Access to Essential Diabetic Medicines

CARPHA Guidelines for Management of Diabetes in Primary Care in the Caribbean

4
The Caribbean Public Health Agency is the Caribbean region’s collective response to strengthening health systems and addressing public health challenges which threaten development.

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Module 1
Evidence-Based Treatment Protocols for Diabetes

Module 2
Healthy Lifestyle Counselling

Module 3
Guidance For Persons With Diabetes (PwD) & Caregivers

Module 4
Access To Essential Medication

Module 5
Systems for Monitoring

CARPHA Guidelines For Management of Diabetes In Primary Care In The Caribbean
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<th>Full Form</th>
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<tr>
<td>ACE</td>
<td>Angiotensin Converting Enzyme</td>
</tr>
<tr>
<td>ACEI</td>
<td>ACE inhibitors</td>
</tr>
<tr>
<td>ADA</td>
<td>American Diabetes Association</td>
</tr>
<tr>
<td>AER</td>
<td>Albumin Excretion Rate</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin Receptor Blockers</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>CARPHA</td>
<td>Caribbean Public Health Agency</td>
</tr>
<tr>
<td>CCFP</td>
<td>Caribbean College of Family Practitioners</td>
</tr>
<tr>
<td>CRS</td>
<td>Caribbean Regulatory System</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td>DCCT</td>
<td>Diabetes Control and Complications</td>
</tr>
<tr>
<td>DKA</td>
<td>Diabetic Ketoacidosis</td>
</tr>
<tr>
<td>DKD</td>
<td>Diabetic Kidney Disease</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>DPN</td>
<td>Distal Symmetric Polyneuropathy</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>DPP-4</td>
<td>Dipeptidyl Peptidase 4 Inhibitor</td>
</tr>
<tr>
<td>EMB</td>
<td>Evidence Based Medicine</td>
</tr>
<tr>
<td>EML</td>
<td>Essential Medical List</td>
</tr>
<tr>
<td>ESRD</td>
<td>End Stage Renal Disease</td>
</tr>
<tr>
<td>FBS</td>
<td>Fasting Blood Sugar</td>
</tr>
<tr>
<td>GDM</td>
<td>Gestational Diabetes</td>
</tr>
<tr>
<td>GLP-1</td>
<td>Glucagon like Peptide 1 Receptor Agonist</td>
</tr>
<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
</tr>
<tr>
<td>HBA1c</td>
<td>Glycosylated Haemoglobin</td>
</tr>
<tr>
<td>HHS</td>
<td>Hyperglycaemic Hyperosmolar Syndrome</td>
</tr>
<tr>
<td>IDF</td>
<td>International Diabetes Federation</td>
</tr>
<tr>
<td>IGT</td>
<td>Impaired Glucose Tolerance</td>
</tr>
<tr>
<td>IFG</td>
<td>Impaired Fasting Glucose</td>
</tr>
<tr>
<td>Meds</td>
<td>Medications/Medicines</td>
</tr>
<tr>
<td>NCD</td>
<td>Non-Communicable Disease</td>
</tr>
<tr>
<td>NGSP</td>
<td>National Glycohaemoglobin Standardization Programmeme</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>-----------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>OECS</td>
<td>Organization of Eastern Caribbean States</td>
</tr>
<tr>
<td>OGTT</td>
<td>Oral Glucose Tolerance Test</td>
</tr>
<tr>
<td>PCP</td>
<td>Primary Care Physician</td>
</tr>
<tr>
<td>PWD</td>
<td>Persons with Diabetes</td>
</tr>
<tr>
<td>OECS PPS</td>
<td>OECS Pharmaceutical Procurement Service</td>
</tr>
<tr>
<td>RPG</td>
<td>Random Plasma Glucose</td>
</tr>
<tr>
<td>T2DM</td>
<td>Type 2 Diabetes Mellitus</td>
</tr>
<tr>
<td>TZDs</td>
<td>Thiazolidinediones</td>
</tr>
<tr>
<td>UHC</td>
<td>Universal Health Coverage</td>
</tr>
<tr>
<td>WDF</td>
<td>World Diabetes Foundation</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WINDREF</td>
<td>Windward Islands Research and Education Foundation</td>
</tr>
</tbody>
</table>
Preface

The CARPHA Guidelines on the Management of Diabetes in Primary Care in the Caribbean provide a strategic approach to improving diabetes health outcomes, by providing simple directives on key aspects of care for persons with diabetes (PWD).

