GUIDELINES FOR PROCUREMENT OF INSULINS AND ASSOCIATED SUPPLIES

NOVEMBER 2021

acciss
Addressing the Challenge and Constraints of Insulin Sources and Supply

HAI HEALTH ACTION INTERNATIONAL

ACCISS Guidelines for Procurement of Insulins and Associated Supplies

Developed by Cecile Macé and Christophe Perrin

November 2021

Disclaimer: The ACCISS Study is supported by The Leona M. and Harry B. Helmsley Charitable Trust. The analysis included in this report is that of the authors alone and does not necessarily reflect the views of the Helmsley Charitable Trust. All references and conclusions are intended for educational and informative purposes and do not constitute an endorsement or recommendation from the Helmsley Charitable Trust.

Table of Contents

ACRONYMS

ACAME	Association des Centrales d'Achats de Médicaments Essentiels
ACCISS	Addressing the Challenge and Constraints of Insulin Sources and Supply
CIP	Cost Insurance Paid
COVID-19	Coronavirus
DAP	Delivered At Place
EURO	WHO Regional Office for Europe
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	Good Manufacturing Practices
HAI	Health Action International
HIV/AIDS	Human immunodeficiency virus infection and acquired immunodeficiency syndrome
HLCM-PN	High-Level Committee on Management Procurement Network
IDA	International Dispensary Association – IDA Foundation
IEHK	Interagency Emergency Health Kit
IMDRF	International Medical Device Regulators Forum
IMRES	International Medical Relief Service
INN	International Non-Proprietary Name
ISPAD	International Society for Paediatric and Adolescent Diabetes
LMICs	Low and Middle-Income Countries
LMIS	Logistic Management Information System
LTA	Long Term Agreement
MDS	Managing Drug Supply
MEG	Medical Expert Group
MoH	Ministry of Health
MSH	Management Sciences for Health
NCD	Non communicable diseases
nEML	National Essential Medicines List
OECS	Organisation of Eastern Caribbean States
PAHO	Pan-American Health Organization
QA	Quality Assurance
SRA	Stringent Regulatory Authorities
UN	United Nations
UNDP	United Nations Development Programme
UNICEF	United Nations Children's Fund
UNICEF SD	United Nations Children's Fund Supply Division
UNOPS	United Nations Office for Project Services
WHO	World Health Organization
WHO PQP	WHO Prequalification Programme

INTRODUCTION

Insulin is a life-saving medicine for people with type 1 diabetes and is used to manage care for an increasing number of people with type 2 diabetes. While insulin is an essential medicine, literature has highlighted its poor availability across the public and private health sectors in most low- and middle-income countries (LMICs)[1], with ranges most often below those set by World Health Organization (WHO) targets for non-communicable disease (NCD) medicines[2]. In terms of supply, the market is dominated by three large multinational insulin manufacturers (Novo Nordisk, Sanofi, Eli Lilly) that control over 90% global market share by volume and value.[3,4] This market structure with limited competition and the lack of transparency on prices are two key reasons why insulin is higher priced than other NCD medicines, showing governments must do more to contain insulin prices and ensure they are affordable for all their citizens living with diabetes.[5]

A study in 13 LMICs[6] found governments were paying far more, particularly for analogues (but also for human insulins in some countries) compared to published 2021 estimates of manufacturers' selling prices (covering production costs, profit, transport, and other costs) for human and analogue insulins.[7] This shows there is room for price reductions. Further, the same study found that for isophane human insulin, only three countries meet in the public sector the WHO target of 80% availability of affordable essential medicines for NCD in any sector.[8] This outcome demonstrates that there is a need for improvement in forecasting and selecting most suitable supply and distribution procedures to the local context.

Together with insulin, diabetes management requires associated supplies, such as insulin syringes and pen needles, and blood glucose meters, test strips and lancets for glucose testing.

