, unexplained high and low sugars; moving to healthy skin often needs a 10–20% lower dose.

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PART II · CHAPTER 11

Starting and Titrating Basal Insulin

The simplest, safest way to start insulin in type 2 diabetes

When to start

- HbA1c above target despite 2–3 oral drugs (or GLP-1 RA)
- HbA1c >10% or glucose ≥300 mg/dL at any stage
- Symptoms, weight loss or ketosis — suspect insulin deficiency (consider LADA/type 1)
- Pregnancy, severe CKD or liver disease, acute illness, steroids

What to continue

- **Continue** metformin, SGLT2i, DPP-4i, GLP-1 RA
- **Reduce** sulfonylurea (or stop if hypoglycaemia)
- **Stop** pioglitazone if oedema or heart failure
- Give a glucometer; teach SMBG of fasting glucose daily during titration

Starting dose

Insulin	Starting dose	Timing
Glargine U-100 / detemir / degludec	10 U/day or 0.1–0.2 U/kg/day	Same time daily (glargine); detemir at bedtime; degludec any time
NPH (human)	10 U or 0.1–0.2 U/kg at bedtime	At bedtime (≈10 pm) to cover the dawn rise; split BD if >30 U
Glargine U-300	0.2 U/kg/day	Same time daily

Titration — fix the fasting glucose first

Clinician-led (2-0-2)

- ↑ **2 U every 3 days** until fasting 80–130 mg/dL
- If fasting >180: ↑ 4 U every 3 days

Patient self-titration

- ↑ **1 U every day** until fasting <110 mg/dL (glargine)
- Or ↑ 2 U every 3 days on average of 3 readings

If hypoglycaemia

- Any glucose <70: ↓ **4 U or 10–20%**
- Find the cause (meal, exercise, SU)

Mean fasting glucose (3 days)	Change basal dose
>180 mg/dL	+4 U (or +10–15%)
140–180 mg/dL	+2–4 U
131–139 mg/dL	+2 U
80–130 mg/dL	No change — target reached
<80 mg/dL or any hypoglycaemia	−4 U (or −10–20%)

OVERBASALISATION — TIME TO INTENSIFY, NOT TO KEEP INCREASING

Basal dose >0.5 U/kg/day · bedtime-to-morning glucose difference ≥50 mg/dL · hypoglycaemia (especially nocturnal) · high glucose variability. If fasting glucose is at target but HbA1c is still high, the problem is post-meal glucose → add prandial insulin or a GLP-1 RA (Chapter 12).

Worked example

A 62-year-old man, 70 kg, HbA1c 9.4% on metformin 2 g + glimepiride 2 mg + sitagliptin 100 mg. Start glargine 10 U at 9 pm; reduce glimepiride to 1 mg. He increases by 2 U every 3 days: fasting falls from 210 to 118 mg/dL at 24 U (0.34 U/kg) after 3 weeks. HbA1c at 3 months 7.1%.

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PART II · CHAPTER 12

Intensifying Insulin — Basal-Plus, Premixed and Basal–Bolus

When fasting glucose is at target but HbA1c is not

A **Basal insulin titrated, fasting at target, HbA1c above target** → first consider adding a **GLP-1 RA** (or a fixed-ratio basal insulin/GLP-1 RA combination where available) — less hypoglycaemia and weight gain. If not possible, choose one of three insulin options:

▼

1 · Basal-plus

- Add rapid/regular insulin before the **largest meal** (usually lunch or dinner in India)
- Start **4 U**, or 0.1 U/kg, or **10% of basal**
- If HbA1c <8%, reduce basal by the same amount
- Titrate ↑ 1–2 U (10–15%) twice weekly to post-meal <180 mg/dL
- Add a second, then third prandial dose ("basal-plus-2/3") as needed

2 · Premixed BD

- Convert total basal dose: give **2/3 before breakfast, 1/3 before dinner** (or 1/2 + 1/2)
- New start: 0.2–0.3 U/kg/day split the same way
- Pre-breakfast dose titrated to **pre-dinner** glucose; pre-dinner dose titrated to **next-morning fasting**
- ↑ 1–2 U (10–15%) twice weekly
- Can add a third (lunch) analogue premix dose

3 · Basal–bolus

- Most flexible and physiological; for type 1 and for type 2 not controlled on premix
- TDD 0.4–0.5 U/kg (type 1: 0.5–0.6)
- **50% basal** once daily; **50% prandial** split over three meals
- Titrate each dose to the next pre-meal or bedtime value

Converting premixed to basal–bolus

Take the total daily premixed dose. Give **50% as basal** and **50% as prandial** split equally over three meals. If control was poor, add 10%; if there was hypoglycaemia, reduce by 10–20%.