In 2018, the OECS Health Unit, as part of the Strategic Pillar ‘Healthy Environments and Health Empowerment,’ and consistent with the emphasis placed on Non-communicable Diseases (NCDs) in the region, collaborated with CARPHA and WINDREF and secured funding from the World Diabetes Foundation for the implementation of the “OECS Diabetes, Prevention and Care Project.” A key component of the project, required to support its implementation, was the updating of clinical practice guidelines for the management of diabetes. The collaborators viewed this project as opportune, as it allowed for the review and update of the CARPHA Management of Diabetes in Primary Care in the Caribbean.

Previous versions of these guidelines were produced in 1995, 1998 and 2006. However, with rapid advancements in research, resulting in new international guidelines and treatment protocols, there was a need for an updated document to be produced. Consistent with its remit to provide an accurate, timely and relevant evidence-base for public health decision-making, the Caribbean Public Health Agency teamed up with the Organisation of Eastern Caribbean States to expedite the production of the revised guidelines, aligning them with current WHO strategies on Non-communicable Disease (NCD) treatment and management, including the WHO HEARTS and WHO’s Package of Essential Package of Non-communicable Disease Interventions (WHO PEN).
High-quality, evidence-informed clinical practice guidelines bridge the gap between policy, best practice, local contexts and client choice. They have been upheld as an essential part of quality medical practice and have been defined as ‘a convenient way of packaging evidence and presenting recommendations to health care decision makers,’ improving effectiveness and quality of care, by standardising clinical practices, and reducing costly and preventable mistakes and adverse events.

This newest version of the CARPHA guidelines has been extensively modified from its previous format and uses a modular approach which includes five modules.

- Module 1: EVIDENCE-BASED TREATMENT PROTOCOLS
- Module 2: GUIDING LIFESTYLE CHANGES
- Module 3: GUIDANCE FOR PERSONS WITH DIABETES (PWD) AND CAREGIVERS
- Module 4: ACCESS TO ESSENTIAL MEDICINES
- Module 5: SYSTEMS FOR MONITORING

These modules are intended for use by clinicians, caregivers, policymakers and programme managers. Each one focuses on complementary aspects of care of diabetes in the health system, and targets different cadres of workers and care providers for management of diabetes. Target users may vary, based on context, existing health systems and national priorities in CARPHA Member States, and recommendations made in each of the modules may require adaptation for implementation at country level. Ultimately, the revised guidelines seek to support the efforts of Ministries of Health, to strengthen and standardise the management of diabetes in primary care and improve outcomes in care of diabetes, regionally.
Acknowledgements

The Caribbean Public Health Agency and the Organisation of Eastern Caribbean States acknowledge, with appreciation, the World Diabetes Foundation (WDF) and the several regional individuals and agencies whose contributions were indispensable to the successful completion of these revised guidelines:

Dr. Avery Hinds and Dr. Lisa Monrose, the Consultants who were instrumental in the development of this revised document.

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• WINDREF - Professor Calum MacPherson and Dr. Satesh Bidaisee
• Ministry of Health Saint Lucia - Dr. Christy Nathaniel and Ms Ira Isaac
• Dr. Rohan Maharaj - University of the West Indies
• Ms. Anica Sanoir – Caribbean Certified Diabetes Educator
• Health Professionals, who participated in the peer review consultations
• Mr. Sherlan Gittens, responsible for the graphics and layout of the guidelines
CARPHA Diabetes Guidelines: The Modular Approach Expanded

The revised CARPHA Guidelines take a modular approach to providing guidance on the Management of Diabetes in Primary Care in the Caribbean.

**Module 1: EVIDENCE-BASED TREATMENT PROTOCOLS**
Targets primary care physicians, nurse-practitioners and any other health care provider who is directly involved in the medical management of diabetes. This module aims to give updated algorithms on care, incorporating the most recent recommendations in the care of diabetes.

**Module 2: GUIDING LIFESTYLE CHANGES**
Intended for all persons on the health team, who provide care and lifestyle-counselling to persons living with diabetes (PWD). It is specifically geared toward physicians, dietitians, nutritionists, nurses, community aides and home-help. This module covers all aspects of lifestyle that directly impact target outcomes. Therefore, diet, physical activity, weight management and mental health are addressed in this module.

