Management of Glycaemic Control in Oncology Patients

Scope of Guidance

Only applicable to adult Oncology patients, with or without known diabetes mellitus (DM). Includes patients receiving glucocorticoids, systemic anti-cancer treatment (SACT) and immunotherapy.

Introduction

It is estimated that 20% of people with cancer have concurrent diabetes mellitus. People with cancer are at increased risk of developing new onset DM or hyperglycaemia, as well as worsening control of pre-existing DM.

Hyperglycaemia may be associated with worse overall survival and increased risk of cancer recurrence in a number of cancer subtypes. Hyperglycaemia may reduce the efficacy of chemotherapy, and diabetic individuals with cancer are at higher risk of developing infections and being hospitalised.

Measuring the HbA1c routinely in one study found 11% of cancer patients met the criteria for a new diagnosis of diabetes.

Glucocorticoid usage

Glucocorticoid therapy is frequently used in Oncology to manage a number of conditions, such as metastatic spinal cord compression, immunotherapy toxicity, brain metastases, supportive treatment during chemotherapy, and in lymphoma and multiple myeloma.

The incidence of steroid-induced hyperglycaemia is 30%, but could be as high as 50%. Significant harm can result if it is missed, such as development of Hyperosmolar Hyperglycaemic State (HHS), hospitalisation and death.

Diagnostic Criteria for Diabetes

	Fasting plasma glucose (mmol/L)	2 hour plasma glucose (mmol/L)	Random plasma glucose (mmol/L)	HbA1c / Glycated haemoglobin (mmol/mol) (%)
Normal	≤6.0	<7.8	<7.8	<42 (<6.0%)
Impaired fasting glucose	6.1-6.9	And <7.8	_	_
Impaired glucose tolerance	<7.0	And 7.8-11.0	_	Pre-diabetes: 42-47 (6.0-6.4%)
Diabetes mellitus	≥7.0	Or ≥11.1	≥11.1	≥48 (6.5%)

Author: Dr Katie Bond, Dr Alison Evans
Approved by: SACT subgroup November 2024

Diabetic Emergencies

HHS (Hyperosmolar Hyperglycaemic State)

This has a significant morbidity and higher mortality than DKA and must be diagnosed promptly and managed intensively.

- Hypovolaemia
- Marked hyperglycaemia (30 mmol/L or more) without significant hyperketonaemia (<3 mmol/L) or acidosis (pH>7.3, bicarbonate >15 mmol/L)
- Osmolality usually 320 mosmol/kg or more (calculated 2[Na+] + Glucose + Urea)

DKA (Diabetic Ketoacidosis)

Indicative of type 1 diabetes, but increasingly being recognised in ketone-prone type 2 diabetes also. Note that euglycaemic DKA can also occur, with relatively low glucose concentrations.

- Ketonaemia ≥3.0 mmol/L or significant ketonuria (more than 2+ on standard urine sticks)
- Blood glucose >11.0 mmol/L or known diabetes mellitus
- Bicarbonate (HCO3-) ≤15 mmol/L and/or venous pH<7.3

Hypoglycaemia

Sweating, fatigue, dizziness, perioral paresthesia, tremor/shaking, palpitations, mood change, pallor, confusion

CBG Monitor Provision and Training

- CBG monitor and patient training will be provided in weekly sessions on Wednesday 3pm-4pm. If these slots are full or urgent training is required there may be adhoc daily slots available too. Please email Chemobookers to book patient into one of these slots.
- Letter to be sent to the GP requesting: Agamatrix WaveSense glucose test strips x 100; Agamatrix Ultra-Fine lancets 33g x 100; Sharp Safe Container

Contact for Diabetes Team for Advice and Referrals

ghn-tr.secretariesdiabeteschelt@nhs.net – Diabetes Team in Cheltenham

ghn-tr.secretariesdiabetesglos@nhs.net – Diabetes Team in Gloucester

Label email as 'Urgent Oncology'