Which glucose reading guides which dose?

Regimen	Dose	Adjust according to
Premixed BD	Pre-breakfast	Pre-dinner (and post-lunch) glucose
	Pre-dinner	Fasting glucose next morning (and 3 am if nocturnal hypo suspected)
Basal–bolus	Basal	Fasting glucose
	Breakfast bolus	Pre-lunch or 2 h post-breakfast glucose
	Lunch bolus	Pre-dinner or 2 h post-lunch glucose
	Dinner bolus	Bedtime or 2 h post-dinner glucose

KEY POINT

When prandial insulin is started, **stop the sulfonylurea**. Continue metformin and, where indicated, SGLT2i or GLP-1 RA.

CLINICAL PEARL

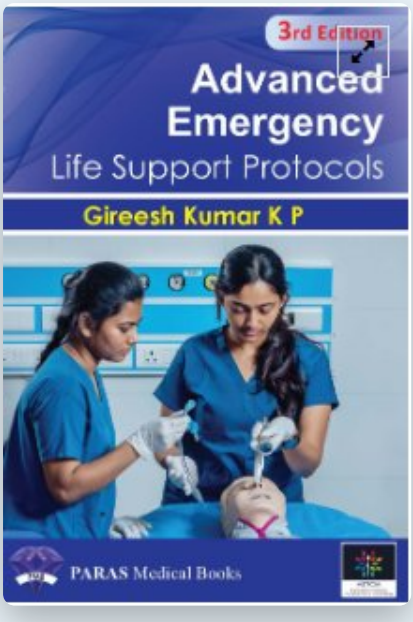
Premixed insulin suits patients with fixed meal times and two main meals, who want fewer injections. Basal–bolus suits those with variable meals, type 1 diabetes and those who can count carbohydrates.

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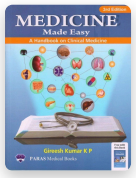
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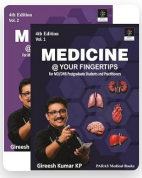
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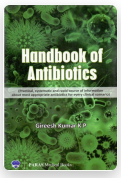
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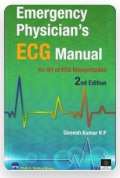
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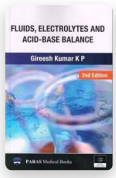
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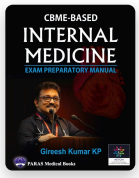
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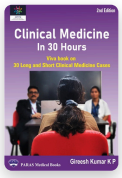
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PART II · CHAPTER 13

Insulin Dose Calculations and Worked Examples

Total daily dose, carbohydrate ratio and correction factor

Total daily dose (TDD)

Situation	TDD
Type 2, starting full insulin	0.3–0.5 U/kg/day
Type 1, new diagnosis	0.4–0.5 U/kg/day
Type 1, established	0.5–0.8 U/kg/day
Obesity, steroids, infection	0.6–1.0 U/kg/day or more
Elderly, eGFR <30, low intake	0.2–0.3 U/kg/day

The rules of 500 and 1800

Parameter	Rapid analogue	Regular insulin
Insulin-to-carbohydrate ratio (g covered by 1 U)	500 ÷ TDD	450 ÷ TDD
Correction (sensitivity) factor (mg/dL fall per 1 U)	1800 ÷ TDD	1500 ÷ TDD

Correction dose = (current glucose − target glucose) ÷ correction factor. Target usually 120 mg/dL (140 in elderly).

Meal dose = carbohydrate in meal (g) ÷ carbohydrate ratio. Add the correction dose to the meal dose.

Correction (supplemental) scale

Add to the scheduled prandial dose; give alone at bedtime only if very high (half dose).