**Module 3: GUIDANCE FOR PERSONS WITH DIABETES (PWD) AND CAREGIVERS**
Aims to inform to persons living with diabetes (PWD) and all persons involved in their care, with or without a medical or health care background. This module should be particularly useful to community nurses, home-help, community aides, and other community caregivers,
especially those involved in caring for PWD in their homes and can serve as a directory of topics relevant to caregivers. It addresses topics such as foot care, self-monitoring of blood glucose, identification and management of low blood glucose (hypoglycaemia) and high blood glucose (hyperglycaemia).

**Module 4: ACCESS TO ESSENTIAL MEDICATION**
Targets physicians, nurses, pharmacists and personnel involved in ensuring the efficiency of health system procurement mechanisms. It provides information on the various classes of medicine available for care of diabetes, issues related to their availability, as well as the risks, benefits and cautions that should be considered in their use.

**Module 5: SYSTEMS FOR MONITORING**
Targets all health care providers but is of particular relevance to Primary Care Managers and those involved in health systems evaluations. It focuses on monitoring and reporting information on the prevention and management of T2DM, and the implementation of the guidelines using standardised indicators and data collection tools.

Table I, below, summarises the scope and highlights the target users of each module.
Table A: Modules of The Guidelines For The Management Of Diabetes In Primary Care In The Caribbean

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<thead>
<tr>
<th>Modules of the Management of Diabetes in Primary Care Guidelines</th>
<th>Who are the target users?</th>
</tr>
</thead>
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<tr>
<td><strong>Module</strong></td>
<td><strong>What does it cover?</strong></td>
</tr>
<tr>
<td>Module 1 Evidence Based Treatment Protocols</td>
<td>Documentation of protocols aimed at standardizing the clinical approach to the management of T2DM in primary care.</td>
</tr>
<tr>
<td>Module 2 Guiding Lifestyle Changes</td>
<td>Information on lifestyle interventions that target the four modifiable risk factors for diabetes.</td>
</tr>
<tr>
<td>Module 3 Guidance for PWD &amp; Caregivers</td>
<td>Information for Persons With Diabetes (PWD) and lay caregivers related to the care of diabetes.</td>
</tr>
<tr>
<td>Module 4 Access to Essential Medications</td>
<td>Information on medicines and technologies available for diabetes management and their supply-chain management at the primary care facility level.</td>
</tr>
<tr>
<td>Module 5 Systems for Monitoring</td>
<td>Monitoring and reporting information, standardized indicators and data collection tools for use in the prevention and management of T2DM.</td>
</tr>
</tbody>
</table>
The Client-Centred Approach to Chronic Care

Diabetes is a chronic illness which extends across an individual’s lifespan. The goal of all clinicians and persons on the health team should therefore be to deliver optimal and evidence-based care and support. The Chronic Care Model, endorsed by PAHO/WHO, emphasises the importance of the team approach to the care of all Chronic Non-communicable Diseases (CNCDs) and further underscores the integral role of high-level policy support in optimising the delivery of care to persons with chronic illnesses. This framework informs the approaches recommended in these guidelines and is both endorsed and encouraged by CARPHA and the OECS as a mechanism for improving the standard of health care delivered to people of the region.

The Chronic Care Model identifies patient-centeredness, effectiveness, efficiency, equity and timeliness as essential elements of efficient health service delivery for people with this chronic illness. From as early as the 1980’s, the approach to the care of “clients” has undergone a paradigm shift from the doctor-centred model, to one which gives more focus, autonomy and involvement to the recipient of health care services, initially called “patient-centred care.” Moria Stewart et al (2003), highlighted that persons receiving care preferred this model and reported improved satisfaction, outcomes, and health care utilisation with this approach. As archetypes, relating to health care delivery continued to evolve, and the shared role of health care providers and recipients in decision-making became more widely accepted, and the terminology describing health care participants was updated. “Patients” are now called “clients,” a term recognising the
more empowered role they play in their own health care. Rather than passively presenting to be “fixed” by a doctor, they are recognised as an integral part of the health care team for their treatment. These guidelines will therefore utilise the terms “persons with diabetes” (PWD) and “clients” in reference to the recipients of health care services for diabetes.

At each visit, health care providers need to remember that clients are individuals, with the circumstances of their lives constantly changing. The natural progression of the disease process also means that recommended management will almost certainly need to be adjusted periodically. Early involvement of the wider team of health professionals in the prevention and management of the complications of diabetes is a critical risk mitigation strategy, the success of which hinges upon the cooperation of educated, motivated clients and integrated, coordinated providers of health care. At each point of care, it behoves the care-provider, to seek an integrated understanding of the client’s world and to solicit feedback alongside the provision of their recommendations for improving management. Each member of the health team must recognise that managing the non-clinical (emotional, social, economic, psychological) needs and life issues of the client plays an important role in ensuring successful outcomes and must understand the relevance of tailoring their care to suit their individual clients.

