

# International Journal of **Diabetes** in Developing Countries

Official Publication of  
**Research Society for the  
Study of Diabetes in India**

RSSDI Clinical Practice Recommendations for  
Management of In-Hospital Hyperglycaemia – 2016





# International Journal of Diabetes in Developing Countries

## Incorporating Diabetes Bulletin

### Founder Editors

M. M. S. Ahuja  
Hemraj B. Chandalia

### Editor-in-Chief

G. R. Sridhar, Visakhapatnam, India

### EDITORIAL COMMITTEE (Associate Editors)

V. Mohan  
K.M. Prasanna Kumar  
R.V. Jaya Kumar  
S.V. Madhu  
P.V. Rao  
Jayant Panda

### Editorial Assistant

Rashi Kushwaha

### RESEARCH SOCIETY FOR STUDY OF DIABETES IN INDIA

founded by Prof. M.M.S. Ahuja in 1972

### THE OFFICE BEARERS IN THE YEAR 2016

#### PATRONS

H.B. Chandalia, Mumbai  
C. Munichoodappa, Bengaluru  
A.K. Das, Puduchery  
B.K. Sahay, Hyderabad  
O.P. Gupta, Ahmedabad  
V. Seshiah, Chennai

#### PRESIDENT

S.R. Aravind, Bengaluru

#### PRESIDENT ELECT

Sarita Bajaj, Allahabad

#### PAST PRESIDENT

S.V. Madhu, New Delhi

#### SECRETARY

Rajeev Chawla, New Delhi

#### JOINT SECRETARY

Banshi Saboo, Ahmedabad

#### TREASURER

B.M. Makkar, New Delhi

#### EXECUTIVE COMMITTEE

Ch. Vasanth Kumar, Hyderabad  
Rakesh Sahay, Hyderabad  
K.R. Narasimha Setty, Bengaluru  
G.C. Reddy, Hyderabad  
Jayant K. Panda, Cuttack  
Vijay Panikar, Mumbai

Jitendra Singh, Jammu  
Jayaprakashai Jana, Nellore

### CO- OPTED

P.V. Rao, Hyderabad

### Aims and Scope

International Journal of Diabetes in Developing Countries targets a readership consisting of clinicians, research workers, paramedical personnel, nutritionists and health care personnel working in the field of diabetes. Original research work and reviews of interest to the above group of readers is considered for publication in the journal.

The journal has a goal of serving as an important resource material in diabetes for its readers, mainly in the developing world.

### Copyright Information

#### For Authors

As soon as an article is accepted for publication, authors will be requested to assign copyright of the article (or to grant exclusive publication and dissemination rights) to the publisher (respective the owner if other than Springer).

This will ensure the widest possible protection and dissemination of information under copyright laws. More information about copyright regulations for this journal is available at [www.springer.com/13410](http://www.springer.com/13410)

#### For Readers

While the advice and information in this journal is believed to be true and accurate at the date of its publication, neither the authors, the editors, nor the publisher can accept any legal responsibility for any errors or omissions that may have been made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

All articles published in this journal are protected by copyright, which covers the exclusive rights to reproduce and distribute the article (e.g., as offprints), as well as all translation rights. No material published in this journal may be reproduced photographically or stored on microfilm, in electronic data bases, on video disks, etc., without first obtaining written permission from the publisher (respective the copyright owner if other than Springer). The use of general descriptive names, trade names, trademarks, etc., in this publication, even if not specifically identified, does not imply that these names are not protected by the relevant laws and regulations.

Springer has partnered with Copyright Clearance Center's RightsLink service to offer a variety of options for reusing Springer content. For permission to reuse our content please locate the material that you wish to use on [link.springer.com](http://link.springer.com) or on [springerimages.com](http://springerimages.com) and click on the permissions link or go to [copyright.com](http://copyright.com) and enter the title of the

publication that you wish to use. For assistance in placing a permission request, Copyright Clearance Center can be contacted directly via phone: +1-855-239-3415, fax: +1-978-646-8600, or e-mail: [info@copyright.com](mailto:info@copyright.com).

© 2016 Research Society for Study of Diabetes in India

### Subscription Information

International Journal of Diabetes in Developing Countries is published 4 times a year. Volume 36 (4 issues) of will be published in 2016.

ISSN 0973-3930 print version  
ISSN 1998-3832 electronic version

For information on subscription rates please contact Springer Customer Service Center: [customerservice@springer.com](mailto:customerservice@springer.com)

The Americas (North, South, Central America and the Caribbean)  
Springer Journal Fulfillment,  
233 Spring Street, New York, NY,  
10013-1578, USA  
Tel. 800-SPRINGER (777-4643); 212-460-1500  
(outside North America)

Outside the Americas  
Springer Customer Service Center GmbH  
Haberstr. 7, 69126 Heidelberg, Germany  
Tel.: +49-6221-345-4303

### Advertisements

E-mail contact: [advertising@springer.com](mailto:advertising@springer.com) or [anzeigen@springer.com](mailto:anzeigen@springer.com) (Germany)

### Disclaimer

Springer publishes advertisements in this journal in reliance upon the responsibility of the advertiser to comply with all legal requirements relating to the marketing and sale of products or services advertised. Springer and the editors are not responsible for claims made in the advertisements published in the journal. The appearance of advertisements in Springer publications does not constitute endorsement, implied or intended, of the product advertised or the claims made for it by the advertiser.

### Journal Website

[www.springer.com/13410](http://www.springer.com/13410)  
Electronic edition: [link.springer.com/journal/13410](http://link.springer.com/journal/13410)

### Office of Publication

Springer Science+Business Media B.V.,  
Van Godewijkstraat 30, 3311 GX Dordrecht,  
The Netherlands

# International Journal of Diabetes in Developing Countries

Volume 36 · Supplement 1 · November 2016

## GUIDELINES

### **RSSDI Clinical Practice Recommendations for Management of In-Hospital Hyperglycaemia – 2016**

V. Panikar · A. Sosale · S. Agarwal · A. Unnikrishnan ·  
K. S · A. Bhattacharya · M. Chawla · A. RM · A. Bhatt ·  
S. Jaggi · B. Sosale · D. Hasnani · J. Vadgama **S1**

**Further articles** can be found at [www.springerlink.com](http://www.springerlink.com)

**Abstracted/Indexed** in *Science Citation Index Expanded (SciSearch)*, *Journal Citation Reports/Science Edition*, *SCOPUS*, *Chemical Abstracts Service (CAS)*, *Google Scholar*, *EBSCO*, *CAB International*, *Academic Search*, *CAB Abstracts*, *CSA Environmental Sciences*, *EMCare*, *Global Health*, *OCLC*, *SCImago*, *Sociedad Iberoamericana de Informacion Cientifica (SIIC) Databases*, *Summon by ProQuest*

**Instructions for Authors** for *Int J Diabetes Dev Ctries* are available at [www.springer.com/13410](http://www.springer.com/13410).

## **Compliance with Ethical Requirements**

International journal of Diabetes in Developing Countries requests that all authors comply with Springer's ethical policies. To view our ethics statements please visit the following:

· Conflict of Interest and Ethical Standards: <http://www.springer.com/authors?SGWID=0-111-6-791531-0>

· Informed Consent: <http://www.springer.com/authors?SGWID=0-111-6-608209-0>

Statement of Human and Animal Rights: <http://www.springer.com/authors?SGWID=0-111-6-608309-0>

# RSSDI clinical practice recommendations for management of In-hospital hyperglycaemia—2016

V. Panikar<sup>1</sup> · A. Sosale<sup>2</sup> · S. Agarwal<sup>3</sup> · A. Unnikrishnan<sup>4</sup> · S. Kalra<sup>5</sup> ·  
A. Bhattacharya<sup>6</sup> · M. Chawla<sup>7</sup> · R. M. Anjana<sup>8</sup> · A. Bhatt<sup>4</sup> · S. Jaggi<sup>9</sup> ·  
B. Sosale<sup>2</sup> · D. Hasnani<sup>10</sup> · J. Vadgama<sup>11</sup>

Published online: 12 November 2016

© Research Society for the study of Diabetes in India - 2016

## Index

Sr. no.	Topics
1	Process and methodology
2	Need for the recommendation
3	Introduction and classification of in-hospital hyperglycaemia
4	Managing diabetes in critically ill patients in the ICU
5	Transition from insulin infusion to SC insulin and/or oral anti-diabetic drugs
6	Glycaemic control in the non-critically ill patient
7	Management in special circumstances
8	Planning discharge from the hospital
9	Hypoglycaemia management
10	References

## Process and methodology

The executive committee of the national RSSDI set up a task force to draft the ‘RSSDI Clinical Practice Recommendations for management of in-hospital hyperglycaemia—2016’.

The topics were divided into six different modules and were assigned to the nominated members. All efforts were made to provide the task force with the available Indian data. Data collated was given special focus by the respective team members, analysed in-depth and referenced in accordance with the contemporary literature. The draft submitted by the task force was reviewed by all group members in a consensus meeting held at Mumbai. Thereafter, the suggestions and thoughts were translated into the recommendations which were further edited, referenced as the final draft. The final draft was circulated to all the executive committee members and KOLs across the country.

**Extended working group** S. V. Madhu, S. Bajaj, R. Chawla, B. Makkar, B. Saboo, R. Sahay, C. Vasanthkumar, J. Panda, J. Jana, N. Shetty, G. Reddy, P. Rao

✉ V. Panikar  
drvijaypanikar@yahoo.com

<sup>1</sup> Department of Endocrinology and Diabetes, Lilavati Hospital, Mumbai, India

<sup>2</sup> Diacon Hospital, Bangalore, India

<sup>3</sup> Aegle Clinic Diabetes Care, Pune, India

<sup>4</sup> Chellaram Diabetes Institute, Pune, India

<sup>5</sup> Department of Endocrinology, Bharti Hospital, Karnal, Haryana, India

<sup>6</sup> Manipal Hospital, Bangalore, India

<sup>7</sup> Asian Heart Institute, Mumbai, India

<sup>8</sup> Dr. Mohan’s Diabetes Specialities Centre, Chennai, India

<sup>9</sup> Action Diabetes Centre, Sri Balaji Action Medical Institute, New Delhi, India

<sup>10</sup> DiaCare—Diabetes Care & Hormone Clinic, Ahmedabad, India

<sup>11</sup> Department of Endocrinology, Lilavati Hospital, Mumbai, India

## In-hospital management of hyperglycaemia—2016

### Need for recommendations

In-hospital hyperglycaemia is a common finding and should be considered an important marker of poor clinical outcome and increased mortality [1].

In-patients with diabetes can be a challenge for the clinician. India is a diverse and vast country with availability of medical facilities ranging from world-class facilities to just basic health care infrastructure.