1. Commencing Glucocorticoid (Steroid) Therapy

- Steroids typically cause an increase in blood glucose levels 4-8 hours after ingestion leading to a peak blood glucose level between midday meal and evening meal if administered in the morning.
- Applicable to a dose of **prednisolone >5 mg per day or equivalent (0.8mg dexamethasone; 4mg methylprednisolone)**.
- NOTE this includes repeated cycles of 2-4 days of high dose steroids as anti-emetics during chemotherapy regimes
- Hyperglycaemia may or may not resolve once steroids are withdrawn and treatment of hyperglycaemia also needs titrating down similarly. A weekly 5mg reduction of prednisolone from 20mg may require a 20-25% reduction in insulin dose, or a 40mg reduction in gliclazide.

Before starting steroids check baseline HbA1c and random plasma glucose for ALL patients

CBG monitor should be provided to:

Baseline plasma glucose ≥12 mmol/L OR High-risk group

Pre-existing type 1 or 2 DM
Impaired fasting glucose or impaired glucose tolerance HbA1c 42-47mmol/mol (pre-diabetes)
Previous development of hyperglycaemia on glucocorticoid therapy

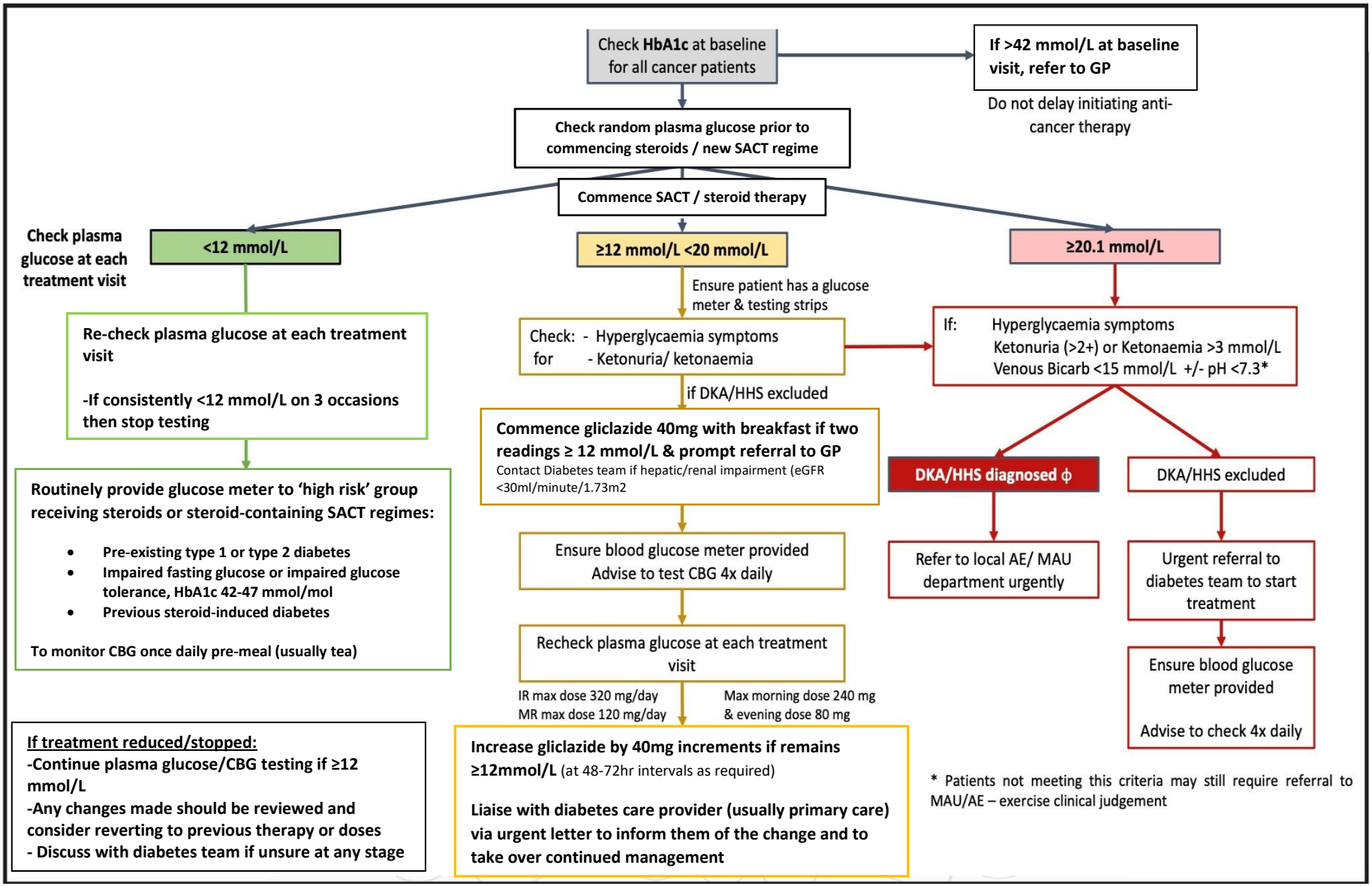
- HbA1c >42 mmol/mol - refer to primary care for ongoing management
- Monitor CBG once daily – prior to evening meal if steroid dose in the morning
- Target glucose 6-10 mmol/L, allowing range of 6-12 mmol/L
- If CBG readings > 12 mmol/L increase monitoring to QDS and use treatment flow chart
- Continue monitoring even after steroids stopped if readings remain over 12 mmol/L