Integrating the individual client-centred approach into the broader framework of the Chronic Care Model will, necessarily, take varying forms in different Member States and will require the adaptation of both systems and individuals to new ways of executing health care functions; but the benefits to be derived at both the individual and the systemic level from improving the quality of health care delivery have been shown, in many other jurisdictions greatly, to outweigh the costs.
MODULE 4
Access to Essential Medication
Introduction

In this Module, essential medicines are defined as those medicines that satisfy the priority health care needs of the majority of a given population and are selected after consideration of their relevance to public health, efficacy and safety, and comparative cost-effectiveness. They are intended to be available within the context of functioning health systems and should be available at all times, in adequate amounts, appropriate dosages, with quality assurance and adequate information, and at a cost that individuals and communities can afford.

Reliable access to essential medicines and health products is dependent on an efficient procurement and supply management system. Consistently available, quality-assured, affordable medicines and technologies is a major strategy for reducing the burden of non-communicable diseases, such as diabetes.

The most common obstruction to the availability of essential medicines and technologies is poor supply chain management. Supply chains are able to deliver essential medicines and technologies as well as provide critical information to planners and policy-makers regarding demand and consumption. Medicines and technologies need to be managed appropriately to ensure that the correct medicines are selected, procured in the right quantities, distributed to facilities on time, and handled and stored in a way that maintains their quality. This is supported by policies that enable sufficient quantities to be procured in order to reduce cost inefficiencies, ensure the reliability and security of the distribution system, and encourage the appropriate use of these health products.

Effective supply chain management avoids stock-outs and the
disruption of treatment. It is dependent on timely procurement, continuous performance monitoring and prompt action in response to problems that may arise. Additionally, medicines must be dispensed correctly and used rationally by the healthcare providers and patients.

This module focuses on access to essential medicines for diabetes management, and includes:

- information on the pharmaceutical management cycle and policies;
- selection of appropriate medicines;
- supply-chain management, including quantification, forecasting, distribution, storage and handling; and
- ensuring supply and accountability.

Pharmaceutical management requires continuous support, including policies and legislative frameworks and the country specific regulatory authority. In countries with no regulatory authority, procurement agencies should prequalify suppliers and manufacturers to ensure medicines are manufactured to international standards and Good Manufacturing Practice (GMP). Countries should also consider medicines approved by the Caribbean Regulatory System (CRS), which is a function which is under the aegis of the Caribbean Public Health Agency (CARPHA).
Section 1: Medicines Used in the Treatment of Diabetes
Access to Essential Diabetic Medications

There are several classes of medicine that are now used worldwide, in the treatment of diabetes. WHO 2nd and 3rd line Medicine in DM Care, and IDF 2018 Clinical Practice Recommendations along with numerous other studies, suggest that metformin should be the first drug to be chosen in the care of PWD. It can be given as monotherapy along with lifestyle changes to newly diagnosed persons with diabetes. To achieve greater client tolerance to the drug, start low and go slow. Recommended start 500mg daily and increase to 2000mg. Slow-release or modified release metformin can also be used if having significant gastrointestinal side effects. At present the modified release metformin is not available through the OECS but a supplier has been identified (APOTEX), and discussions are ongoing to add it to the formulary.

If metformin is not tolerated or adequate blood glucose control is not obtained with monotherapy, then advance to dual therapy by adding another glucose lowering drug (Module 1, Algorithm 2). If weight loss is a major issue, give a choice that promotes weight loss. Newer classes of glucose lowering medicine GLP-1 (Glucagon like peptide) or SGLT-2 (sodium-glucose cotransporter Type 2 inhibitors), are recommended as they are associated with achieving weight loss.