The objective of these recommendations is to address the resource gaps and enhance the standards of care, while attempting to bring uniformity of care across the varied and diverse health care landscape of India, covering both the resource intense and the limited resource setting.

### Introduction

The burden of diabetes globally stands at 415 million translating to one in every 11 adults being affected with diabetes. Recent data from the International Diabetes Federation 2015 states that India has over 69.2 million adults with diabetes and it is estimated that India is housing about 97,700 children with type 1 diabetes mellitus (T1DM). By 2040, India is projected to have over a hundred million adults with diabetes [2, 3].

Acute illness results in a number of physiological changes like increase in stress hormones or therapeutic choices like steroid therapy that can exacerbate hyperglycaemia. This, in turn, causes some pathological changes that can worsen the acute illness such as decreased immune function and increased oxidative stress leading further to a vicious cycle of worsening illness and poor glycaemic control. A systematic approach to in-hospital management of hyperglycaemia has consistently demonstrated better patient outcomes and reduced burden on the health care system.

### Definition: hyperglycaemia in a hospitalised patient

Hyperglycaemia in the hospital has been defined as any blood glucose that is >140 mg/dl [4].

### The burden of hyperglycaemia in the hospital setting

In a review of medical records of roughly 2000 patients admitted in a hospital in the USA, 38% of patients had been documented to have hyperglycaemia, out of which 26% had a known history of the disease and 12% had no history of diabetes prior to admission [1]. Observational studies have reported a prevalence of hyperglycaemia ranging from 32 to 38% in community hospitals, 70–80% patients with acute coronary syndrome and CABG surgery patients [5].

In summary, the prevalence of diabetes in hospitalised adults is dependent on the criteria and the methodology utilised to define the representative patient population, which on a conservative estimate, is usually 12–25% [6].

### Classification of hyperglycaemia during hospitalisation [6]

Hyperglycaemia in a hospital setting can be classified into

1. *Previously diagnosed/known diabetes*: Diabetes has been previously diagnosed, prior to admission.
2. *Previously undiagnosed diabetes/diagnosed upon admission (HbA1c > 6.5%)*: Hyperglycaemia (fasting plasma glucose (FPG) >126 mg/dl or random blood glucose (RBG) >200 mg/dl) occurring during hospitalisation and confirmed as diabetes after hospitalisation by standard diagnostic criteria.
3. *Stress hyperglycaemia (normal HbA1c)*: Hyperglycaemia (fasting PG >126 mg/dl or random BG >200 mg/dl)

occurring during the hospitalisation that reverts to normal after hospital discharge.

---

#### Classification of hyperglycaemia during hospitalisation

Previously diagnosed	Existing hyperglycaemia prior to hospitalisation
Previously undiagnosed	At admission: Fasting plasma glucose (FPG) >126 mg/dl Random blood glucose (RBG) >200 mg/dl HbA1c >6.5%
Stress hyperglycaemia	At admission: HbA1c <5.7% During hospitalization: FPG >126 mg/dl RBG >200 mg/dl Post discharge: normoglycaemia

---

#### Recognition of inpatient hyperglycaemia [5]

- Laboratory PG (Plasma Glucose) testing should be done for all patients on admission.
- If PG >140 mg/dl in non-diabetes patients
  - Monitor with capillary blood glucose (CBG) for 1–2 days
- Monitor CBG for 1–2 days in non-diabetes patients on
  - Glucocorticoids, Octreotide, Enteral nutrition (EN) or Parenteral nutrition (PN)

**HbA1c to be tested at admission** [5]: Every hyperglycaemic hospitalised patient should have an HbA1c test done at admission if it has not been done in the last 2–3 months. This will

1. Assist with differentiation of newly diagnosed diabetes from stress hyperglycaemia
2. Assess glycaemic control prior to admission

3. Facilitate design of an optimal regimen at the time of discharge

#### Monitoring [5]

- Bedside CBG is a preferred method.
- In which types of patients and when?
  - *In those who are eating:*
    - Test before meals (as close to meal as possible and not earlier than 1 h before meal) and at bedtime
  - *In those receiving continuous EN or NPO:* every 4–6 h
  - *More frequently in:* patients with continuous insulin infusion (CII), glucocorticoids use, abrupt stoppage of EN or PN or frequent hypoglycaemia.

**Issues with CBG monitoring:** One study from the Centers for Disease Control and Prevention (CDC) of five commonly used glucose meters showed mean differences from a central laboratory method to be as high as 32% and a coefficient of variation of 6 to 11% with a single-trained medical technologist [5].

- In the ICU, factors that can affect glucose meter readings
  - Hypotension or other perfusion problems in trauma/shock
  - Extremes of haematocrit
  - High oxygen tension (in patients receiving oxygen therapy)
  - Medications such as aspirin, paracetamol, vitamin C, dopamine and mannitol
- If CBG value does not correlate with the patient's clinical status
  - Confirm through lab testing of plasma glucose

**Clinical practice recommendations for management of in-hospital hyperglycaemia can be further classified into care of the diabetic patient in the following three categories:**

1. Critically ill (ICU)
2. Non-critically ill (non-ICU)
3. Special circumstances
  - Peri-operative conditions
  - Patients on enteral/parenteral nutrition
  - Patients on glucocorticoid therapy
  - Chronic kidney disease (CKD) patients
  - Transplant patients
  - Peri-partum situations

#### **Targets: recommendations based on the landmark trials**

The NICE-SUGAR [8] (Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation) is a large multi-centre randomised control trial which demonstrated that in medical ICU, intensive glucose control targets of 81–108 mg/dl in comparison to the conventional target of <180 mg/dl led to more deaths. This concluded that the target of blood glucose in ICU should remain between 140 and 180 mg/dl [8]. The recommended targets are summarised in Table 1. The American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) [7] recommends that insulin therapy should be initiated for treatment of persistent hyperglycaemia, starting at a threshold of no greater than 180 mg/dl.

Once insulin therapy has been started, a glucose range of 140–180 mg/dl is recommended for the majority of critically ill patients.

**Table 1** Glycaemic targets in ICU and non-ICU settings

Level of care	Glycemic target
ICU	140–180 mg/dl
Non-ICU	Fasting PG 80–120 mg/dl Pre-meal BG <140 mg/dl Post-meal BG <180 mg/dl
Special circumstances	Refer to the relevant section

Special requirement patients like those with acute myocardial infarction, patients on glucocorticoid therapy, pregnancy and labour, etc., can have individualised targets abiding with the guidelines and recommendations [4, 8, 9]. Post-transplant patient should be treated as surgical inpatients and should have the same targets [9].

Patients on parenteral mode of nutrition can be maintained on blood glucose targets in accordance with their condition [8].

All these targets have been derived through numerous trials and studies with expert opinions and extensive patient experience.

The management of hyperglycaemia in hospitalised patients is relatively easier as compared to an outpatient setup provided there is interdisciplinary coordination within the hospital. The correct use of insulin and insulin analogues, using intravenous (IV) or subcutaneous (SC) regimes that are required to achieve normoglycaemia, ensures better therapeutic outcomes. Training of health care providers; education of the support staff; using simple, uniform guidelines; and a good feedback system are essential for the successful management of diabetes in hospital setting.

#### **Summary**

- A systematic approach to the in-hospital management of diabetic patients has been associated with better outcome for the patient and reduced disease burden on the health care system as a whole.
- Hyperglycemia in the hospital has been defined as 'any blood glucose' >140 mg/dl.
- Every hospitalised patient should have an HbA1c test done at admission, if it has not been done in the last 2-3 months, this will assist in differentiating between known, unknown and stress diabetes and facilitate planning of the treatment at discharge.
- Target of blood glucose recommended in ICU setting is between 140-180 mg/dl.



**Table 2** Preparation for insulin infusion in intensive care unit [9]

Preparation	50 U of regular insulin dissolved in 50 ml normal saline (NS) in a 50-ml disposable syringe
Mode of administration	Intravenous infusion with an electronic pump/infusion pump
The choice of IV insulin	Short-acting regular human insulin
Primary target	To maintain blood glucose level between 140 and 180 mg/dl
Control methodology	Blood glucose to be controlled gradually in case of severe hyperglycaemia by titrating the dose of intravenous insulin
Prerequisites	Initially, 15–20 ml of solution should be flushed through plastic tubing to saturate the insulin binding sites in the tubing
Targets	Dose should be adjusted as per the levels of the blood glucose
Monitoring	<ul style="list-style-type: none"> <li>• Either by CBG or from the venous site/central line, every 1 h until BG stability has been demonstrated</li> <li>• Monitor serum potassium levels</li> <li>• Check regularly for blockage/disconnection/infusion pump malfunctioning</li> </ul>

### Managing diabetes in critically ill patients in the ICU

Hyperglycaemia is significantly associated with increased mortality and morbidity in critically ill individuals, independent of the severity of illness, diabetes diagnosis or length of stay in the ICU. Hyperglycaemia is a correctable abnormality and thus is a therapeutic target to improve outcomes in hospitalised patients [1, 9].

- Well-experienced and staffed centre
- Cardiac surgery
- Patient with stable glycaemic control—if can be achieved without hypoglycaemia

- *Glucose level of <110 or >180 mg/dl is not recommended*

#### *In-hospital management of hyperglycaemia aims to:*

- Restore stable glycaemia
- Minimise disruption of the metabolic state
- Minimise adverse outcomes

#### **Insulin in critical care**

- Based on the available evidence, for the majority of critically ill patients in the ICU setting, insulin infusion should be used to control hyperglycaemia, and BG >180 mg/dl should trigger insulin initiation.
- Once intravenous insulin is started, the glucose level should be maintained between 140 and 180 mg/dl.

#### *Recommended glycaemic targets in the ICU setting are*

- 140–180 mg/dl in majority
- 110–140 mg/dl in select few

#### **IV insulin infusion protocol**

Several published insulin infusion protocols appear to be both safe and effective, with low rates of hypoglycaemia. Some examples are the Portland Protocol [10], Yale Protocol [11], Markovitz Protocol [12], Medanta [13, 14], Mayo [15], Smart Phone Protocol [16], etc. The exact protocol is probably less important, what is important is its presence in an institution and adaptation to the individual hospital needs.

For the sake of ease and simplicity, the following insulin protocol is suggested as an example (Table 2).

#### **Starting an IV insulin infusion**

- Give a priming bolus of regular insulin 0.1 U/kg body wt. if the initial BG >300 mg/dl.

**Infusion initiation (U/h):** Initial rate of infusion = current BG divided by 100 [11, 17]

### Example

- Patient's BG = 200 mg/dl, then initial infusion rate =  $200 / 100 = 2$  units/h. (Since each ml of insulin infusion consists of 1 U of insulin, the rate will be 2 ml/h).