If blood plasma glucose is ≥12 mmol/L on TWO occasions → Commence gliclazide 40mg in the morning

NB Avoid gliclazide in severe hepatic impairment and renal impairment (<30ml/minute/1.73m^2), and contact Diabetes team as insulin will usually be required

- Educate patient on symptoms and management of possible hypoglycaemia – leaflet available – and provide blood glucose monitor
- Advise patient to contact primary care team as soon as possible for ongoing care and send cover letter to GP. Advise patient that they will require an HbA1c test 12 weeks after completing Oncology treatment (if appropriate).

Starting any SACT or glucocorticoid therapy in cancer patients WITHOUT a prior diagnosis of diabetes



2. Commencing Systemic Anti-Cancer Therapy (without Immune Checkpoint Inhibition)

Before starting any new SACT regime or steroid-containing regimes (>5mg prednisolone equivalent) check baseline HbA1c and random plasma glucose for ALL patients

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Check random venous plasma glucose during outpatient visits or with each cycle of treatment

Can consider stop testing if result <12 mmol/L on 3 occasions

- HbA1c >42 mmol/mol - refer to GP but do not delay SACT
- Target glucose 6-10 mmol/L, allowing range of 6-12 mmol/L

If blood plasma glucose is ≥12 mmol/L on TWO occasions → Commence gliclazide 40mg in the morning

NB Avoid gliclazide in severe hepatic impairment and renal impairment (<30ml/minute/1.73m^2), and contact Diabetes team

↓

If remains >12 mmol/L --- Increase gliclazide in 40mg dose increments (max dose 240mg in the morning). Evening dose of gliclazide may be started (up to max daily dose of 320mg).

- Educate patient on symptoms and management of possible hypoglycaemia and provide blood glucose monitor
- Advise patient to contact primary care team as soon as possible for ongoing care and send cover letter to GP. Advise patient that they will require an HbA1c test 12 weeks after completing Oncology treatment (if appropriate).

3. Commencing Checkpoint Inhibitors

- Immune checkpoint inhibitors (ICP), such as cytotoxic T-lymphocyte associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1) inhibitors, may induce de novo diabetes, although this is at a low frequency of <1%.
- May present as new-onset insulin-dependent diabetes or sudden worsening pre-existing type 2 diabetes, but mechanism is considered similar to type 1 diabetes
- 75% of patients developing ICP-induced DM present with DKA
- Explain clearly the signs/symptoms of hyperglycaemia, advising urgent medical help if they occur.