The use of Sulphonylureas continues to remain a 2nd line of treatment in the Caribbean, because of the low cost of these medications. WHO supports its use from a public health standpoint, for that same reason. However, the first generation Sulphonylureas such as Glibenclamide, should be avoided because of the high associated
<table>
<thead>
<tr>
<th>Class of Drug</th>
<th>Drug</th>
<th>MOA</th>
<th>Efficacy</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguinide</td>
<td>Metformin 250/500/850mg</td>
<td>Hepatic glucose output</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Delays glucose absorption</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulphonylurea</td>
<td>Gliclazide 30mg MR tab</td>
<td>↑ Insulin release (Major complication is</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>(2nd Generation)</td>
<td>60mg SR tab Glyburide</td>
<td>hypoglycemia esp in first generation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Repaglinide Nateglinide</td>
<td>↑ Insuline Release</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>(glinides)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha Glucosidase</td>
<td>Acarbose</td>
<td>↓ Intestinal absorption of carbohydrates</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TZDs Thiazolidinedions</td>
<td>Rosiglitazone</td>
<td>↑ Insulin sensitivity</td>
<td>High</td>
<td>Moderate</td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
<td>Sitagliptin</td>
<td>Enhances insulin secretion in response</td>
<td>Intermediate</td>
<td>High</td>
</tr>
<tr>
<td>(dipeptidyl peptidase-4 inhibitors)</td>
<td>Vildagliptin</td>
<td>to meals</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saxagliptin</td>
<td>↓ Glucagon secretion (Glucose dependant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GLP-1 Receptor</td>
<td>Exenatide</td>
<td>Augments Insulin secretion after meal</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Agonist</td>
<td>Liraglutide</td>
<td>ingestion</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exenatide ER</td>
<td>Suppresses glucagon release</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduces hepatic glucose production</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLGT-2 inhibitors</td>
<td>Canagliflozin</td>
<td>Reduce plasma glucose by inducing</td>
<td>Intermediate</td>
<td>High</td>
</tr>
<tr>
<td>Sodium-glucose</td>
<td>Dapagliflozin</td>
<td>glycosuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cotransporters Type 2</td>
<td>Empagliflozin</td>
<td>(Thus major complication is UTI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibitors</td>
<td>Ipragliflozin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
risk of hypoglycaemia.

Physicians are encouraged to customize prescribing, by considering the patient’s profile (age, weight, and any complications that pre-exist). The risk and benefits of each glucose lowering medication should also be considered before prescribing. (Table 2 & 4). Combinations of classes of medicine, of different mechanisms of action, are frequently required for optimum control.

With so many returning nationals and tourists who visit our shores with the medicine they have been prescribed in their home countries, primary care physicians must be aware of global trends and recommendations whilst providing to clients in limited resource settings. The current cost of newer medicine in the Caribbean such as thiazolidinedione (TZDs), meglitinides and DPP-4 inhibitors, may in cases be prohibitive.

Chlorpropamide and Glibenclamide, both long-acting Sulphonyleureas are no longer recommended. Where still available, it should be used with extreme caution in the elderly and should be avoided in those

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<table>
<thead>
<tr>
<th>Class of Drug</th>
<th>Drug</th>
<th>MOA</th>
<th>Efficacy</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile Acid sequestrants</td>
<td>Colesevelam</td>
<td>Acts by a hepatic mechanism in decreasing hepatic glucose output</td>
<td>Very High</td>
<td></td>
</tr>
<tr>
<td>Amylin mimetics</td>
<td>Pramlintide</td>
<td>Glucagon secretion slows gastric emptying</td>
<td>Very High</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Profile of presently Available Glucose Lowering Agents Not including Insulin

AVOID first generation sulphonylureas such as Glibenclamide, due to high associated risk of hypoglycaemia!
with renal disease. It is the suggestion of these guidelines that it should be taken off the formulary to diminish risks to our population.

Bromocriptine (a Dopamine 2 agonist), which is outdated in its use as a glucose lowering drug as well as alpha glucosidase inhibitors such as Arcabose have been discontinued in several OECS territories, because of their relatively limited effect on the lowering of HBA1c.

**Oral Glucose Lowering Agents**

Therapy with oral agents should be introduced simultaneously with diet and exercise. The majority of PWD will eventually require drug therapy in increasing dosages and often in multiple drug regimens as T2DM is a progressive disorder. Many persons will also subsequently require the addition or substitution of insulin to achieve glycaemic control. T2DM, may require insulin for control somewhat at the time of diagnosis, if the patient is very symptomatic and/or has severe hyperglycaemia or high HbA1c of >11.0%.