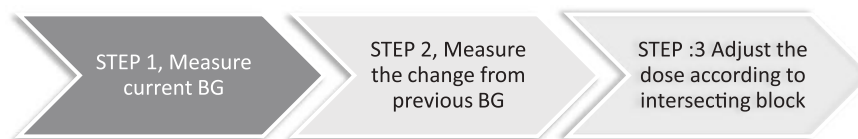


Chart adapted from Marie E. McDonnell and Guillermo E. Umpierrez [17].

**Table 3** Adjusting the insulin infusion rate

BG (mg/dl)	↑BG from prior BG	BG ↓ <30mg/dl	BG ↓ >30mg/dl from prior BG
≥241	↑rate 3U/h	↑rate 3U/h	No Change
211–240	↑rate 2U/h	↑rate 2U/h	No Change
181–210	↑rate 1U/h	↑rate 1U/h	No Change
141–180 (target)	if BG ↑ by >30 mg/dl, ↑ rate by 25%	if BG ↓ by 10–30mg/dl, ↓ rate by 25%	if BG ↓ 30–50mg/dl, ↓ rate by 25%
	If previously in target range, continue the same	If previously in target range, continue the same	If previously in target range, continue the same
	if BG ↑ by < 30mg/dl, continue same and recheck in 1 h	if BG ↓ by < 10mg/dl, continue same	if BG ↓ by >50mg/dl, ↓ rate by 50%
110–140	No Change	↓rate by 50%	↓ rate by 50%
91–109	No Change	Suspend Insulin <sup>a</sup>	Suspend Insulin <sup>a</sup>
71–90	Suspend Insulin <sup>b</sup>		
≤ 70	Suspend Insulin, give 25% dextrose; dose (ml) = $(100 - \text{BG}) \times 0.8^c$		

<sup>a</sup> Check BG q 1 h. Restart infusion at 50% of the previous rate when BG increases >140 mg/dl

<sup>b</sup> Check BG q 30 min till BG >90 mg/dl and then check BG q 1 h. Restart infusion at 50% of the previous rate when BG increases >140 mg/dl

<sup>c</sup> Example: BG = 40 mg/dl, give  $(100 - 40) \times 0.8 = 60 \times 0.8 = 48$  ml of 25% dextrose IV and check BG after 15 min [17]

- If BG <70 mg%, give the calculated dose of 25% dextrose and then check BG q 15 min.
- If BG >70 mg%, check BG q 30 min till BG >90 mg%.
- If BG >90 mg%, check BG q 1 h.
- If BG >140 mg/dl, restart infusion at 50% of previous rate.

In patients with chronic kidney disease with elevated creatinine or needing dialysis, caution is advised as chances of hypoglycaemia may be more.

*The choice of IV insulin should be regular human insulin. Short-acting analogues have no advantage over regular insulin when given intravenously but have been found to be safe if preferred.*

**In adjusting the insulin infusion rate**, refer to Table 3

Monitor Capillary blood glucose (CBG) hourly.

1. Rate adjustment considers the rate of change (or lack of change) between the current and previous glucose values and the current rate of insulin infusion.

- a. If the BG decreases >30 mg/dl, continue the same dose as shown in the table.
- b. If the BG decreases <30 mg/dl, increase the dose of insulin appropriately as shown in the table.
- c. If the BG increases above the initial BG, increase the dose of insulin appropriately as shown in the table.

Monitor BG hourly; adjust the dose of insulin infusion till target BG of 140–180 mg/dl is achieved. Once a stable BG (two consecutive readings within target) is achieved, monitoring of BG can then be done every 2–3 h.

Administer 5D/DNS at 80–120 ml/h if not receiving any nutrition; supplement K<sup>+</sup> if no contraindication.

**Recommendations for the limited care settings** [9, 17]

In the limited care and resource-constrained setting, where insulin pump facility is not available, 25 units of regular

insulin in 500 ml of normal saline is recommended to be delivered intravenously through an IV drip set as explained in Table 4. (This would give 0.05 units/ml).

To measure the rate, we must know

- a. The number of drops which is equal to 1 ml, e.g. macro-drip IV set 15 drops = 1 ml
- b. Time in minutes

The formula for working out flow rates is

$$\frac{\text{volume (ml)} \times \text{drop factor (gtts/ml)}}{\text{time (min)}} = \text{gtts*/min}$$

\*gtts = Latin for drops

Calculation for 20 ml/h = (20 × 15) / 60 = 5 drops/min

**Transition to SC insulin is required when patient begin eating regular meals or when transferred to lower intensity care.**

- BG >180 mg/dl should trigger insulin initiation
- Continuous IV insulin infusion (CII) is the most effective method.

Insulin infusion rate ( U/hr )	Drip rate ( ml/hr )	Drop rate/min By regular macro-drip IV set
1	20	5
2	40	10
3	60	15
4	80	20
5	100	25
6	120	30
7	140	35

- For Blood Transfusion**  
Set: 1ml = 10 drops/min
- For Regular Macro Drip**  
Set: 1ml = 15 drops/min
- For Micro Drip Set:**  
1ml = 60 drops/min

**Table 4** Insulin infusion rate and the drop rate/min

**Transition from insulin infusion to SC insulin and/or oral anti-diabetic drugs**

**Introduction**

The transition from IV to SC insulin is an important step in the care of a critically ill patient, usually occurring after clinical improvement has taken place. Abrupt discontinuation of IV insulin often leads to rebound hyperglycaemia. Hence, the transition orders from IV to SC insulin should be made carefully and only after it is clear that the patient exhibits stable glycaemic control.

**Safety indicators for transition from IV to SC insulin [18]**

1. Stable blood glucose levels <180 mg/dl for at least 4–6 h
2. Resolution of acidosis in DKA
3. Haemodynamically stable without the use of vasopressors
4. Stable nutrition plan
5. Stable IV drip rates (low variability)

Transition is more likely to be successful if blood glucose levels are between 140 and 180 mg/dl with an insulin drip rate of <2 units/h [19]. Transition may prove challenging in elderly patients, those with high pre-admission HbA1c, those with high variability of blood glucose in the 24-h preceding transition, those on corticosteroids and subjects with fluctuating concomitant illnesses.

**Process of transition**

The *total insulin dose* (TDD) should be calculated when we transition from IV to SC insulin. Subcutaneous insulin administration in hospitalised patient should include three components to be effective:

- *Basal insulin* (to inhibit hepatic gluconeogenesis)
- *Bolus* or nutritional insulin (to facilitate mealtime glucose metabolism)
- *Correctional insulin* (to provide real-time adjustment of insulin dosing based on the patient’s insulin sensitivity). (Refer to Table 5)

Various factors influence insulin requirement such as post-surgical stress, pain, variable oral intake, infection and underlying insulin resistance. The safest method to calculate the TDD is to find a time interval of several hours (ideally, 4–6-h duration), during which the blood glucose values are

**Table 5** Calculation of the total daily dose (TDD) of insulin

TDD calculation	Dose 80% of calculated TDD
<b>From IV to SC transition</b>	Use 80% of calculated TDD for starting SC insulin
• Calculate insulin needed for stable control of BG for previous 6 h and multiply by 4	Give Basal insulin is 50%
Or	Bolus insulin is 50%
• Calculate the total amount of insulin needed in previous 24 h	

**Table 6** Calculation of basal/bolus dose including the correctional dose

Basal dose		Correctional bolus (CB)
Glargine	OD dose	$BG - 100 = CB$
Detemir	OD or BD dose	Correction factor (CF) (of regular/rapid-acting insulin)
NPH	BD dose	$CF = 1500/TDD$ (regular insulin)
<b>For basal dose correction</b>		Or
<b>PM basal:</b> check FPG every day, ↑ 2 U of basal till FPG of 80–120 mg/dl is achieved		$CF = 1800/TDD$ (insulin analogue)
<b>AM basal:</b> check pre-dinner glucose every day, ↑ 2 U of basal till BG <140 mg/dl (for BD dose of NPH/detemir)		
Bolus dose		
Total bolus dose ÷ 3	With breakfast, lunch, dinner <sup>a</sup>	
For bolus: regular, aspart, glulisine or lispro can be used		

CF Correction Factor

<sup>a</sup>Note that if specific calorie count of each meal is available, doses may be varied according to the meal

stable and at target. The insulin requirement during this stable period can be extrapolated to a 24-h time period [18].

**Choice of insulin**

On transition, regular human insulin/neutral protamine Hagedorn (NPH) or short- and long-acting insulin analogues can be used, based on affordability.

The half-life of IV insulin is less than 5 min. To prevent the recurrence of hyperglycaemia during the transition to subcutaneous insulin, the insulin infusion should be continued after the dose of SC insulin is given. For regular or rapid-acting insulin given subcutaneously, continue insulin infusion for 1–2 h and long-acting insulin 2–3 h.

**Transition basal/bolus regime examples**

1. For patients who are not receiving significant amount of calories (e.g. patients who are on liquid diet alone), the basal dose can be given as a single dose of long-acting insulin (e.g. glargine, detemir) or two doses of intermediate-acting insulin (NPH) every 12 h. Correctional short-acting insulin (regular) or rapid-acting insulin (e.g. aspart, glulisine, lispro) can be added as needed depending on nutritional intake and glucose levels [20].
2. For patients who are allowed oral intake, 50% of the calculated dose of insulin is administered as the basal dose and the rest is divided evenly between the three meals as the bolus dose [20, 21] (refer to Table 6).

**Glucose monitoring after transition to SC therapy [18]**

The first 24 h after the transition is crucial to assess the patient’s insulin requirement as this may continue to change with clinical improvement. Hence, BG should be monitored at least five times daily for patients who are on multiple daily injections, that is

- Before each meal
- At bedtime
- At 3 a.m.

**Table 7** Maintenance of the target BG

Level of care	Target
ICU setting	140–180 mg/dl
Non-ICU setting	Fasting 80–120 mg/dl Pre-meal <140 mg/dl Post-meal <180 mg/dl
Special circumstances	Refer to the relevant section

The target BG should be maintained as per Table 7.

In case the glucose levels are above pre-determined targets at any time, *supplemental doses (correction boluses)* need to be given. Correction insulin refers to the administration of supplemental doses of short- or rapid-acting insulin together with the usual dose of bolus insulin for BG above the target range.

The supplemental insulin dose is calculated using CF which is the degree of BG lowering expected from 1 unit of insulin.

**Calculating the CF and correction dose (Table 6)**

Correction factor is equal to 1800 divided by the TDD if insulin analogue is used or 1500 divided by the TDD if regular insulin is used. (Refer to Tables 6 and 8).