People living with diabetes using insulin require several glucose tests strips per day and need to replace their blood glucose meters every few years. In many contexts, replacement of strips and meters can be extremely challenging. Indeed, suppliers limit the compatibility of proprietary test strips with particular meter models, such that test strips do not work with other meter brands, or often even with other models within the same brand. Therefore, a specific attention needs to be paid when making centralised purchases of blood glucose meters and strips at country level to ensure sustainable supply of compatible strips and meters. This supply challenge becomes even more complex when suppliers provide meters for free to encourage consumers to switch over to their platform, thereby driving up test strip sales as well as treatment management costs.[9]

The Addressing the Challenges and Constraints of Insulin Sources and Supply (ACCISS) Study guidelines for procurement of insulins and associated supplies were developed as a tool to provide strategies and methods to increase transparency and efficiency in procurement mechanisms, and thus to secure a stable supply of insulins, that is affordable and quality assured. These strategies have been informed by a study recently completed by ACCISS in Pacific countries, as well as through the review of the procurement of insulin and associated supplies through multi-country and global pooled procurement mechanisms.[10]

[1] https://www.thelancet.com/journals/landia/article/PIIS2213-8587(15)00521-5/fulltext
[2] https://www.who.int/nmh/ncd-tools/target9/en/
[3] https://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf
[4] https://gh.bmj.com/content/bmjgh/4/3/e001410.full.pdf
[5] https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf
[6] https://gh.bmj.com/content/bmjgh/4/3/e001410.full.pdf
[7] https://gh.bmj.com/content/bmjgh/3/5/e000850.full.pdf
[8] https://gh.bmj.com/content/bmjgh/4/3/e001410.full.pdf
[9] https://haiweb.org/wp-content/uploads/2021/09/Market-Report_Self-monitoring-Devices-in-LMICs.pdf
[10] Analysis of pooled procurement mechanisms and their applicability for insulin and associated supplies in small state countries or countries with limited needs (with Pacific as a case study), 2021

OBJECTIVE

The objective of these ACCISS guidelines is to provide guidance to LMICs and specifically public sector procurers on how to improve procurement of insulins and associated supplies.

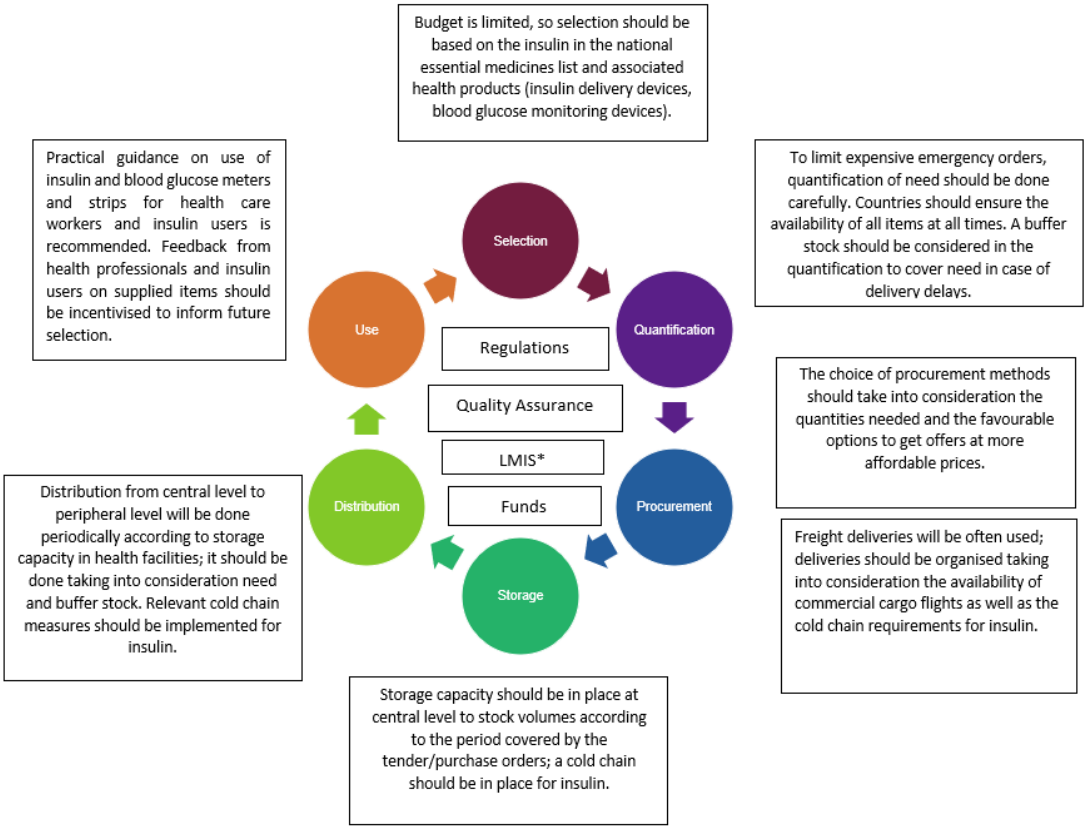
They will highlight the important aspects to consider for guaranteeing a continuous supply of quality-assured insulin and associated supplies at affordable prices. These guidelines could be used by staff involved in procurement activities to review their procurement process or as one tool to help guide the development and implementation of procurement strategies for insulin and associated supplies.