The therapeutic options for the treatment of T2DM are:

- Biguanides- increases insulin sensitivity;
- Thiazolidinediones- increases insulin sensitivity;
- Sulfonylureas- increases insulin release;
- Meglitinides- increase insulin release;
- Alpha-glucosidase inhibitors- modifies intestinal absorption of carbohydrates;
- Dipeptidyl-peptidase 4 Inhibitors (DPP-4 inhibitors) – augments the release of insulin;
<table>
<thead>
<tr>
<th>Medicine</th>
<th>Hypo</th>
<th>Weight</th>
<th>GI Side Effects</th>
<th>Major CV Events</th>
<th>Chronic Heart Failure</th>
<th>Other Side Effects</th>
<th>Chronic Kidney Disease STG3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Neutral</td>
<td>Slight loss</td>
<td>Moderate</td>
<td>Benefit</td>
<td>Neutral</td>
<td>Nil</td>
<td>Reduce dose in 3A</td>
</tr>
<tr>
<td>Sulphonylurea</td>
<td>Moderate</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Nil</td>
<td>Caution high risk hypo stg3A, B</td>
</tr>
<tr>
<td></td>
<td>Severe (1st Gen)</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Nil</td>
<td>Contraindicated except glipizide and glicazide</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>Neutral</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Risk</td>
<td>Edema &amp; Bone loss</td>
<td>Neutral</td>
</tr>
<tr>
<td>Alpha-Glucosidase Inhibitors</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Nil</td>
<td>Neutral stg3A, 3B</td>
</tr>
<tr>
<td>DPP4-Inhibitors</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Pancreatitis</td>
<td>Neutral but must reduce dose except linagliptin</td>
</tr>
<tr>
<td>GLP1 Receptor Agonists</td>
<td>Neutral</td>
<td>Loss</td>
<td>Moderate</td>
<td>Benefit (2RCT)</td>
<td>Neutral</td>
<td>Nil</td>
<td>Caution with exenatide ER stg3A, 3B</td>
</tr>
<tr>
<td>SLGT2 Inhibitors</td>
<td>Neutral</td>
<td>Loss</td>
<td>Neutral</td>
<td>Benefit</td>
<td>Neutral</td>
<td>Mycotic genital infections, fractures, amputation</td>
<td>Contraindicated stg3B</td>
</tr>
</tbody>
</table>

Table 2: Risks and Benefits of Common Glucose Lowering Agents
• Glucagon-like, Peptide-1 receptor agonist (GLP-1 receptor agonist) – enhances glucose-stimulated insulin, biosynthesis and secretion, suppresses post-prandial glucagon release, decreases appetite and food intake, delays gastric emptying;
• Sympatholytic D2-Dopamine Agonist: Cycloset (Bromocriptine mesylate) - inhibits excessive sympathetic tone within the central nervous system resulting in a reduction in post meal plasma glucose;
• Sodium, Glucose Cotransporter-2 Inhibitors (SLGT-2) – reduces plasma glucose concentration by inducing glycosuria.
• Insulins- replaces insulin deficiency.

Table 3 looks at the risks and benefits of the oral glucose lowering agents available for treatment of diabetes.

**Insulin for T2DM**

Insulin is indicated in all persons with T1DM and T2DM, who don’t achieve control on oral diabetic medicine. There are several types of insulin presently available as indicated in the table below (Table 4). The newest being the ultra-Lente insulins which are concentrated and have very long half-lives. The main side effect of insulin is hypoglycaemia as well as weight gain but poses no risk of CVD (Table 5).
<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid acting</td>
<td>Insulin lispro/insuline glulisine</td>
</tr>
<tr>
<td></td>
<td>Insulin aspart</td>
</tr>
<tr>
<td>Short acting</td>
<td>Human Regular</td>
</tr>
<tr>
<td>Intermediate Human NPH</td>
<td>(Neutral Protamine Hagedon)</td>
</tr>
<tr>
<td>(Basal Insulins)</td>
<td></td>
</tr>
<tr>
<td>Glargine</td>
<td></td>
</tr>
<tr>
<td>Detemir</td>
<td></td>
</tr>
<tr>
<td>Ultralente</td>
<td></td>
</tr>
<tr>
<td>Pre-mixed</td>
<td>70% / 30% NPH / Regular</td>
</tr>
<tr>
<td></td>
<td>80% / 20% Lente / Regular</td>
</tr>
<tr>
<td>Biphasic Insulin</td>
<td>75% Protamine Lispro: 25%</td>
</tr>
<tr>
<td></td>
<td>Insulin Lispro</td>
</tr>
<tr>
<td>Concentrated</td>
<td>U-500</td>
</tr>
</tbody>
</table>