*Correction dose* is the actual BG minus 100 divided by the CF. (Refer to Table 6).

**Table 8** Calculation of correction factor and correction dose

Example	
<b>Total calculated daily dose is 30 U</b>	<b>Additional correctional bolus:</b>
- Basal 15 U	Estimated pre-meal BG 250 mg/dl
- Bolus 15 U	$CF = 1500/30 = 50$ U
Bolus 5 U-5 U-5 U before each 3 meals + additional correctional bolus for BG not at target at any meal	$CB = 250 - 100 = 150 = 3$ U $CF = 50$
	Total meal dose 5 U + 3 U = 8 units

Unexpected hyperglycaemic excursions are common, and the use of correction insulin remains a pervasive and arguably logical practice. If correction insulin is used, it should be ordered as a separate step after considering basal and nutrition insulin needs. The doses of scheduled insulin should be adjusted regularly if correction insulin is required consistently. There is no evidence to support the routine use of continuous glucose monitoring.

### Transition in stress hyperglycaemia

If the patient requires less than 1 U/h of IV insulin, it is prudent to monitor blood glucose levels and institute SC insulin only if glucose levels are consistently >180 mg/dl.

### Safety markers for transition to oral anti-diabetic drugs [22]

It is advisable to transition patients administered IV insulin in hospital to subcutaneous insulin therapy after stabilisation.

### Transition to oral anti-diabetic agents in combination with insulin is done when

1. Patient is on normal diet
2. Glycaemic control is stable with no ketoacidosis
3. In post-surgical patients where expected tissue damage is minimal
4. There are no serious co-morbid conditions

### *Transition to oral agents alone is not preferred in hospitalised patients who have a prolonged stay because*

- Sulfonylureas and other insulin secretagogues (e.g. meglitinides) could lower glucose rapidly, increasing the risk of hypoglycaemia.
- Efficacy and side effects of Alpha-Glucosidase Inhibitors (AGI) limit their use.
- For patients who have been on metformin, dipeptidyl peptidase (DPP)-IV inhibitors, sodium-glucose co-transporter (SGLT)-2 inhibitors or a thiazolidinedione before admission, these agents often are restarted in the post-operative period when oral intake of medications is possible and hepatic and renal function are stable.

### Summary

- Discontinuation of IV insulin often leads to rebound hyperglycemia. Hence the transition orders from IV to SC insulin should be made carefully and only after it is clear that the patient exhibits stable glycaemic control.
- Transition is more likely to be successful if blood glucose levels are between 140-180 mg/dl with insulin drip rates being constant.
- It should be ensured that there is continuity between IV insulin infusion and the first dose of SC insulin.
- The calculation of the total daily insulin requirement can be best ascertained during a time interval of 4-6 hours during which the blood glucose values are at goal and IV insulin rates are not particularly elevated or variable.
- Regular insulin or rapid acting analog should be used for the bolus/prandial insulin and the supplemental insulin. The basal insulin requirement should be met using NPH, insulin detemir or glargine.

### Glycaemic control in the non-critically ill patients

In general, insulin is the preferred treatment for hyperglycaemia in hospitalised patients with diabetes. Patients with type 1 diabetes must be maintained on insulin therapy at all times to prevent diabetic ketoacidosis (DKA).

The targets for the majority of non-critically ill patients are pre-meal BG <140 mg/dl and post-meal BG <180 mg/dl [6, 7].

### Insulin initiation in hospital

Common approaches to insulin dosing in the hospital are the sliding scale insulin (SSI) approach and the use of basal insulin dosing with prandial and correctional doses. Medical articles have questioned the effectiveness of SSI since at least in 1970. A Medline search of 52 trials from 1966 to 2003 showed no clinical trials demonstrating benefit from SSI, and most experts currently question the effectiveness and safety of traditional SSI. The largest prospective cohort study to date revealed that SSI regimens failed to adequately control hyperglycaemia, resulting in high rates of hypoglycaemia, and were associated with longer hospital stays. SSI regimens do not allow for basal or mealtime insulin requirements and grossly underestimate total daily insulin requirements. Furthermore, SSI regimens respond to hyperglycaemia after it has happened, rather than preventing it, and the sliding scale depends on the inaccurate assumption that insulin sensitivity is uniform among all patients.

- Subcutaneous (SC) insulin administration in the non-ICU hospitalised patient should include three components to be effective:
  - Basal insulin
  - Nutritional (bolus) insulin
  - Correctional insulin

### Other insulin regimes which can be followed in the hospital

The following insulin regimes can be initiated in the non-critical care settings:

- Basal/bolus therapy

- NPH and regular insulin
- Long-acting and rapid-acting insulin analogues

- Pre-mixed insulin analogues
- Use of incretin-based therapy with basal insulin with supplemental rapid-acting insulin as required

For most patients in the hospital, basal bolus is the preferred regime. However, if patients have been well controlled on pre-mixed insulin, they can be continued on the same regime. These patients require frequent monitoring.

Recently, there are increasing reports of the use of glucagon-like peptide-1 receptor agonist (GLP-1 RA) in hospitalised patients as they can reduce the total daily dose of insulin and minimise the risk of hypoglycaemia. They can be used if there are no contraindications to incretins.

### Estimating SC insulin dose

- Patients, who were well controlled on insulin prior to admission, can usually be maintained on their home insulin regimen with specific adjustments made for differences in meals and activity levels, the effects of illness and the effects of other concomitant medications.
- In patients who were on an insulin infusion and now transferred to non-critical care settings, the TDD of insulin can be calculated from the insulin requirement in previous 6 h of stable control of BG and multiplied by 4 to get the TDD in 24 h or the actual total insulin requirement in the last 24 h.
- For insulin-naïve patients or when no IV insulin therapy has been given, the TDD of insulin can be calculated as shown in Tables 9, 10 and 11.

### Insulin dose modification in hospital

- In patients who are NPO or unable to eat, bolus insulin must be withheld until nutrition is resumed. However, doses of correction insulin can be continued to treat BG above the desired range.
- Adjustments of scheduled basal and bolus insulin can be based on total doses of correctional insulin administered in the previous 24 h.

**Table 9** Estimation of the TDD of insulin

TDD calculation		Dose 80% of calculated TDD
<b>For insulin naïve</b>	<b>Total dose as per body weight</b>	Use 80% of calculated TDD for starting SC insulin
Ideal body weight	0.4–0.5 U/kg	Give when
Obese	0.5–0.6 U/kg	Basal insulin is 50%
Lean or renal compromised	0.3–0.4 U/kg	Bolus insulin is 50%
<b>From IV to SC transition</b>		
Calculate the insulin requirement in the previous 6 h of stable control of BG and multiply by 4 to get the TDD in 24 h or the actual total insulin requirement in the last 24 h		

**Table 10** Calculation of the dose with correctional factor

Basal dose		Correctional bolus (CB)
Glargine	Single dose AM/PM	BG – 100 = CB
Detemir	Given in 12-h split dose	CF
NPH	Given in 12-h split dose	CF = 1500/TDD (regular insulin)
<b>For basal dose correction</b>		Or
<b>PM basal:</b> check FPG every day, ↑ 2 U of basal till FPG of 80–120 mg/dl is achieved		CF = 1800/TDD (insulin analogue)
<b>AM basal:</b> check pre-dinner BG every day, ↑ 2 U of basal till BG <140 mg/dl (for BD dose of NPH/detemir)		
Bolus dose		
Total bolus dose ÷ 3	With breakfast, lunch and dinner	
For bolus dose: regular, aspart, glulisine or lispro can be used		

- Sliding Scale Insulin (SSI) (defined as the administration of a pre-established amount of short-acting insulin in response to hyperglycaemia) as the sole regimen for the management of hyperglycaemia in the hospital setting is ineffective and, therefore, is *not recommended*.

### Role of oral anti-diabetic drugs/non-insulin injectables in non-critically ill patients

The use of oral and other non-insulin therapies presents unique challenges in the hospital settings, because there are frequent contraindications to their use in many inpatient situations (sepsis, NPO status, IV contrast dye, pancreatic disorders, renal failure, etc.)

Selected patients may be candidates for continuation of previously prescribed oral anti-diabetic drug (OAD) therapy in the hospital, those who are clinically stable and eating regular meals and who have no contraindications to the use of these agents.

Conversion to basal bolus insulin therapy based on BG values results to a better management of hyperglycaemia.

#### *Common problems encountered with OADs*

- Sulfonylureas
  - May cause severe and prolonged hypoglycaemia, particularly in elderly, renal-impaired patients and patients with poor oral intake

- For long-acting SUs, dose adjustments may be difficult.
- Skipping a meal poses a severe risk of hypoglycaemia.
- Metformin
  - Must be discontinued in patients with decompensated congestive heart failure, severe renal insufficiency, hypoperfusion or chronic pulmonary disease and in patients who are at risk of developing renal failure and lactic acidosis, as such may occur with the administration of IV contrast dye or surgery
  - Discontinue temporarily before major surgery or IV contrast use; restart after 48 h if kidney function is normal.
- Thiazolidinediones (TZDs)
  - May take several weeks to be effective, thus limiting the usefulness of these agents for achieving glycaemic control in the hospital.
  - They are contraindicated in patients with congestive heart failure, hemodynamic instability or evidence of hepatic dysfunction.
  - If the patient is previously taking TZDs, they may be continued in the absence of any contraindications.
- DPP-IV inhibitors/GLP-1 RA
  - Contraindicated in patients with pancreatic illness, medullary thyroid carcinoma and gastroparesis

**Table 11**

Example	Additional correctional bolus
<b>Total calculated daily dose: 30 U</b>	
- Basal 15 U	Estimated BG 250
- Bolus 15 U	CF 1500/30 = 50 U
Bolus 5U - 5U - 5U before each 3 meals + additional correctional bolus for BG not at target at any meal	CB 250 – 100 = 150 = 3 U
	CF 50 50
	Total meal dose 5 U + 3 U = 8 units

- SGLT-2 inhibitors
  - Higher incidence of genitourinary infections
  - Possible risk of diabetic ketoacidosis
  - Contraindicated prior to major surgery
  - Insufficient data in hospitalised patients

**For limited care settings:** Human insulin rather than analogues may be used.

### Management in special circumstances

#### Minor procedures

The management of in-hospital hyperglycaemia includes special circumstances like minor day-care procedure including dental interventions and cataract surgery. All procedures which do not require patients to be in the hospital overnight and are anticipated to miss not more than one meal are considered minor procedures, e.g. cataract surgery, some therapeutic or diagnostic procedures requiring overnight fasting for more than 8–10 h.