They are based on WHO good practices and international references for procurement, as well as information available in the ACCISS toolkit.

PROCUREMENT CYCLE FOR HEALTH PRODUCTS AND RELATED REFERENCE GUIDELINES

The procurement of insulins and associated supplies in all countries follows a classic procurement cycle for any health product, as described in the Figure 1.

Figure 1. Procurement cycle for health products (proposed as an adaptation of WHO and MSH procurement cycles) highlighting specifics for insulins and associated supplies.



*: LMIS = Logistic Management and Information System

When working through this procurement cycle, the rules set by national regulations for procurement must be fulfilled including Quality Assurance (QA) criteria, and WHO norms and standards for health products. It entails collecting, monitoring, analysing and using logistic data to quantify needs and inform the procurement and distribution processes. Funds also need to be available at the right time in the procurement process to place orders and pay suppliers on time.

When procuring insulins and associated supplies, there are specific concerns that should be considered in terms of selection, quantification, procurement, storage, distribution and use. These conditions are outlined in the procurement guidelines below.

REFERENCE GUIDELINES IN HEALTH PROCUREMENT

Over the past 20 years, the WHO[11] and other international organisations, such as Management Sciences for Health (MSH), and the members of the Interagency Pharmaceutical Coordination Group,[12] involving pharmaceutical advisers from technical partners and donors entities working in health procurement (e.g., WHO, various United Nations (UN) agencies, Global Fund to fight AIDS, Tuberculosis and malaria (GFATM), World Bank, etc) have developed several guidelines advising how procurement of heath products should be managed in order to secure proper access and optimal outcomes.

The main guidelines developed in this field are the following:

- WHO Operational principles for good pharmaceutical procurement, 1999[13]
- WHO Model Quality Assurance system for procurement agencies, 2014[14]
- WHO Good Storage and Distribution practices for medical products, 2020[15]
- MDS3 - Managing Access to Medicines and Health Technologies, 2014.[16]

In addition, the UN Procurement Practitioner's handbook published by the UN High Level Committee on Management's Procurement Network (HLCM-PN)[17] is a common reference for good procurement practices in the UN system. It describes the common and typical guiding principles, policies, procedures, and practices that govern UN procurement activities and can be used as a reference for national procurement reforms. As such, the five above-mentioned references have informed the content of these ACCISS guidelines.

[11] https://www.who.int/medicines/areas/access/supply/en/
[12] https://www.who.int/medicines/areas/policy/ipc/en/
[13] https://www.who.int/3by5/en/who-edm-par-99-5.pdf
[14] https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS986annex3.pdf?ua=1
[15] https://www.who.int/publications/m/item/trs-1025-annex-7-gdp-medical-products
[16] https://www.msh.org/resources/mds-3-managing-access-to-medicines-and-health-technologies
[17] UN Procurement Practitioner's Handbook ver. 2017 (ungm.org)

SELECTION

The selection of insulin and associated supplies should be done according to the National Essential Medicines List (nEML) and national treatment guidelines for diabetes. Considering that the available budget will be often limited in LMICs, it is important to make the best use of available funds exclusively for health products showing the best scientific evidence.