*Table 3 Types of Insulin Available*
### Table 4: Risks Of Insulin

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting or analogue (Lispro, aspart, glulisine)</td>
<td>5-15min</td>
<td>45-90min</td>
<td>2-4h</td>
</tr>
<tr>
<td>Short-acting (regular)</td>
<td>0.5-1h</td>
<td>2-4h</td>
<td>4-8h</td>
</tr>
<tr>
<td>NPH insulin</td>
<td>1-3h</td>
<td>4-10h</td>
<td>10-18h</td>
</tr>
<tr>
<td>Detemir</td>
<td>1-2h</td>
<td>None</td>
<td>12-24h</td>
</tr>
<tr>
<td>Glargine</td>
<td>2-3h</td>
<td>None</td>
<td>20-24+h</td>
</tr>
<tr>
<td>Premixed Insuline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70% NPH / 30% regular</td>
<td>0.5-1h</td>
<td>2-10h</td>
<td>10-18h</td>
</tr>
<tr>
<td>50% NPH/50% regular</td>
<td>0.5-1h</td>
<td>2-10h</td>
<td>10-18h</td>
</tr>
<tr>
<td>75% NPL /25% lispro</td>
<td>10-20min</td>
<td>1-6h</td>
<td>10-18h</td>
</tr>
<tr>
<td>50% NPL/50% lispro</td>
<td>10-20min</td>
<td>1-6h</td>
<td>10-18h</td>
</tr>
<tr>
<td>70% NPA/30% aspart</td>
<td>10-20min</td>
<td>1-6h</td>
<td>10-18h</td>
</tr>
</tbody>
</table>

### Table 5 Pharmacokinetic properties of insulin Products
Pharmacovigilance

WHO has defined pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. An adverse medicine reaction is any noxious change which is suspected to be due to medicine, occurs in doses normally used by humans, requires treatment or decrease in dose or indicates caution in the future use of the same medicine.

The aim of pharmacovigilance is described below:

• to improve patient care and safety regarding the use of medicines (Patient Care); and

• to contribute to the assessment of benefit/harm, effectiveness and risk of medicines, encouraging their safe, rational and cost-effective use (Risk Benefit Assessment).

An adverse event reporting consists of four elements:

1. An identifiable patient
2. An identifiable reporter
3. A suspect medicine
4. A suspected adverse event

OECS/PPS has implemented a regional adverse reaction form which health care workers can submit by post or online to OECS/PPS (Appendix I). Moreover, OECS adverse reaction forms are subsequently channelled to Vigicarib, the Caribbean network located at CARPHA, Trinidad, which finally deposits the reports into Vigibase, the global WHO Pharmacovigilance Centre in Uppsala, Sweden.

Physicians are encouraged to report any adverse effects reported
by patients on the website be https://carpha.org/What-We-Do/Caribbean-Regulatory-System/VigiCarib
### Introduction

A holistic approach needs to be taken in trying to reduce the impact of diabetes through prevention, diagnosis, care and management. A key component is having a list of essential medications that are affordable and easily available when required. An essential list of medicines allows for easier procurement of the correct quantities thus avoiding shortages. Systems must always be put in place for the correct handling, storage and distribution of medicines in a manner that does not compromise the integrity of the medications.

### Medicine Supply Chain Management

Medicine Supply Chain Management (MSCM) is a critical component
in managing diabetes to ensure patients have regular access to quality medicines at competitive prices. The important components of supply chain management are illustrated in the following chart:

Selection

The cornerstone of an efficient pharmaceutical supply system is the selection of cost-effective medicines to be available to prescribers and clients. Moreover, access to medicines is a basic human right and is enshrined in countries’ constitutions. The advantages of a list of essential medicines are four-fold: drug therapy is improved, procurement is enhanced, purchasing power is strengthened and inventory holding cost is contained.

Procurement

An effective procurement process should encompass the following activities:

- procuring the right drugs in the right quantities;
- obtaining the lowest possible purchase price;
- ensuring that all drugs procured meet recognized standards of quality;
- arranging timely delivery to avoid shortages and stock-outs;
- ensuring supplier reliability with respect to service and quality; and
- setting the purchasing schedule and formulas for inventory control.

Given the impact of procurement activities on the operation and
effectiveness of health services, it is critical that these activities be performed by trained staff using sound procedures, and with access to reliable inventory and consumption information.

**Inventory Management**

Inventory management is central to an efficient pharmaceutical supply, because proper inventory management leads to an optimization of financial resources, consistent availability of vital supplies, and improvement in the quality of patient care. Supply systems usually maintain either a manual or electronic inventory system (Appendix VII).