#### Targets for therapy are categorised as pre, intra and post procedure [23]

There are no pre-requisites for emergency life-saving procedures. A stable glycaemic control prior to the elective procedure with HbA1c target of <8% (corresponding to mean plasma glucose of 180 mg/dl) is acceptable. If the HbA1c is >9% or blood glucose >200 mg/dl and the surgery cannot be postponed, it is advised to first achieve blood glucose control prior to the procedure (Tables 12) [23].

#### Glycaemic management in regard to the timing of the surgery [23–28]

Ideally, patients with diabetes should be posted in the morning, preferably as the first case. Considering the prevalence of diabetes, it may not always be feasible to finish all procedures on patients with diabetes in the morning, especially in a high turnover centre or diabetes specialty hospital. Hence, the protocol for patients posted in the morning and afternoon is provided.

**Table 12** Pre-procedure glycaemic control

	Ideal	Acceptable	For intensification
FPG (mg/dl)	80–120	<140	>140
PPBG (mg/dl)	<160	<180	>200
HbA1c (%)	<7	<8	>9

BG targets during the procedure are 140–180 mg/dl with avoidance of hypoglycaemia.

#### For morning procedures

On the day prior to procedure, patients should be advised to take full dose of anti-diabetes medications including insulin and OADs at dinner. The patient will remain NPO till the procedure is complete in the morning. Patient should take their usual dose of insulin and/or OADs when they have breakfast by mid-morning.

If the procedure is delayed unexpectedly and the blood glucose levels are above the target (>180 mg/dl), insulin infusion can be started. If the facility for infusion is not available, subcutaneous correction dose of short-acting insulin may be given followed by a close monitoring to avoid hypoglycaemia.

#### For patients who are not on insulin (on OADs or GLP-1 RA)

All OADs and GLP-1 RA can be continued as usual on the day prior to procedure but should be omitted on the morning of procedure. OADs and GLP-1 RA can be restarted once the patients resume their diet. Metformin may not be discontinued for minor procedures unless there is renal, cardiac or hepatic impairment. For procedures requiring IV radio-contrast administration, it is recommended to discontinue metformin 24 h prior to the procedure. Metformin can be restarted after confirming normal renal function after 48 h.

Patients with long-duration type 2 diabetes and those receiving more than two OADs are likely to deteriorate after discontinuation of anti-diabetes medications. Similarly, dysglycaemia is more likely in patients with poor pre-procedural glycaemic control and if the procedure is unexpectedly prolonged or complicated. These patients should be treated with insulin infusion during procedure and may require subcutaneous insulin for a short duration after the procedure (Tables 13 and 14).

#### Insulin regimes for hyperglycaemia management in post-op period

##### A. Immediate post-op period:

IV insulin protocol

##### B. Enteral feeding:

Basal plus or basal bolus with correction bolus

##### C. Tube feeding:

Low-dose basal with short-acting insulin every 6 h or rapid-acting insulin every 4 h as correction bolus

OR

NPH with short-acting regular insulin every 8 or 12 h

##### D. Parenteral nutrition:

Add 0.1 U of regular insulin per gram of dextrose in non-diabetic patients and 0.15 U of regular insulin per gram of dextrose in diabetic patients to the parenteral solution as IV infusion

OR

Basal with short-acting insulin every 6 h if BG >180 mg/dl



**Table 13** Recommendation for peri-operative adjustment of insulin (short starvation period—no more than *one* missed meal)

Insulin	Day prior to admission	Day of surgery	
		Morning surgery	Afternoon surgery
Once daily (evening) Basal insulin	No dose change	No dose change Check BG 6 h	No dose change Check BG 6 h
Once daily (morning) Basal insulin	No dose change	No dose change Check BG 6 h	No dose change Check BG 6 h
Twice daily Pre-mixed	No dose change	Halve the usual morning dose. Check BG 6 h. Leave evening dose unchanged	Halve the usual morning and evening dose. Check BG 6 h
Twice daily Separate short- + intermediate- acting insulin	No dose change	Calculate the total dose of both morning insulin and give half as intermediate acting only in the morning. Check BG 6 h. Leave evening dose unchanged. Supplement correction doses with short-acting insulin as required	Calculate total dose of both morning insulin and give half as intermediate acting only in the morning. Check BG 6 h and post-op and supplement correction doses with short-acting insulin as required
3, 4 or 5 injections daily	No dose change	<b>Basal bolus regimens:</b> Omit the morning and lunchtime short-acting insulin. Keep the basal unchanged based on BG values. <b>Pre-mixed insulin (morning dose):</b> Halve the morning dose and omit lunchtime dose (if any). Check BG 6 h	Take the usual morning insulin doses. Omit lunchtime dose. Check BG 6 h and supplement correction doses with short-acting insulin as required

**Evaluation for emergency surgery****Pre-op assessment**A. *Metabolic status:*

Measure plasma glucose, pH, urea, Sr. creatinine, Sr. Na and K and urine ketones

B. *Volume status:*

Check for orthostatic hypotension, elevated BUN and/or creatinine, urine output, osmolality and adequacy of peripheral circulation

C. *Cardio-respiratory status:*

ECG, chest X-ray, 2D ECHO

**Preoperative treatment**

- Delay surgery if possible until metabolic control and volume status are stabilised.
- Optimise blood glucose, electrolytes and acid–base status.

**Steroid-induced diabetes****Introduction**

The use of steroids in clinical practice is a common practice. The relationship between steroids and diabetes can be in the form of

**Table 14** Recommendation for peri-operative adjustment of non-insulin medications (short starvation period—no more than *one* missed meal)

Tablets	Day prior to admission	Day of surgery	
		Morning surgery	Afternoon surgery
Acarbose	Take as normal	Omit morning dose if NPO	Give morning dose if eating
Meglitinide	Take as normal	Omit morning dose if NPO	Give morning dose if eating
Metformin	Take as normal	Take as normal	Take as normal
Sulfonylureas	Take as normal	For once daily: omit AM dose For twice daily: omit AM dose	For once daily: omit AM dose and give PM dose For twice daily: half AM dose and give PM dose
DPP-IV inhibitors	Take as normal	Take as normal	Take as normal
GLP-1 RA		Omit on the day of surgery	Omit on the day of surgery

1. Chronic use of steroids leading to diabetes
2. Use of steroids in a patient with pre-existing diabetes
3. Increased endogenous secretion of glucocorticoids

In either of the situations, it is important to achieve good glycaemic control to improve outcomes and prevent adverse events. Commercial preparations of steroids are available as mentioned in Table 15.

### Management of steroid-induced diabetes

#### Monitoring of blood glucose

##### A. *In patients with no history of diabetes*

- In patients perceived to be at high risk (family history, obesity, other ADA risk factors) or with symptoms suggestive of *hyperglycaemia*, check HbA1c prior to starting steroids.
- After starting steroid, recommend BG once daily, pre or post meal.
- If the CBG is <200 mg/dl, consider the patient to be at low risk and record the CBG daily post meal.
- If CBG consistently <180 mg/dl, consider cessation of CBG testing.
- If CBG is found to be >200 mg/dl, the frequency of testing should be increased to a minimum of three times a day and treatment should be initiated accordingly.

##### B. *In a known case of diabetes*

- If a CBG is found to be >200 mg/dl, the frequency of testing should be increased to a minimum

of three times a day and treatment should be initiated accordingly.

### Treatment protocols

#### A. *Single-dose prednisolone in morning*

- BG rise within 4–8 h after administration of oral steroids and earlier with IV steroids. The most commonly prescribed steroid is prednisolone in the morning, resulting in the rise of blood glucose levels by late morning.
- Hence, the anti-hyperglycaemic management should be tailored to combat daytime hyperglycaemia and to avoid nocturnal hypoglycaemia.

### Insulin therapy

- Intermediate-acting insulin (NPH or detemir) administered at the same time of steroid ingestion may best manage hyperglycaemia with a once daily oral steroid.
- The starting dose of NPH can be calculated as per steroid equivalent dose by the formula given in Table 16 [30].
- Increase the daily dose of insulin by 10–20% based on blood glucose level.
- For patients on non-insulin therapy, a single dose of short-acting sulfonylurea such as gliclazide 40 mg for every 5 mg of prednisolone (or equivalent steroid) (max one-time dose 240 mg) taken before breakfast may best manage hyperglycaemia from a once-daily oral steroid treatment. If not controlled by OADs, intermediate-acting insulin (NPH or detemir) may be added in the morning. If the hyperglycaemia is continued late in the evening or overnight, an additional dose of gliclazide or intermediate-acting insulin can be given in the evening [29].
- Current evidence does not support the use of DPP-IV inhibitors, GLP-1 RA or SGLT-2 inhibitors in the management of steroid-induced diabetes.

**Table 15** Steroid dose equivalents [29]

Steroids	Steroid potency (equivalent doses), mg	Duration of action (half-life in hours) [40]
Hydrocortisone	20	8
Prednisolone	5	16–36
Methylprednisolone	4	18–40
Dexamethasone	0.75	36–54
Betamethasone	0.75	26–54

N.B. potency relates to anti-inflammatory action, which may not equate to hyperglycaemic effect

#### B. **Patient taking multiple hydrocortisone injections or dexamethasone or methylprednisolone pulse therapy**

- a. Hyperglycaemia is observed throughout the 24-h period.
- b. Insulin therapy is usually recommended. Subcutaneous insulin using a basal or multiple-dose daily injection regimen is the choice of treatment.

**Table 16** Calculation of NPH dose

Glucocorticoids	Frequency	Insulin dosing
Prednisolone or methylprednisolone	Every day	NPH 0.5 U/mg glucocorticoid (range 0.25–1 U) Administered at the time of the glucocorticoid dose
Prednisolone or methylprednisolone	≥2 times a day	NPH 0.5 U/mg glucocorticoid (range 0.25–1 U) in divided doses twice daily Or Use 130–140% of basal and bolus insulin doses
Dexamethasone		NPH 3 U/mg glucocorticoid equivalent (range 2–5 U) in divided doses twice daily Or Use 140–150% of basal and bolus insulin doses
Hydrocortisone	Once a day	NPH 0.125 U/mg administered at the time of the glucocorticoid dose
Hydrocortisone	Twice a day	NPH 0.125 U/mg administered twice a day at the time of the glucocorticoid dose

- c. Insulin can be given as twice daily pre-mixed (with an increase in the morning insulin dose), basal bolus or individualised regimen having OADs and insulin both.
- d. If on basal insulin, consider switching to morning administration and increase dose in 2–4-unit increments (or by 10–20%) every 24–48 h.
- e. In acutely unwell patients, IV insulin infusion may be required for a short duration.
- f. Intravenous insulin infusion may be used for the estimation of TDD of insulin requirement with steroids, which can be used from the next day as basal/bolus injections.