Check random plasma glucose with each treatment cycle

AND

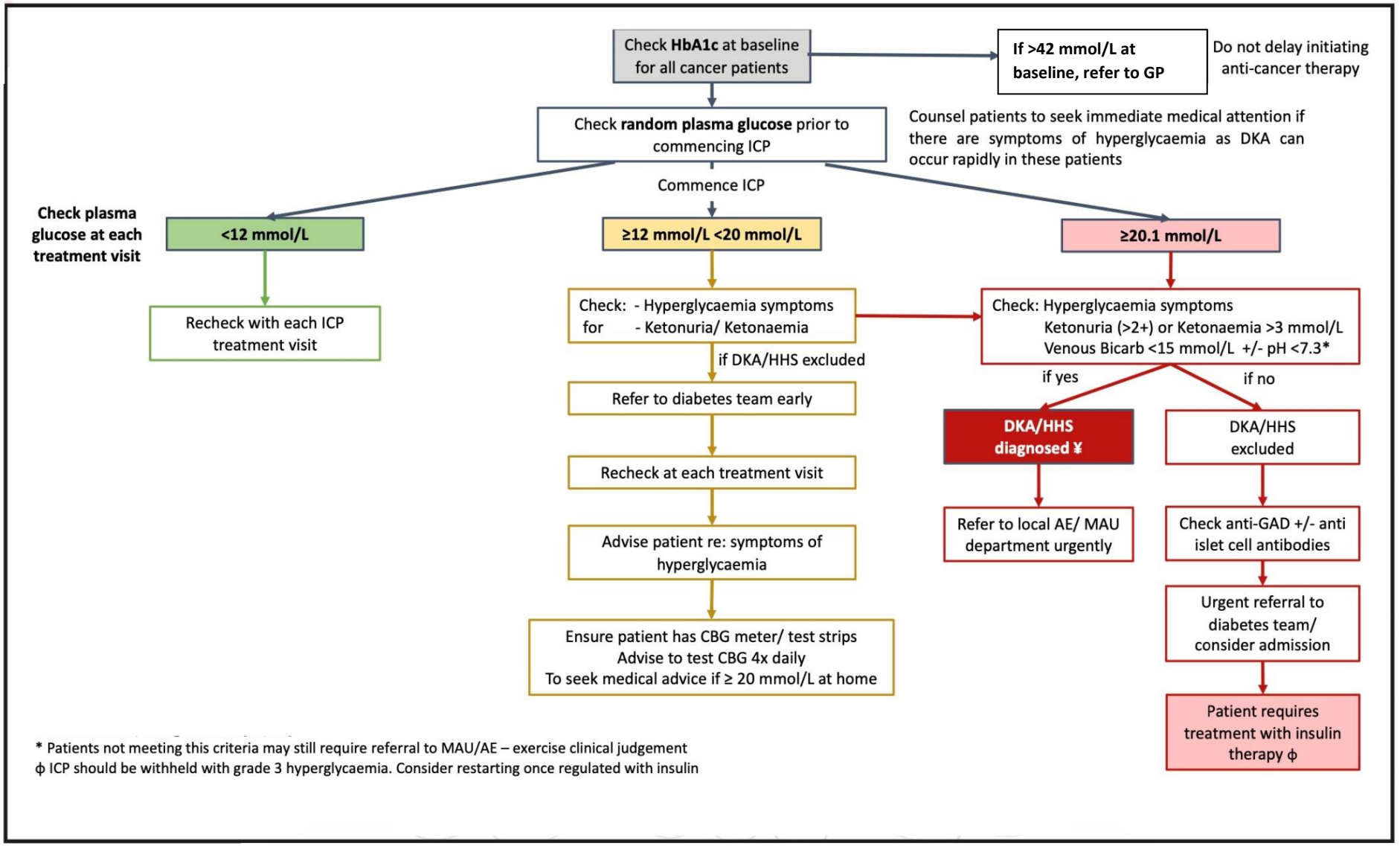
If hyperglycaemic symptoms develop

Continue with checking throughout the duration of ICP treatment – DO NOT STOP

Management

- High dose steroid therapy has not been shown to reverse ICP-induced pancreatic toxicity and diabetes, and could also worsen hyperglycaemia
- Refer to local ICP guidelines or ESMO guidelines
- Urgent management of hyperglycaemia is necessary. If plasma glucose is ≥ 20mmol/L or there are suggestive symptoms, rule out DKA/HHS.
- Check pancreatic antibodies (eg. GAD65, Zn transporter 8 or anti-islet cell)
- Prompt referral to specialist diabetes team and commencement of insulin therapy is almost always required.
- Withhold ICP if evidence of ICP-induced diabetic emergency
- Consider restarting ICP once management for hyperglycaemia has been instigated