Efficient inventory management systems incorporate objective decisions regarding order frequency and quantity, accurate stock records, and systematic performance monitoring. In these cases, there are systematic procedures and rules to guide staff, assisted by an understanding of the basic principles of effective inventory management. To implement good inventory management, procurement staff must use mathematical formulas as models to set policies for stock levels, re-order frequency, and re-order quantity. Several simple formulas have been developed to calculate the various parameters of inventory control.

The ideal inventory control model is shown in Figure 2. In this ideal model, supplies are issued in response to demand, and stock on hand steadily declines until an order is placed. The stock on hand consists of two components, the working stock and the safety stock (SS). In the ideal model, the supplier operates according to plan, the shipments arrive on time, the quantity ordered (Qo) is received, and the inventory level reverts to its starting maximum point. Working stock varies from zero to the quantity ordered, and represents the stock used to satisfy demand between deliveries.
Standard Re-ordering Formulas

Using this approach, one defines a theoretical maximum stock for each item, to provide sufficient but not excessive stock to last between orders; minimum stock level or re-order level determines at what point an order should be placed. Safety stock should be included in the minimum stock level. Variables for consideration include:

- Average monthly consumption, adjusted for stock-outs (CA);
- Supplier lead time (LT);
- Procurement period - time until the next order will be placed (PP);
Safety stock - additional stock to cope with variability in consumption and lead time (SS), usually between 1 and 2 months of stock and

Stock on hand in inventory.

The equation of calculating the minimum stock ($S_{MIN}$) is:
Minimum stock = (LT x CA) + SS

Maximum (target) stock level ($S_{MAX}$) can be calculated as the minimum stock plus the procurement period multiplied by the average consumption;

The Equation is:
$S_{MAX} = S_{MIN} + (PP \times CA)$

**Pricing**

The price of essential medicines for the care of diabetes is an indication of the access to treatment for PWD. As a result of bulk purchasing medicines obtained from government health care facilities tends to be the most affordable to the clients. Economies of scale allow better value for money keeping medicines affordable.

**Storage**

It is essential for medicines and other relevant medical equipment to be stored in a manner that allows for optimal performance at
use. Adequate storage should also protect the physical stability and efficacy of the medication, so that it reaches clients in a stable condition. Many countries have central procurement units responsible not only for the purchasing of medicines but also adequate central storage. All central storage units provide a temperature controlled, dry environment for the medicines until they are dispensed to the local health centres. The health facilities must also have adequate dry, cool designated pharmacy areas for storage at the facilities. Special care is taken with insulins that need to follow a strict cold chain.

Systems for monitoring and evaluation are in place to ensure that there is a constant supply of required medications and that shortages do not occur.

Supply During Disasters

Consideration should be given to national comprehensive plans that speak to availability and distribution of medications during times of disaster. Ongoing efforts in the Caribbean region will specifically aim to answer these questions and develop disaster preparedness plans for distribution of medication. A minimum requirement of any such plan should be the implementation of back-up generators at the central procurement storage facilities to ensure that even in a disaster, the integrity of the medications in storage will not be affected by temperature changes and the cold chain for stored insulins will not be interrupted.
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Appendices
An ADR is a response to a medicine which is noxious and unintended, and which occurs at normal doses.

### Patient Information

<table>
<thead>
<tr>
<th>Initials:</th>
<th>Address:</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.O.B.: (dd/mm/yy)</td>
<td>Gender: M / F</td>
</tr>
</tbody>
</table>

### Adverse Reaction

**Date of Onset** (dd/mm/yy)

**Outcome**

- [ ] Hospitalized
- [ ] Disabled
- [ ] Recovered
- [ ] Died (dd/mm/yy)
- [ ] Other

**Describe reaction or problem**

Relevant laboratory data and medical history (e.g. allergies, pregnancy, smoking, alcohol use, renal/hepatic dysfunction)

### Health Product / Medication History (including vaccines, herbal medicines)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Manufacturer</th>
<th>Mark X for Suspect drug(s)</th>
<th>Dose and Frequency</th>
<th>Route</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

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51
Appendix I: Adverse Reporting Form
Consumption Method

FACTORS

Lead-time (LT) = 3months
Procurement period (PP) = 12months
Monthly consumption (CA) = 100units of medicines

ASSIGNMENT

Calculate
- Safety stock
- Minimum Stock
- Maximum Stock

Morbidity Method

FACTORS:

Daily dose of lopinavir ritonavir = two tablets two times a day
Length of treatment = 12 months
Number of patients = 200 patients

ASSIGNMENT: Calculate the annual requirements for lopinavir ritonavir.