#### • Tapering and discontinuation

Conversely, glucose levels drop to normal in previously non-diabetic individuals within 24 h after discontinuation of IV steroids. This may take several weeks in a dose-dependent manner if oral steroids are weaned over several weeks. The dose of anti-hyperglycaemic agents needs tapering accordingly. A weekly reduction of 5 mg of prednisolone (or equivalent steroid) roughly requires reduction in the total daily dose of insulin by 20–25% or reduction in the dose of gliclazide by 40 mg.

#### Management of hyperglycaemia during obstetric procedures, caesarean section and vaginal delivery [31, 32]

Most obstetric procedures (e.g. cervical cerclage, amniocentesis, D&C) are day-care procedures and do not require more than 6–8 h of overnight fasting. The aim is to maintain blood glucose levels between 70 and 140 mg/dl during and immediately after the procedure.

#### Intra-partum glucose management

Insulin requirements significantly reduce during active labour due to reduced hepatic gluconeogenesis and increased calorie requirement. Uncontrolled maternal hyperglycaemia during the labour can lead to foetal hyperinsulinism, consequently resulting in neonatal hypoglycaemia. Feasible target levels of maternal blood glucose levels during delivery for prevention of neonatal hypoglycaemia are 70–140 mg/dl.

#### Glycaemic management during vaginal delivery [31]

Maintenance of target blood glucose levels during labour requires a balanced administration of insulin and glucose preferably in the form of separate infusions. Depending on the glycaemic status, insulin infusion can be started at the rate of 0.5 to 1 units/h. Glucose-containing fluid (in the form of 5% dextrose or dextrose normal saline (DNS)) can be started to provide glucose at the rate of 80–125 ml/h. Glucose infusion can be started either simultaneously with insulin infusion or when blood glucose levels fall below 70 mg/dl. Where facility of infusion is not available, subcutaneous short-acting insulin every 4–6 h may be given.

#### Glycaemia management during caesarean section and induction of labour

A planned caesarean section should be posted early in the morning. Patient should take usual dose of night-time insulin (short as well as intermediate or long acting) and OADs on the day prior to surgery. The

morning dose of insulin as well as OADs should be withheld on the day of surgery, and blood glucose levels should be monitored closely. A similar protocol should be followed for induction of labour which again should be planned early in the morning. If the procedure is expected to get delayed (may take 8–12 h for induction of labour especially in primigravida) and a light breakfast is allowed by obstetrician, half the usual dose of insulin can be administered subcutaneously in the form of intermediate-acting insulin. Insulin and glucose infusions may be administered as required to maintain blood glucose levels between 70 and 140 mg/dl, if prolonged fasting is anticipated. In the post-partum phase, blood glucose levels may normalise in patients with gestational diabetes while the insulin requirement may drastically come down for patients with type 1 and type 2 diabetes. If appropriate, the insulin regimen and doses can be deescalated.

### Insulin in renal-compromised patients

Insulin requirements show a biphasic course in patients with diabetes and renal disease (Table 17). In the beginning, glucose control deteriorates because of insulin resistance; therefore, more insulin is needed to achieve glycaemic control. In advanced renal failure with creatinine clearance below 50 ml/min, the need for insulin is lower or even the cessation of insulin may be necessary. The need for insulin is decreased because of less caloric intake in uremic patients. With the institution of haemodialysis, the need for insulin changes because the insulin sensitivity and liver metabolism improve.

Most patients who are renal compromised need a lower total daily dose of insulin and have less stringent glycaemic targets. In non-critical care situation, the preferred insulin is short-acting insulin analogue over regular insulin. Patients with normal GFR with

albuminuria or post-transplant patients may need tighter control albeit without the risk of hypoglycaemia [36].

### Insulin therapy

Multiple doses of rapid-acting insulin analogues are best suited for patients with estimated glomerular filtration rate (eGFR) <30 ml/min to deal with poor and unpredictable food intake, nausea and vomiting. Most patients with advanced CKD (eGFR <30 ml/min) do not require basal insulin. Multiple-dose insulin injection therapy with two to three rapid-acting insulin (preferably analogues) and one to two basal insulin injections may be required for patients with eGFR between 30 and 60 ml/min.

### Oral anti-diabetic agents

The use of oral insulin-sensitising agents in addition to insulin may improve glycaemic control in patients with CKD (Table 18). Occasionally, few patients with milder hyperglycaemia may get controlled with only OADs. Most OADs require dose adjustment with declining renal function. Insulin therapy remains the mainstay of treatment in diabetic patients on hemodialysis. On the day of dialysis, the usual dose of short- or rapid-acting insulin should be administered after the session of dialysis.

### Peri-operative management of transplant patient [31, 33, 34]

Care of glycaemic status during a pre-transplant period involves patients with pre-existing diabetes as well as new-onset diabetes after solid organ transplantation (NODAT). For a planned transplant in patients with pre-existing diabetes, it is advisable to achieve optimal blood glucose control prior to a procedure. Glycaemic control in the peri-procedural period is achieved with insulin infusion which may be continued till the patients resume solid diet.

**Table 17** Glycaemic targets for renal patients [36]

	HbA1c (%)	FPG (mg/dl)	2 h PPBG (mg/dl)
Normal GFR, microalbuminuria +	6.5–7	80–120	<180
Pre-dialysis (CrCl <10)	<7.5	100–120	<180
Dialysis	7.5–8	100–140	<200
Post renal transplant	6.5–7	80–120	<180

**Table 18** Safety of anti-hyperglycaemic medications in patients with diabetes and CKD [36]

eGFR (ml/min/1.73 m <sup>2</sup> )	Safe without dose adjustment	Can be used in reduced dose	Contraindicated
More than 60	Insulin Almost all OADs Liraglutide		
30–59	Insulin (caution for longer-acting preparations) Acarbose Linagliptin Gliclazide Nateglinide Repaglinide Pioglitazone <sup>a</sup> Liraglutide	Metformin (max 1 g/day) Saxagliptin (2.5 mg) Sitagliptin (50 mg) Exenatide (5 mcg BD)	Glibenclamide GLP-1 RA SGLT-2 inhibitors
15–29	Insulin (caution for longer-acting preparations) Linagliptin Nateglinide Repaglinide Pioglitazone <sup>a</sup>	Sitagliptin (25 mg) Saxagliptin (2.5 mg) Gliclazide	Acarbose Voglibose Metformin Glibenclamide GLP-1 RA SGLT-2 inhibitors
Less than 15 or dialysis	Insulin (avoid longer-acting preparations) Linagliptin Nateglinide Repaglinide Pioglitazone <sup>a</sup>	Sitagliptin (25 mg) Gliclazide	Acarbose Voglibose Metformin Glibenclamide Saxagliptin GLP-1 RA SGLT-2 inhibitors

<sup>a</sup> Risk of volume overload

Care of glycaemic status during a post-transplant period additionally involves patients with NODAT. Hence, blood glucose monitoring should be done regularly in all individuals with or without pre-existing diabetes. The threshold for the diagnosis of NODAT is the same as described by the American Diabetes Association using fasting plasma glucose (FPG) >125 mg/dl and post-meal blood glucose >200 mg/dl. Treatment of post-transplant diabetes is the same as that of type 2 diabetes.

#### Management of CKD patient on hemodialysis [35, 36]

Insulin is generally the choice of treatment for uncontrolled diabetes with CKD, but few OADs can be used safely after dose adjustment for milder hyperglycaemia. The target as well as threshold to start anti-hyperglycaemic agents in patients with CKD is HbA1c >7%. A less stringent target may be chosen in individuals with chronic co-morbidities or limited life expectancy with acute co-morbidities and risk of hypoglycaemia.

#### Management in special feeding [37]

- Total parenteral nutrition (TPN)
- Enteral feeding via Ryle's tube/jejunostomy feeds

Usually, insulin is added along with the nutrition in patients receiving TPN. Initially, a separate IV infusion of regular insulin may be required to estimate the TDD of insulin. Subsequently, the separate insulin infusion can be stopped, and 80% of the 24-h infusion insulin dose can be placed in the TPN bag as regular insulin. Correctional dose may be given subcutaneously for unusual hyperglycaemia (as discussed in earlier sections). Long-acting insulin should never be added to TPN bag.

If continuous feeds are given through Ryle's tube or jejunostomy, insulin can be administered as a basal bolus regimen with multiple daily subcutaneous injections. Fifty percent of TDD (determined by IV infusion initially) is given as long-acting insulin and 50% as short-acting insulin. Regular insulin at an interval of 6 h is preferred over rapid-acting analogues for their longer duration of action. Patients receiving bolus enteral feeds

are typically treated with basal bolus regimen the same as patients who are eating regular meals, taking care to match the timing of short-acting insulin with the enteral feeds.

### Planning discharge from hospital

The discharge plan of a patient with diabetes should begin well before the discharge to ensure smooth transition of care between hospital and home. Different factors to incorporate into discharge plan include educational status, affordability, patient and family competence, psychological state, social and religious beliefs, co-morbidities and accessibility to health care [38, 39].

### Recommended care (Table 19)

The following aspects can be integrated [7, 30, 40–42]

1. Diabetes self-management must be reviewed.
2. The discharge summary must include information on the type of diabetes, individualised targets, hypo- and hyperglycaemic emergencies, sick day rules, lifestyle modifications with medical nutrition therapy and exercise.
3. A detailed medication summary must be given to all patients in clear writing which should include the medications, formulations, dosage, instructions for use and duration of therapy.
4. Those on insulin should be sufficiently adept with insulin injection rotation technique, site rotation, frequency of self-monitoring of blood glucose, insulin dosage adjustments to achieve glycaemic targets and hypoglycaemia management.
5. Patients must be encouraged to take their insulin themselves during hospital stay especially in those for whom insulin has been recently initiated.