Starting immune checkpoint inhibitors (ICP) in cancer patients WITHOUT a prior diagnosis of diabetes



4. Commencing SACT or steroids in patients with KNOWN diabetes

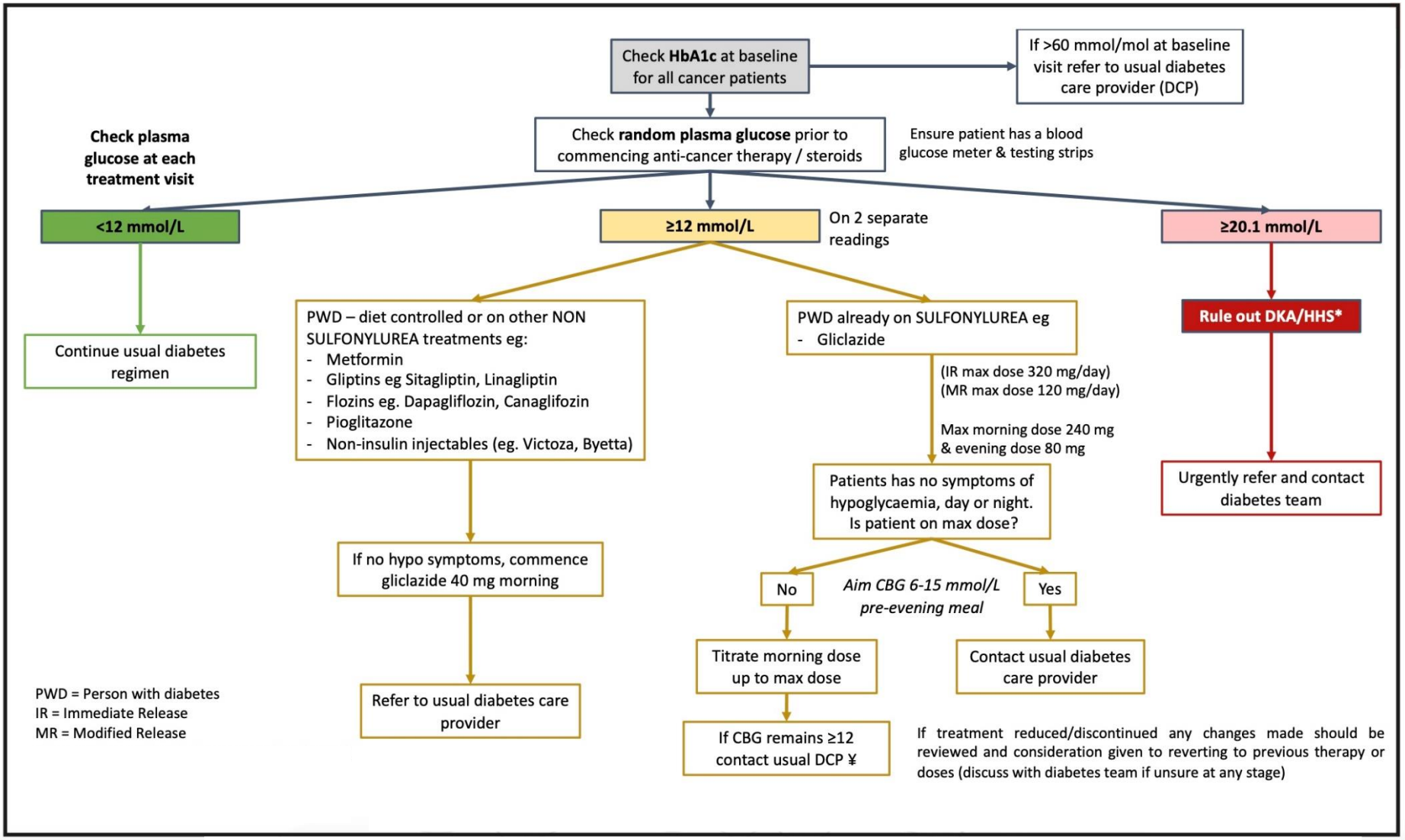
- **Ensure patient has a blood glucose monitor** and they should undertake more frequent CBG testing
- Document type of diabetes, any pre-existing diabetes complications, whether patient has hypoglycaemic awareness
- **Test baseline random plasma glucose and check HbA1c** (if not tested within 3 months)
- **Ensure patient contacts their usual diabetes care provider for ongoing diabetes management**, and send letter to make them aware that patient is commencing SACT / steroids so requires closer follow-up
- The flow charts below provide a guide to ongoing management, if clinician feels confident to make changes before patient sees their usual diabetes care provider.
- Make patient aware of likely exacerbation of hyperglycaemia whilst on anti-emetic therapy
- Type 3c Diabetes (Pancreatogenic DM) – consider early referral of these patients to the Diabetes team, as can behave similar to Type 1 Diabetes.