The analysis of 100 nEMLs from LMICs by ACCISS demonstrates that, with very few exceptions, all countries list both short-acting and intermediate-acting insulin, which are recommended by the WHO Model List. See ACCISS Insulin Market Profile.

Countries could use the outcomes of the WHO Expert Committee on Selection and Use of Essential Medicines[18], as well as the last updates of the WHO Model List of Essential Medicines[19], to select the insulins that are necessary according to their epidemiological context. The WHO guidance on selection of essential medicines at country level could be used when reviewing the nEML.[20] They can also refer to the guidelines for insulin use developed by ACCISS to know more about the different types of insulin and their clinical use.[21]

Animal insulin was the first type of insulin to be used on humans in 1922. It is derived from pigs or cows (known as 'porcine or bovine insulin' respectively). Porcine insulin is still available, but only a limited number of manufacturers still produce it. It is used because of allergies to other insulin types, or personal preference.

Human insulin is synthetically grown in a laboratory within common bacteria. It mimics insulin that is already in humans. Types of human insulin include short-acting, intermediate acting and pre-mixed insulins.

Analogue Insulin

Similar to human insulin, analogue insulin is made from recombinant DNA. The difference is that it is modified to change the absorption rates of the insulin. This allows the insulin to be released more quickly, or slowly, into the bloodstream.

[18] Expert Committee on Selection and Use of Essential Medicines (who.int)
[19] eEML - Electronic Essential Medicines List (essentialmeds.org)
[20] Selection of essential medicines at country level (who.int)
[21] Guidelines for Insulin Use - Haiweb - Acciss Toolkit

WHO recommends human insulins (short-acting and intermediate-acting), and added long-acting analogue insulin to the EML in October 2021. Wealthier countries also purchase analogue insulin at higher prices despite the evidence showing no added benefits over human insulin[22,23], which has a serious impact on limited budgets. With the same budget, LMICs will be able to treat more people when supplying human insulins.[24]

To administer insulin and to monitor treatment outcomes on blood glucose levels, it is also necessary to have insulin delivery devices, i.e., insulin syringes for use with the vials, insulin pens for the cartridges, insulin pen needles, blood glucose meters, associated test strips and lancets. It will be important to distinguish blood glucose meters for use in health facilities and for self-monitoring.

To ensure continuous availability of all the items simultaneously, it may be beneficial for countries to consider bundling items at the time when they are purchased or procuring all these items as a lot. This approach is described further below in the section related to tender/bidding documents and important elements for consideration during procurement.

QUANTIFICATION

Poor quantification at the national level can lead to government tenders that do not match the actual insulin need, thus causing stock-outs or over-stocks. Accurate quantification not only avoids these stock problems but can also improve trust with suppliers, who may be more willing to offer the lowest competitive price on an accurately estimated-quantity supply contract.

In most of the countries included in the ACCISS Study, public health facilities where insulin should be available struggle to avoid stock-outs. This is particularly true for the health facilities further from the big cities or the capital where central stock(s) are managed. There are several reasons for this situation depending on the context, but a frequent challenge can be properly maintaining registries of people living with diabetes in need of insulin and quantifying need. These are two important pre-conditions to ensure that centralised purchases of insulin match the demand in all areas of a country.

As for any other health products[25], collecting past consumption of insulin and associated supplies is the most reliable way to predict and quantify future demand, taking into consideration existing stock-outs often seen in the national supply chain, and that consumption records are reasonably accurate throughout key national stakeholders, such as hospitals and health facilities in districts, provinces/regions, and the capital. Central Medical Stores, when they exist, can also provide distribution data. No specific quantification tool exists for quantifying the needs for insulin and associated supplies like for TB, HIV/AIDS, malaria, or reproductive health medicines. However, general quantification tools already used in countries would be helpful.