**Table 19** On-discharge recommendations

Review <i>self-management</i> with the patient
Issue <i>discharge summary</i> with clear instructions
Discuss about <i>prescribed drugs</i> —description, dosages, possible adverse events
Instruct on <i>SMBG</i> and keeping of proper record of measured BG
Clear instructions regarding <i>insulin treatment</i> —dose, technique, frequency, various formulations
Instruct regarding <i>hypoglycaemia</i> and its treatment and measure to avoid it
Discuss regarding <i>BG targets</i> required for good control
Importance of regular <i>follow-up</i>

### 6. Medications at discharge

- A. In a patient *previously diagnosed to have diabetes*, the medications at discharge can be based on the HbA1c at admission or the pre-admission HbA1c [42].
  - HbA1c <8%—The patient's baseline medications may be continued. HbA1c >8%—Changes include the addition of an oral anti-diabetic medication, intensification of the doses of pre-existing medications (or insulin) and/or initiation of basal insulin for patients not on insulin.
  - In cases where HbA1c is not available and the patient has fair glycaemic control, the pre-admission anti-diabetic medication may be continued. In those with poor glycaemic control, the pre-admission medications may be up-titrated.
- B. In a patient with *previously undiagnosed diabetes*, a similar approach may be followed. [43, 44]
  - HbA1c 6.5–7%—Lifestyle modification and follow-up are recommended. Monotherapy with an oral glucose-lowering agent may be considered.
  - HbA1c >7%—Use of oral anti-diabetic and/or insulin where indicated
- C. Patient with *stress hyperglycaemia*
  - HbA1c <5.7%—Follow-up is recommended.
  - HbA1c 5.7–6.4%—Must be treated as per recommendations for pre-diabetes.

**Table 20** Protocol for discharge management

HbA1c	Action to take
<b>Previously diagnosed</b>	
<8%	Pre-discharge medications to be continued
>8%	Intensify treatments with OADs, insulin
No A1c available	
Good glycaemic control	Re-introduce pre-admission treatments
Poor glycaemic control	Intensify pre-admission treatment
<b>Previously undiagnosed</b>	
6.5–7%	Lifestyle modification, metformin, follow-up
>7%	Continue treatment with OADs/insulin as per guidelines
<b>Stress hyperglycaemia</b>	
<5.7%	Maintain follow-up
5.7–6.4%	Treatment as recommended for pre-diabetes

7. A follow-up appointment must be scheduled within 15 days of discharge with the

specialist and/or primary care physician (Table 20).

#### SUMMARY

- Different factors to incorporate into discharge plan include educational status, affordability, family support, co-morbidities and accessibility to health care.
- Integrated care is important; diabetes self-management must be reviewed, with a follow-up appointment scheduled within 15 days of discharge, with the medications summary at discharge.
- HbA1c levels of 8% should be cut-off to determine the future course of medications at discharge in most cases.
- Limited care settings determine a customized approach with emphasis on the education on insulin technique and blood glucose monitoring.

#### *Hypoglycaemia management*

**Definition:** The American Diabetes Association (ADA) defines hypoglycaemia as BG <70 mg/dl. This could present as symptomatic or asymptomatic hypoglycaemia.

*Severe hypoglycaemia* requires assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions.

#### **Treatment of hypoglycaemia**

Adults who are experiencing hypoglycaemia symptoms but have a blood glucose level >70 mg/dl should be treated with a small carbohydrate snack only, e.g. one medium banana, a slice of bread or normal meal, if due.

All adults with a BG <70 mg/dl with or without symptoms of hypoglycaemia should be treated as outlined below.

A. *Adults who are conscious, oriented and able to swallow*

1. Give 15–20 g quick-acting carbohydrate of the patient's choice where possible. Some examples are
  - Commercially available glucose tablets or liquids

- 150–200 ml pure fruit juice, e.g. orange (not applicable for patients with CKD)
- Three to four heaped teaspoons of sugar dissolved in water (for patients on alpha-glucosidase inhibitors, glucose is recommended since they cannot breakdown complex carbohydrates)

2. Repeat CBG measurement 10–15 min later. If it is still <70 mg/dl, repeat dose
3. If CBG remains <70 after 30–45 min or 3 cycles, then give 25% dextrose, as described below.

B. *Severe hypoglycaemia: unconscious/unable to eat/requires assistance of another person for treatment*

1. Check airway (and give oxygen), breathing, circulation and blood glucose.  
If the patient is on an insulin infusion, stop it immediately.
2. If IV access is available, give 25% dextrose IV [5].

Amount of 25% dextrose to be infused (ml) = (100 – current BG) × 0.8

Repeat capillary blood glucose measurement 15 min later and recalculate the dose of second bolus 25% dextrose if BG is <100 mg/dl.

- Following the bolus of 25% dextrose, infusion of 10% dextrose in water (D/W) may be needed.
  - *For ICU patients on insulin infusion:* After reaching the target blood glucose, resume insulin infusion at half the previous rate [5].
  - *Patients on subcutaneous insulin and NPO:* After reaching the target blood glucose, resume insulin regimen after appropriate insulin adjustment if needed.
3. Once blood glucose is >70 mg/dl and the patient has recovered, give a long-acting carbohydrate of the patient's choice where possible.
- Some examples are
- Two biscuits
  - One slice of bread/toast
  - 200–300 ml glass of milk
  - Normal meal if due
4. *Do not omit insulin injection if due.* However, revision of insulin dose may be required.
  5. Document event in patient's notes.
  6. Ensure regular capillary blood glucose monitoring is continued for 24 to 48 h.
  7. Give hypoglycaemia management education to the patient and family
  8. Find the cause

### SUMMARY

- The treatment of hypoglycemia is guided by the ADA definition of hypoglycemia with a cut off plasma glucose concentration of 70 mg/dl.
- If the patient is conscious, oriented and able to swallow, initial 15–20 gm quick acting carbohydrate would suffice, with the monitoring and the step-up approach depending on the response for the increase in the plasma glucose.
- If the patient is unconscious, IV access or an infusion pump is preferred to provide 100–200 ml of 10% glucose over 15 minutes (e.g. 400–500 ml/hr), with monitoring to repeat till the plasma glucose is 70mg/dl.

**Acknowledgements** RSSDI thanks the *Sanofi India Ltd. for extending their unrestricted educational grant to RSSDI and for all the logistic support.*

### References

1. Umpierrez GE, Isaacs SD, Bazargan N, et al. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab.* 2002;87(3):978–82.
2. Nam Han Cho. IDF diabetes atlas 2015, 7th edition. <http://www.idf.org/idf-diabetes-atlas-seventh-edition>. Last accessed 4 Oct 2016.
3. KM Prasanna Kumar. *Indian J Endocrinol Metab.* 2015;19(Suppl-1).
4. ADA. Diabetes care in the hospital, nursing home, and skilled nursing facility. Sec. 13. In: Standards of medical care in diabetes—2015. *Diabetes Care* 2015;38(Suppl. 1):S80–S85.
5. Umpierrez GE, Hellman R, Korytkowski MT. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2012;97:16–38.
6. Clement S, Braithwaite SS, Magee, et al. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care.* 2004;27:553–91.
7. Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association Consensus statement on inpatient glycemic control. *Endocr Pract.* 2009;15(4).
8. Finfer S et al. NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med.* 2009;360(13):1283–97.
9. Bajwa SS, Baruah MP, Kalra S, Kapoor MC, et al. Interdisciplinary position statement on management of hyperglycemia in perioperative and intensive care. *J Anaesthesiol Clin Pharmacol.* 2015;31(2):155–64.
10. Furnary AP, Wu YX, Bookin SO, et al. Effect of hyperglycemia and continuous intravenous insulin infusions on outcomes of cardiac surgical procedures: the Portland Diabetic Project. *Endocr Pract.* 2004;10 Suppl 2:21–33.
11. Goldberg PA, Siegel MD, Sherwin RS, et al. Implementation of a safe and effective insulin infusion protocol in a medical intensive care unit. *Diabetes Care.* 2004;27(2):461–7.



12. Markovitz LJ, Wiechmann RJ, Harris N, et al. Description and evaluation of a glycemic management protocol for patients with diabetes undergoing heart surgery. *Endocr Pract.* 2002;8(1):10–8.
13. Bansal B, Mithal A, Carvalho P, Mehta Y, Trehan N, et al. Feasibility, efficacy, and safety of a simple insulin infusion protocol in a large volume cardiac surgery unit in India. *Indian J Endocrinol Metab.* 2015;19(1):47–51.
14. Bansal B, Mithal A, Carvalho P, Mehta Y, Trehan N, et al. Medanta insulin protocols in patients undergoing cardiac surgery. *Indian J Endocrinol Metab.* 2014;18(4):455–67.
15. Pattan V, Parsaik A, Brown JK, et al. Glucose control in Mayo Clinic intensive care units. *J Diabetes Sci Technol.* 2011;5(6):1420–6.
16. Karippacheril JG, Mathai RT, Abraham SS. Insulin IP Calc: a smartphone application for insulin infusion protocol in intensive care units. *Indian J Anaesthesia.* 2015;59(12).
17. McDonnell ME, Umpierrez GE. Insulin therapy for the management of hyperglycemia in hospitalized patients. *Endocrinol Metab Clin North Am.* 2012;41(1):175–201.
18. Kreider KE, Lien LF, et al. Transitioning safely from intravenous to subcutaneous insulin. *Curr Diab Rep.* 2015;15:23.
19. Braithwaite SS. The transition from insulin infusions to long term diabetes therapy: the argument for insulin analogs. *Semin Thorac Cardiovasc Surg.* 2006;18:366–78.
20. Bode BW, Braithwaite SS, Steed RD, et al. Intravenous insulin infusion therapy: indications, methods, and transition to subcutaneous insulin therapy. *Endocr Pract.* 2004;10 Suppl 2:71–80.
21. Umpierrez GE, Smiley D, Hermayer K, et al. Randomized study comparing a basal-bolus with a basal plus correction insulin regimen for the hospital management of medical and surgical patients with type 2 diabetes: basal plus trial. *Diabetes Care.* 2013;36:2169–74.
22. Gangopadhyay KK, Bantwal G, Talwalkar PG, et al. Consensus evidence-based guidelines for in-patient management of hyperglycaemia in non-critical care setting as per Indian clinical practice. *JAPI Suppl.* 2014;62.
23. Australian Diabetes Society. Peri-operative diabetes management guidelines. July 2013.
24. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes.* 2013;37 suppl 1:S1–212.
25. Garber AJ et al. American College of Endocrinology position statement on inpatient diabetes and metabolic control. American College of Endocrinology Task Force on Inpatient Diabetes Metabolic Control. *Endocr Pract.* 2004;10 Suppl 2:4–9.
26. Alan J. Garber. American College of Endocrinology and American Diabetes Association Consensus Statement on Inpatient Diabetes and Glycemic Control. *Diabetes Care.* 2006; 29(8).
27. JBDS-IP (Joint British Diabetes Societies for in-patient care). Management of adults with diabetes undergoing surgery and elective procedures: Improving standards. Summary. Revised Sept 2015.
28. Marks JB. Perioperative management of diabetes. *Am Fam Physician.* 2003;67:93–100.
29. JBDS-IP (Joint British Diabetes Societies for in-patient care). Management of hyperglycaemia and steroid (glucocorticoid) therapy. October 2014.
30. Cecilia C. Low Wang, Boris Draznin, et al. Insulin use in hospitalized patients with diabetes: navigate with care. *Diabetes Spectrum.* 2013;26(2).
31. Lazar HL, Chipkin SR, Fitzgerald CA, Bao Y, Cabral H, Apstein CS. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. *Circulation.* 2004;109(12):1497–502.
32. Kalra P, Anakal M. Peripartum management of diabetes. *Indian J Endocrinol Metab.* 2013;17(Suppl1):S72–6.
33. Wilkinson A, Davidson J, et al. Guidelines for the treatment and management of new-onset diabetes after transplantation. *Clin Transpl.* 2005;19:291–8.
34. Marvin MR, Morton V. Glycemic control and organ transplantation. *J Diabetes Sci Technol.* 2009;3(6):1365–72.
35. KDOQI clinical practice guideline for diabetes and CKD: 2012 update. *Am J Kidney Dis.* 2012;60(5):850–886
36. Hahr AJ, Molitch ME. Management of diabetes mellitus in patients with chronic kidney disease. *Clin Diabetes Endocrinol.* 2015;1(2):2–9.
37. Gosmanov AR, Umpierrez GE. Management of hyperglycemia during enteral and parenteral nutrition therapy. *Curr Diab Rep.* 2013;13(1):155–62.
38. Houlden R et al. Canadian diabetes association clinical practice guidelines expert committee in-hospital management of diabetes. *Can J Diabetes.* 2013;37:S77–81.
39. Roman SH, Chassin MR. Windows of opportunity to improve diabetes care when patients with diabetes are hospitalized for other conditions. *Diabetes Care.* 2001;24:1371–6.
40. ADA Standards of Medical Care in Diabetes 2016; *Diabetes Care* 2016;39(S1):1–119.
41. Shepperd S, Lannin NA, Clemson LM, et al. Discharge planning from hospital to home. *The Cochrane Library.* 2013.
42. Umpierrez GE, Reyes D, Smiley D, et al. Hospital discharge algorithm based on admission HbA1c for the management of patients with type 2 diabetes. *Diabetes Care.* 2014;37:2934–9.
43. Greci LS, Kailasam M, Malkani S, et al. Utility of HbA(1c) levels for diabetes case finding in hospitalized patients with hyperglycemia. *Diabetes Care.* 2003;26(4):1064–8.
44. Workgroup on Hypoglycemia, American Diabetes Association. Defining and reporting hypoglycemia in diabetes: a report from the ADA Workgroup on Hypoglycemia. *Diabetes Care.* 2005;28(5):1245–9.
45. Joslin Diabetes Center and Joslin Clinic. Guideline for in-patient management of surgical and ICU patients with diabetes. (Pre-, Peri- and Postoperative Care) 12-30-2015.