Nausea/Vomiting Management

Standard anti-emetic schedules should be amended to avoid agents causing hyperglycaemia.

- In highly and moderately emetogenic chemotherapy regimes, NK1 antagonists with a long-acting 5HT3 inhibitor (e.g. ondansetron) should be offered.
- In highly emetogenic regimes, consider the use of glucocorticoids in the first cycle.
- The dose should be reduced or steroids withdrawn with subsequent cycles based on emetic control and on blood glucose monitoring.

Starting SACT / glucocorticoid therapy in cancer patients with known type 2 diabetes on oral glucose lowering therapies



Starting SACT / glucocorticoid therapy in cancer patients with diabetes treated with insulin

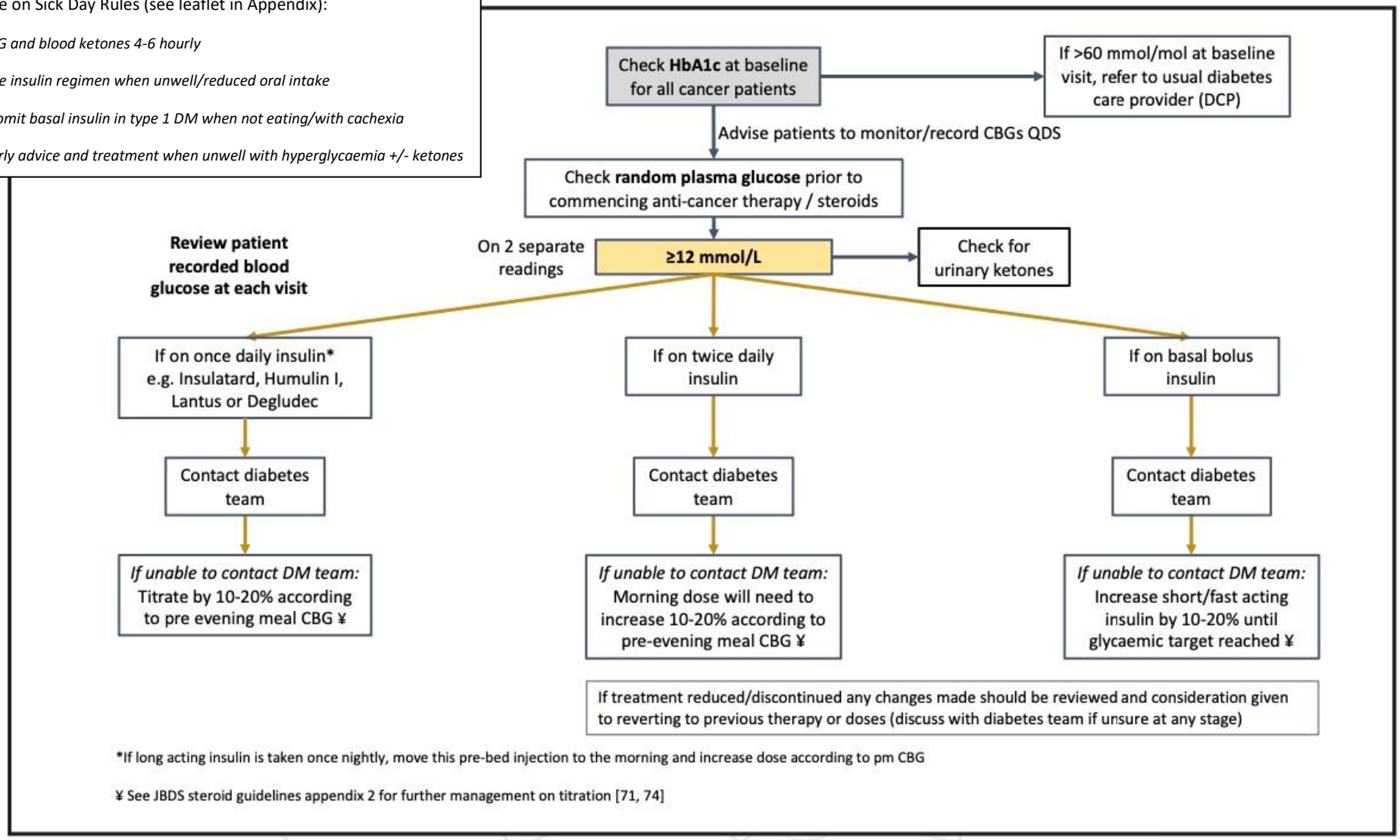
Educate on Sick Day Rules (see leaflet in Appendix):