Pre-meal glucose (mg/dL)	Insulin-sensitive (thin, elderly, CKD)	Usual	Insulin-resistant (obese, steroids)
141–180	+1 U	+2 U	+3 U
181–220	+2 U	+4 U	+6 U
221–260	+3 U	+6 U	+8 U
261–300	+4 U	+8 U	+10 U
301–350	+5 U	+10 U	+12 U
>350	+6 / +12 / +14 U and check ketones; inform doctor		

ADJUSTING THE REGIMEN

If correction doses are needed on most days, add 50–100% of the average daily correction to the scheduled doses.

Worked example 1 — starting basal–bolus in type 2

Weight 80 kg, HbA1c 10.8% on premix 30/70 18 U + 12 U (TDD 30 U), poor control. New TDD = 0.4 U/kg × 80 = 32 U. Basal (glargine) = 16 U at 10 pm. Prandial (aspart) = 16 U → breakfast 4 U, lunch 6 U, dinner 6 U (largest meals get more). Titrate: basal by fasting glucose every 3 days; each bolus by the next pre-meal reading twice weekly.

Worked example 2 — carbohydrate ratio and correction in type 1

TDD 40 U (aspart). Carbohydrate ratio = 500 ÷ 40 = **1 U per 12.5 g**; correction factor = 1800 ÷ 40 = **1 U lowers glucose by 45 mg/dL**. Lunch of 3 chapatis + dal + vegetables ≈ 75 g carbohydrate → 75 ÷ 12.5 = 6 U. Pre-lunch glucose 255, target 120 → (255 − 120) ÷ 45 = 3 U. **Lunch dose = 6 + 3 = 9 U**.

Worked example 3 — converting NPH to glargine

NPH 20 U BD (40 U/day) → glargine **32 U once daily** (reduce total by 20% when changing from BD NPH). NPH once daily → glargine same dose.

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PART II · CHAPTER 14

Insulin in Hospital — Ward, IV Infusion, DKA/HHS and Surgery

Basal–bolus in the ward; fixed-rate IV insulin for emergencies

Non-critically ill ward patient

- Target **140–180 mg/dL**; check glucose before meals and at bedtime (4–6 hourly if nil by mouth)
- Stop most OHAs on admission if unwell; continue in stable patients eating normally (hold metformin and SGLT2i if acute illness, contrast or surgery)
- **Basal–bolus + correction** — TDD 0.3 U/kg (age >70, eGFR <30), 0.4 U/kg (glucose 140–200), 0.5 U/kg (glucose 201–400); half basal, half prandial
- Poor oral intake: basal + correction only
- **Sliding scale alone is not recommended** — it treats hyperglycaemia after it has happened
- Steroids: morning NPH 0.1 U/kg per 10 mg prednisolone (max 0.4 U/kg) for afternoon–evening hyperglycaemia

Variable-rate IV insulin infusion

50 U regular insulin in 50 mL 0.9% saline = **1 U/mL**. Prime the line. Check capillary glucose hourly. Run with a glucose-containing fluid when not eating (e.g. 5% dextrose in 0.45% saline with KCl).

Glucose (mg/dL)	Rate (U/h) — standard
<72	Stop; treat hypoglycaemia; restart 0.5 when >72
72–108	0.5
109–144	1
145–216	2
217–288	4
289–360	5
361–432	6
>432	8 — check ketones; review

Use a reduced scale for insulin-sensitive and an increased scale for resistant patients. **Continue the patient's basal insulin** during the infusion.

Insulin in DKA and HHS (adults)

	DKA	HHS
Before insulin	Fluids first: 0.9% saline 1 L over the first hour. K^+ <3.5 mmol/L → replace K^+ before starting insulin	Fluids are the mainstay; replace gradually over 24 h
Insulin	**Fixed-rate** IV regular insulin **0.1 U/kg/h** (no bolus needed); continue basal analogue	Start **0.05 U/kg/h** only if glucose is not falling with fluids alone, or if ketotic
Glucose falls	When <250 mg/dL add 5–10% dextrose and reduce to 0.05 U/kg/h; keep 150–250 until resolution	Aim fall 90–180 mg/dL in 24 h; keep 180–270 initially
Resolution	Ketones <0.6 mmol/L and pH ≥7.3 (or bicarbonate ≥18)	Osmolality <300, mentation normal
Transition	Give SC basal (and meal-time) insulin **1–2 h before stopping** the infusion; restart previous dose or use 0.5–0.6 U/kg/day	