For patient requiring rapid control  
of prandial glucose

Add

# Apidra<sup>®</sup>

*insulin glulisine*

An Apt Rapid Acting Insulin



ONLY<sup>1,2</sup>  
ZINC-FREE  
INSULIN<sup>0</sup>



Fast<sup>1,2</sup>



Flexible<sup>3,4</sup>



Physiological<sup>5,6</sup>

1. Arnolds S et al. Exp Clin Endocrinol Diabetes 2010;118:662-664. 2. Becker RH et al. Exp Clin Endocrinol Diabetes 2005; 113:435-443. 3. Apidra API Dated October 2015. 4. Lankisch MR, et al. Diabetes ObesMetab2008; 10:1178-1185. 5. Steven Edelman. Osteopathic Medicine and Primary Care 2007, 1:9. 6. Brange J et al. Diabetes Care 1990;13:923-954.

**APIDRA<sup>®</sup>**  
INSULIN GLULISINE INJECTION (Monocomponent Insulin Glulisine)

#### Abridged Prescribing Information

**COMPOSITION:** 1 ml contains 3.5 mg insulin glulisine, corresponding to 100 IU human insulin. Each pre-filled disposable pen (SoloStar®) contains 3 ml, equivalent to 300 IU insulin. Each vial contains 10 ml equivalent to 1000 IU. **THERAPEUTIC INDICATIONS:** Treatment of adults, adolescents and children of 6 years or older with diabetes mellitus, where treatment with insulin is required. **DOSAGE & ADMINISTRATION:** The dosage of Apidra should be individually adjusted. Apidra should normally be used in regimens that include a longer-acting insulin or basal insulin analogue. Blood glucose monitoring is recommended for all patients with diabetes. Apidra should be given by injection within 15 minutes before or immediately after a meal. Apidra is intended for subcutaneous administration by injection or by external infusion pump. Apidra can also be administered intravenously. There is insufficient clinical information on the use of Apidra in children younger than the age of 6 years. Hypoglycaemia may be difficult to recognize in the elderly. **SAFETY-RELATED INFORMATION CONTRAINDICATIONS:** Hypersensitivity to insulin glulisine or to any of the excipients. **WARNINGS & PRECAUTIONS:** Patients with diabetes will also require a longer-acting insulin or insulin infusion pump therapy to maintain adequate glucose control. Any change of insulin should be made cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, species or method of manufacture may result in the need for a change in dosage. Concomitant oral antidiabetic treatment may need to be adjusted. Insulin requirements may be altered during intercurrent conditions such as illness, emotional disturbances, or stress. The time of occurrence of hypoglycaemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen is changed. Apidra requirement may be reduced in renal and hepatic impairment. Apidra cartridges should be used with Allstar™ and not with any other reusable pen as dosing accuracy has only been established with Allstar™. Patients using continuous subcutaneous insulin infusion pump therapy must be trained to administer insulin by injection and have alternate insulin delivery system available. For intravenous use, Apidra should be used at a concentration of 1 unit/ml insulin glulisine in infusion systems with the infusion fluid sterile 0.9% sodium chloride solution. Apidra was found to be incompatible with Dextrose solution and Ringers solution and, therefore, can not be used with these solution fluids. **PREGNANCY AND LACTATION:** No adequate data are available. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters and decline after delivery. It is unknown whether Apidra® is excreted in human milk. Lactating women may require dose and diet adjustment. **ADVERSE REACTIONS:** Hypoglycaemia is the most frequent undesirable effect of insulin therapy. Injection site reactions and local hypersensitivity reactions may occur. Severe cases of generalised allergy, including anaphylactic reaction, may be life-threatening. Lipodystrophy may occur at the injection site. Medication errors have been reported in which other insulins, particularly long-acting insulins, have been accidentally administered instead of insulin glulisine. **Date:** October 2015 **Source:** CCDS Version 9 dated 23rd April 2013.

For full prescribing information please write to Sanofi India Ltd., Sanofi House, CT Survey No 117-B, L&T Business Park, Saki Vihar Road, Powai, Mumbai 400072.



Sanofi India Ltd., Sanofi House, CT Survey No 117-B, L&T Business Park, Saki Vihar Road, Powai, Mumbai 400072.

Transforming  
insulin management  
since  
**15** years<sup>1</sup>

## The most widely used basal insulin<sup>2</sup>



**>15 YEARS**  
since launch<sup>3</sup>

**~11 MILLION\***  
patients treated in 2015<sup>3</sup>

**~89 MILLION\***  
patient-years since launch<sup>3</sup>

**>200,000**  
participants in clinical and  
observational studies<sup>3</sup>

\*based on IMS data and assuming average daily dose of 25 U Lantus<sup>1</sup>

1. Data on file. 2. IMS-MAT, 2015. 3. Lantus DSUR No. 5, 2016.

### LANTUS®

#### INSULIN GLARGINE INJECTION I.P.

##### Abridged Prescribing Information

**COMPOSITION:** Lantus 100 IU/ml solution for injection of insulin glargine I.P. is available in vials, cartridges and cartridge systems. **INDICATION:** For the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above. **DOSAGE AND ADMINISTRATION:** Lantus should be administered subcutaneously once daily at any time but at the same time each day. The dosage and timing of dose of Lantus should be individually adjusted. In patients with type 2 diabetes mellitus, Lantus can also be given together with orally active antidiabetic products. When changing from a treatment regimen with an intermediate or long-acting insulin to a regimen with Lantus, the amount and timing of short acting insulin or fast acting insulin analogue or of the dose of any oral antidiabetic drug may need to be adjusted. Close metabolic monitoring is recommended. Lantus is administered subcutaneously, should not be administered intravenously and must not be mixed with any other insulin or diluted. Lantus is not the insulin of choice for the treatment of diabetic ketoacidosis. **SAFETY-RELATED INFORMATION:** Contraindications: Hypersensitivity to insulin glargine or to any of the excipients. **Precautions:** Insulin treatment requires constant alertness to the possibility of hyper- and hypoglycaemia. Patients and their relatives must know what steps to take if hyperglycaemia or hypoglycaemia occurs or is suspected, and they must know when to inform a physician. Hypoglycaemia may occur. The time of occurrence of hypoglycaemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen is changed. As with all insulins, particular caution should be exercised, and intensified blood glucose monitoring is advisable, in patients in whom sequelae of hypoglycaemic episodes might be of particular clinical relevance. In patients with renal impairment or severe hepatic impairment, insulin requirements may be diminished due to reduced insulin metabolism. In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements. Hypoglycaemia can generally be corrected by immediate carbohydrate intake. So that initial corrective action can be taken immediately, patients must carry a minimum of 20 grams of carbohydrates with them at all times. Intercurrent illness requires intensified metabolic monitoring. In many cases urine tests for ketones are indicated, and often it is necessary to adjust the insulin dose. Lantus cartridges should be used with Allstar and not with any other reusable pen as dosing accuracy has only been established with the above listed pens. **Pregnancy & Lactation:** There are no randomized controlled clinical studies on the use of insulin glargine in pregnant women. A large number (more than 1000 retrospective and prospective pregnancy outcomes) of exposed pregnancies from Post Marketing Surveillance indicate no specific adverse effects of insulin glargine on pregnancy or on the health of the foetus and newborn child. Lantus can be used during pregnancy, if clinically needed. Insulin requirements may decrease during the first trimester and generally increase during the second and third trimesters. Immediately after delivery, insulin requirements decline rapidly. Careful monitoring of glucose control is essential in such patients. Patients with diabetes must inform their doctor if they are pregnant or are contemplating pregnancy. **Adverse Reactions:** Most frequent: Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement, temporary visual impairment may occur. Lipodystrophy may occur at the injection site. Injection site reactions including redness, pain, itching, hives, swelling or inflammation. For full prescribing information please write to Sanofi India Ltd., Sanofi House, CT Survey No 117-B, L&T Business Park, Saki Vihar Road, Powai, Mumbai 400072. **Dated:** April 2016. **Source:** CCDS Version 17 dated 23rd May 2014.

For the use only of a Registered Medical Practitioner or Hospital or a Laboratory