Adjustments to insulin consumption can still be needed in line with changes in morbidity and prescribing patterns. Also, where consumption data are incomplete or do not reflect real demand, estimation of procurement requirements can be done according to standard treatment protocols and epidemiological data.

[22] Short-acting insulin analogues versus regular human insulin for type 1 diabetes mellitus | Cochrane
[23] Short-acting insulin analogues versus regular human insulin for type 2 diabetes mellitus | Cochrane
[24] https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013498.pub2/epdf/abstract
[25] mds3-ch20-quantifying-mar2012.pdf (msh.org)

To avoid emergency orders, which significantly increase the cost of health products, pharmacists, or staff in charge of procurement should have access to reliable logistics data from health facilities nationwide. This requires the availability and proper use of either a paper-based system to collect consumption data or, better still, extraction of data from electronic Logistic Management Information Systems. Providing to health facilities a standard template to be used when preparing their orders help them to take into consideration the stock at hand, the period to be covered by the order, the quantity necessary to have a buffer stock and the exact quantity to be ordered. This template could also help the person preparing the order at country level to double check the calculation done by health facilities and to adjust quantities, if needed. This standard template should also include the expiry date of stock available and could help to identify over stock in health facilities, and to move stock in other health facilities in need.

It is also important to define the level of buffer stock for each health product (e.g., insulin and associated supplies) needed to avoid stock out situations and to compensate for delivery time (which could be long due to logistic aspects). This requires having a budget in place to cover the needs and the buffer stock.

PROCUREMENT

An effective procurement process seeks to ensure the availability of the right medicines and other health products in the right quantities, at reasonable prices, and at recognised standards of quality. It should also apply to the procurement of insulin and associated supplies.

In several low- and middle-income countries, issues have been observed in the procurement of insulin and associated supplies, including:

- bidding documents that are not specific to pharmaceuticals but could apply to any commodity purchased by a government,
- specifications for insulin by brand name or specifications that were set by national experts in a non-transparent manner and in non-compliance with international standards for diabetes care,
- contract awards to suppliers of insulin without national marketing authorisation at the time of the analysis of the bidding documents in compliance with existing waivers that may lead to supply unregistered insulin when bids are awarded,
- disconnect between the amount of insulin vials and related syringes, or insulin cartridges and related pens and/or pen needles purchased,
- insufficient budget to purchase the amounts of insulin needed throughout the duration of supply agreements signed with manufacturers.

To review their procurement process for insulin and associated supplies, countries would benefit from the Interagency Operational principles for good pharmaceutical procurement[26], the managing procurement and managing the tender process chapters in the MSH guidelines[27] and the UN Procurement Practitioner's handbook[28].

National Regulations

Procurement of insulins and associated supplies should be carried out according to national procurement regulations. In some countries, public procurement is done through annual tenders, particularly when the amount of procurement is above a specific threshold. Restricted tenders should be preferred to open tenders for medicines and associated supplies according to the WHO Operational Principles for Good Pharmaceutical Practices.[29]

Some countries may decide to get the support from procurement partners at regional or global level to buy insulin and associated supplies, for instance because their needs are too small to attract offers from suppliers. This may require an adaptation of the national procurement regulations to do direct procurement from a pooled procurement mechanism at regional level or through UN agencies for example. However, in many LMICs, similar support is already provided for other categories of products such as TB, malaria, HIV/AIDS, or reproductive health products and this could be used to support the establishment of a similar mechanism for insulins and associated supplies. In this case, an agreement needs to be signed between the country and the procurement partner to define the roles and responsibilities of each party, describe the procurement steps to be followed and clarify the financial requirements. See page 18.