Perioperative — night before and day of surgery

Drug	Action	Drug	Action
Metformin	Omit on day of surgery	SGLT2i	Stop 3 days before (ertugliflozin 4)
SU / meglitinide	Omit on day of surgery	DPP-4i	May continue
Basal analogue	Give 75–80% of dose the night before / morning	NPH	Give 50% of morning dose
Premix	Give 50% of usual morning dose; IV insulin if long fast	Rapid/regular	Omit while nil by mouth

Target 100–180 mg/dL peri-operatively; weekly GLP-1 RA — inform anaesthetist (aspiration risk).

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PART II · CHAPTER 15

Hypoglycaemia and Insulin in Special Groups

Recognise and treat hypoglycaemia; adapt insulin to pregnancy, CKD, the elderly and type 1

Hypoglycaemia

Level	Definition	Treatment
Level 1	Glucose <70 mg/dL and ≥54 mg/dL	**Rule of 15:** 15–20 g fast-acting glucose (3–4 glucose tablets, 150 mL fruit juice or regular soft drink, 3 teaspoons sugar in water). Recheck after 15 min; repeat if <70. Then a snack or the next meal
Level 2	Glucose <54 mg/dL	
Level 3 (severe)	Altered mental or physical state needing help from another person	IV **25% dextrose 50–100 mL** (or 50% dextrose 25–50 mL) then 10% dextrose infusion; or **glucagon 1 mg** IM/SC (nasal glucagon 3 mg where available). Recheck in 15 min

AFTER ANY SEVERE EPISODE

Find the cause (missed meal, alcohol, exercise, wrong dose, CKD, SU). Reduce the responsible insulin dose by 10–20%. SU-induced hypoglycaemia needs admission and prolonged monitoring. Teach family to use glucagon.

HYPOGLYCAEMIA UNAWARENESS

Common in long-standing diabetes, elderly and β-blocker users. Relax targets, avoid any hypoglycaemia for 2–3 weeks to restore awareness, and use CGM where available.

Insulin in special groups

Pregnancy (pre-existing and GDM)

- Targets: fasting <95, 1 h <140, 2 h <120 mg/dL
- Safe insulins: human regular, NPH, aspart, lispro, detemir, glargine, degludec
- GDM: start NPH or long-acting at bedtime for high fasting; rapid insulin before meals for high post-meal values
- Requirement rises steeply after 24 weeks (up to 1–1.5 U/kg); falls abruptly after delivery — **stop insulin in GDM after delivery**, halve the pre-pregnancy dose in pre-existing diabetes

Type 1 diabetes

- Always basal–bolus (or pump) from diagnosis
- **Never stop basal insulin** — even when not eating
- Teach carbohydrate counting, correction doses and ketone testing

Chronic kidney disease

- Insulin clearance falls — reduce dose by ~25% at eGFR 10–50 and ~50% at <10
- Prefer analogues (less hypoglycaemia); HbA1c may be unreliable — use SMBG/CGM
- Dialysis days: glucose may fall — reduce pre-dialysis prandial dose

Elderly

- Once-daily basal analogue in the morning (less nocturnal hypoglycaemia)
- Simplify: avoid complex basal–bolus if self-care is limited; involve carers
- Target fasting 90–150 mg/dL; HbA1c <8%

Glucocorticoid therapy

- Morning steroid → afternoon/evening hyperglycaemia → morning NPH or extra lunch/dinner prandial insulin; taper as the steroid is tapered

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PART II · CHAPTER 16

Injection Technique, Storage, Sick-Day Rules and Quick Reference

Good technique is part of the prescription

Injection technique

- Use **4 mm pen needles** (or 6 mm syringe) at 90° — no skin pinch needed for most adults; pinch with 6–8 mm needles or very thin patients
- Sites: **abdomen** (fastest; preferred for prandial), thighs (slower; good for NPH), buttocks, back of upper arm
- **Rotate** within a site, 1 cm apart; check sites for **lipohypertrophy** at every visit — injecting into lumps gives erratic absorption
- Pens: prime 2 U; hold needle in skin for 10 s after injecting; new needle each injection
- Cloudy insulins (NPH, premix): roll and tip 10–20 times until uniformly milky
- Mixing in one syringe (regular + NPH): draw clear before cloudy. Never mix glargine, detemir or degludec