Test CBG and blood ketones 4-6 hourly

Continue insulin regimen when unwell/reduced oral intake

Do not omit basal insulin in type 1 DM when not eating/with cachexia

Seek early advice and treatment when unwell with hyperglycaemia +/- ketones



*If long acting insulin is taken once nightly, move this pre-bed injection to the morning and increase dose according to pm CBG

¥ See JBDS steroid guidelines appendix 2 for further management on titration [71, 74]

References

Adapted from 'The Management of Glycaemic Control in People with Cancer Guidance for the oncology and diabetes multidisciplinary team' - January 2023

UK Chemotherapy Board and Joint British Diabetes Societies for Inpatient Care.
JBDS_17_Oncology_Guideline_with_QR_code_January_2023.pdf (abcd.care)

TREND UK Know Diabetes website TREND UK | Know Diabetes

Further Resources

- 'The Management of Glycaemic Control in People with Cancer Guidance for the oncology and diabetes multidisciplinary team' - January 2023. UK Chemotherapy Board and Joint British Diabetes Societies for Inpatient Care

JBDS_17_Oncology_Guideline_with_QR_code_January_2023.pdf (abcd.care)

- Management of Hyperglycaemia and Steroid (Glucocorticoid) Therapy

JBDS 08 Steroids and DM Guideline with qr code.pdf (amazonaws.com)

- The Management of Hyperosmolar Hyperglycaemic State (HHS) in Adults

JBDS 06 The Management of Hyperosmolar Hyperglycaemic State (HHS) in Adults FINAL.pdf (amazonaws.com)

- The Management of Diabetic Ketoacidosis in Adults

JBDS 02 DKA Guideline with qr code.pdf (amazonaws.com)

- The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus

JBDS 01 Hypo Guideline with qr code.pdf (amazonaws.com)

Useful Printable Documents and Patient Information Sheets

Type 2 Diabetes and Steroid Tablets Patient Leaflet - a5_steroids_grx_trend.pdf (knowdiabetes.org.uk)

Hypoglycaemia Patient Leaflet - a5_6pp_hypo_trend_connect.pdf (knowdiabetes.org.uk)