Procurement Strategies

Standard strategies

In most of the countries, procurement of insulin and associated supplies will be done with the general procurement of health products at national level either by a procurement department under the Ministry of Health (MoH) or through a national procurement centre having some autonomy. Procurement will then be done on behalf of public health facilities in a centralised manner according to national procurement regulations for the public sector. In countries where decentralization of health services is implemented, it may also include the decentralisation of procurement activities for health products. Governments should however consider that the absence of economies of scale may lead to higher prices.

Among the countries that are part of the ACCISS Study, the MoH in Peru delegates centralised drug procurement for public health structures to an entity within the MoH called CENARES. It oversees the purchasing of insulin to cover nationwide needs through international restricted tenders every two years. In case of stock-outs or need for specific medicines which are not listed on the current nEML, after an approval of a technical committee sitting at the MoH, public health structures can procure medicines directly on the Peruvian market in a decentralised mode through institutional purchase orders.

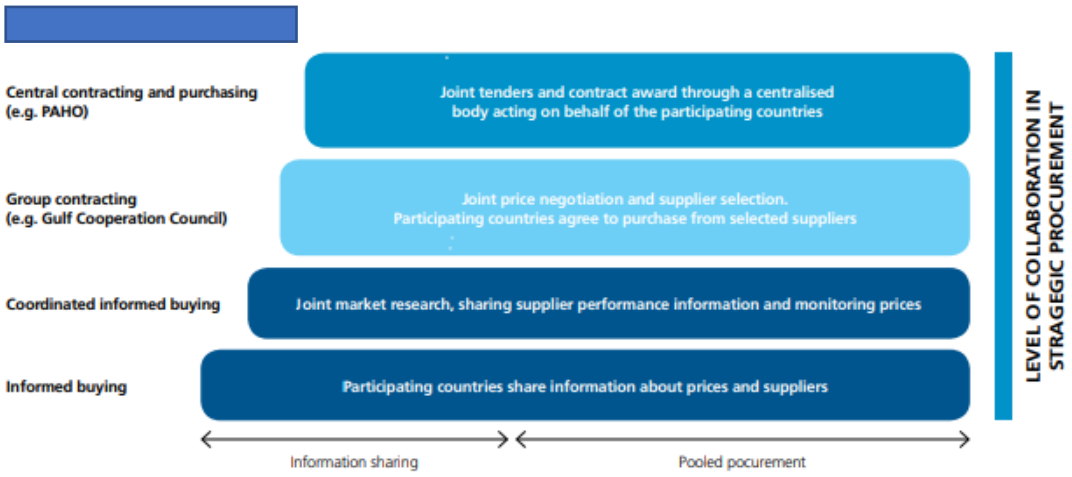
[26] https://www.who.int/3by5/en/who-edm-par-99-5.pdf
[27] https://www.msh.org/resources/mds-3-managing-access-to-medicines-and-health-technologies
[28] UN Procurement Practitioner's Handbook ver. 2017 (ungm.org)
[29] who-edm-par-99-5.PDF

Alternative strategies

Some countries with limited needs or procurement capacity might decide to partner with other countries to do multi-country pooled procurement (e.g., Gulf Cooperation Council[30] or Organization of Eastern Caribbean States[31]). Detailed analysis of these pooled procurement mechanisms for insulin and associated supplies is available in a report available in the ACCISS toolkit.[32]

The term "pooled procurement" covers several concepts, from information sharing to centralised procurement through a centralised body on behalf of several countries according to the scheme proposed below in Figure 2. It is extracted from a report published by the WHO Office for Europe (EURO)[33] and adapted from a model proposed by MSH. [34]

Figure 2. Levels of collaboration in strategic procurement



Note: PAHO = Pan American Health Organization.
Source: Modified from Management Sciences for Health *(22)*.

[30] https://www.gcc-sg.org/en-us/Pages/default.aspx
[31] https://caricom.org/institutions/organisation-of-eastern-caribbean-states-oecs/
[32] Analysis of pooled procurement mechanisms and their applicability for insulin and associated supplies in small state countries or countries with limited needs (with Pacific as a case study), 2021
[33] Challenges and opportunities in improving access to medicines through efficient public procurement in the WHO European Region, WHO 2016.
[34] Managing procurement. In: MDS-3: managing access to medicines and health technologies. Arlington, VA: Management Sciences for Health; 2012.