Storage

- Unopened: refrigerator 2–8 °C — never freeze; do not use if frozen
- In use: room temperature <25–30 °C for up to 28 days (some products longer — check label); keep away from heat and sunlight
- In hot weather without a fridge: a clay pot with water or an insulated pouch keeps insulin cool; carry insulin in hand luggage when travelling

Sick-day rules

- Never stop basal insulin; check glucose every 4 h, and ketones if glucose >250 mg/dL or in type 1
- Drink 150–250 mL fluid hourly; if not eating, take carbohydrate fluids
- **Pause** while dehydrated or vomiting — "**SADMANS**": **S**U, **A**CEi, **D**iuretics, **M**etformin, **A**RB, **N**SAIDs, **S**GLT2i; restart 24–48 h after eating and drinking normally
- Extra rapid insulin: 10–20% of TDD every 2–4 h if glucose >250 with ketones
- Seek help: vomiting >6 h, ketones ≥1.5 mmol/L, glucose persistently >300, drowsiness or breathlessness

Prescription checklist

- Name, type and device of insulin (brand, pen/vial, U-100)
- Dose and timing in relation to meals
- Titration rule written for the patient
- Glucometer, strips, needles; SMBG plan
- Hypoglycaemia education and glucose tablets
- Follow-up date; HbA1c every 3 months until stable

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Quick reference

Task	Rule	Task	Rule
Start basal	10 U or 0.1–0.2 U/kg	Titrate basal	+2 U every 3 days to FBG 80–130
Start prandial	4 U or 10% of basal	Premix BD	2/3 morning, 1/3 evening
Basal–bolus TDD	0.4–0.5 U/kg, 50:50	Hypoglycaemia	−10–20%; rule of 15
Carb ratio	500 ÷ TDD (g/U)	Correction factor	1800 ÷ TDD (mg/dL/U)
DKA insulin	0.1 U/kg/h fixed rate	Ward target	140–180 mg/dL

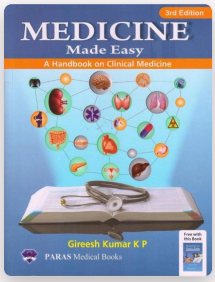
Key sources: ADA Standards of Care in Diabetes 2025 · ADA/EASD consensus report on management of hyperglycaemia in type 2 diabetes (2022) · RSSDI clinical practice recommendations for type 2 diabetes · ADA/EASD/JBDS/AACE consensus on hyperglycaemic crises in adults (2024) · JBDS-IP guidelines on inpatient and perioperative care · product information of individual drugs.

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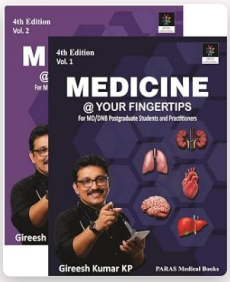
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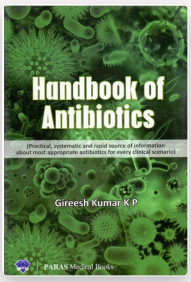
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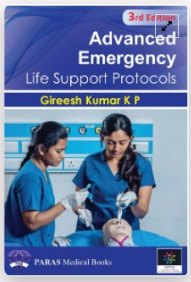
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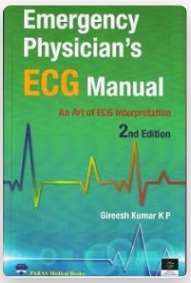
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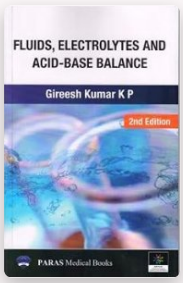
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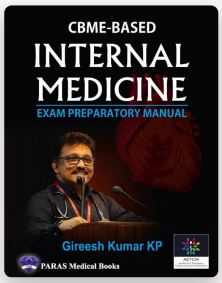
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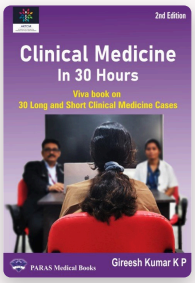
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