Type 1 DM Sick Day Leaflet - a5_t1illness_trend_final.pdf (knowdiabetes.org.uk)

Type 2 DM Sick Day Leaflet - a5_t2illness_trend_final.pdf (knowdiabetes.org.uk)

'Developing high blood glucose (blood sugar) on anti-cancer therapy in a person not known to have diabetes' - JBDS_17_Oncology_Guideline_with_QR_code_January_2023.pdf (abcd.care)

'Starting anti-cancer treatment/steroids in a person with diabetes' -
JBDS_17_Oncology_Guideline_with_QR_code_January_2023.pdf (abcd.care)

ACTION CARD

TITLE: MANAGEMENT OF GLYCAEMIC CONTROL IN ONCOLOGY PATIENTS RECEIVING SACT AND STEROIDS

FOR USE BY: Oncology clinical staff, CGH Outpatient nursing team	**LIAISES WITH:** Diabetes team

Rationale: Patients receiving SACT are at increased risk of developing new onset DM or hyperglycaemia, as well as worsening control of pre-existing DM. Patients receiving steroid-containing treatment are also at risk of steroid-induced diabetes mellitus.

Baseline HbA1c testing and random plasma glucose should be considered for all patients receiving SACT and for those receiving steroids at a dose of prednisolone >5mg/day or equivalent. Ongoing random plasma glucose monitoring at clinic visits should take place as per guidelines.

Capillary blood glucose (CBG) monitoring should be considered for all patients with pre-diabetes, diabetes and previous steroid-induced diabetes, who are receiving steroids/steroid-containing SACT regime. Diabetes treatment should be commenced when appropriate. See full guideline for more detailed information.

Liaise with the patients' diabetes care provider (usually primary care; diabetes team if on insulin) via urgent letter to inform of any change in management and to take over continued care.

CLINIC APPPOINTMENT		
Check baseline HbA1c (review previous result if within 3 months)	**<42**	Normal
	42-47	Pre-diabetes, refer to GP, commence CBG monitoring[1]
	≥48	Diabetes, refer to GP, commence CBG monitoring[1]
Check plasma glucose	**<12**	Re-check at each treatment visit If consistently <12 on 3 occasions, stop monitoring Re-check if SACT regime alters or commencing steroids
	12-20	Commence CBG monitoring and follow treatment guidelines[1] Check for hyperglycaemia symptoms (see guideline if symptomatic) Check urinary ketones (see guideline if >2+) Refer to GP
	≥20.1	Rule out DKA/HHS (See guideline) Urgent referral to diabetes team for treatment

Action card continued overleaf

ACTION CARD	
TITLE: MANAGEMENT OF GLYCAEMIC CONTROL IN ONCOLOGY PATIENTS RECEIVING SACT AND STEROIDS	
FOR USE BY: Oncology clinical staff, CGH Outpatient nursing team	**LIAISES WITH:** Diabetes team

CBG MONITORING[1]	
Indication	Pre-existing diabetes or previous steroid-induced diabetes HbA1c 42-47 Random plasma glucose ≥12
Process	Ensure patient has glucose meter & testing strips Book into education session via Chemobookers (Wed 3-4pm) and send template letter to GP HbA1c test with GP 12 weeks after Oncology treatment completed (if appropriate)
Monitoring	Check once daily prior to evening meal If ≥12, increase monitoring to qds
Gliclazide	If ≥12 on TWO occasions, consider commencing gliclazide 40mg om (excludes those on pre-existing diabetic medications and immune checkpoint inhibitors - refer to specific guidelines) Discuss with diabetes team if severe liver impairment or eGFR<30 If persistently ≥12, increase gliclazide by 40mg increments (not more frequently than 48hrly) Max. dose 320mg/day (max. 240mg am and 80mg pm)

Referrals

Gloucester Diabetes team - ghn-tr.secretariesdiabetesglos@nhs.net

Cheltenham Diabetes team - ghn-tr.secretariesdiabeteschelt@nhs.net

Mark as 'Urgent Oncology Patient'