Multi-country pooled procurement will be valid for a group of countries having similar procurement challenges to attract the market. However, several conditions will need to be in place for a successful outcome, as per the box below.

Multicountry pooled procurement (PP) will require:

- Political will at the highest level in each country,
- A signed agreement to confirm each country's commitment to honour the conditions of the agreement,
- Adaptation of national procurement law/regulations to use the PP mechanism
- Harmonisation of regulatory requirements with other countries,
- A financial commitment from each government for the establishment of the PP mechanism and to pay suppliers on time,
- Use a similar currency than other countries while having a central national bank is helpful,
- Full support by each country to a permanent and autonomous common secretariat
- The support for expertise in procurement and QA at central level,
- Standardised needs with other countries,
- An effective communication channel established to reinforce trust between countries and the PP mechanism,
- Commitment to favor the PP mechanism for items in its scope in comparison to national procurement systems,
- Alignment of procurement cycles with other countries,
- Support for transparency on prices obtained through the PP mechanism.

More initiatives of pooled procurement are under discussion in other parts of the world, such as the Southern African Community[35], Scandinavian countries[36], Eastern European and Central Asian countries, etc. and could include insulin.

Other countries will choose to use regional or global pooled procurement mechanisms available through UN agencies (*e.g.*, PAHO Strategic Fund[37], UNICEF Supply Division[38], UNDP[39]).

UNICEF Supply Division (SD) is one of the UN agencies that has agreements in place for human insulin and associated supplies (particularly insulin syringes). Countries who are considering using UNICEF procurement services can check UNICEF SD catalogue (unicef.org) to find the price currently offered for human insulin. UNICEF SD has also put in place in its warehouse in Copenhagen a stock of insulin and all necessary procedures in place to guarantee the quality of the shipments under cold chain conditions.

[35] https://www.sadc.int/files/6614/1890/8516/SADC___SADC_POOLED_PROCUREMENT_OF_ESSENTIAL_MEDICINES_AND_MEDICAL_SUPPLI....pdf
[36] https://www.eversana.com/2020/02/18/first-joint-nordic-tendering/
[37] https://www.paho.org/en/paho-strategic-fund
[38] https://www.unicef.org/supply/
[39] https://www.undp-capacitydevelopment-health.org/en/capacities/focus/procurement-and-supply-chain-management/

These mechanisms are already experienced in procuring insulins and associated supplies through ad-hoc past procurement or Long-Term Agreements (LTA) in place with manufacturers/suppliers. Also, countries could benefit from the economies of scale and from the expertise and QA systems when buying through these mechanisms.

> An LTA is a written agreement between an organisation and a supplier that is established for a defined period of time for specific goods or services at prescribed prices or pricing provisions. It could include legal obligation to order any minimum or maximum quantities, but not always (*e.g.,* LTAs established by UN agencies do not include legal obligation to order minimum or maximum quantities).

In the case of emergency situations, some countries can also get the support of the WHO Global Supply Policies department[40] and will get insulin as part of kits developed by WHO. However, countries need to go back to a regular procurement process as quickly as possible to avoid over-stock of some items and loss due to expiry.

> The WHO Global Supply Policies department provides procurement support to countries through WHO Country Offices. It is mainly done using donor funds given to specific countries in emergency situations. Therefore, the procurement priority of WHO is mainly to the supply kits.
>
> Insulin and associated supplies (insulin syringes, insulin pens and needle pens, blood glucose meters, blood glucose test strips and lancets) are part of the Interagency Emergency Health Kit (IEHK). These items are also part of the NCD kit used mainly with displaced populations to maintain their treatment. Kits are supplied by WHO under Long Term Agreements in place with international suppliers (IDA, IMRES, MEG).

Some countries may also benefit from donations from pharmaceutical companies in specific circumstances (e.g., human insulin in the context of COVID-19 or through access programs) but this should not be seen as a sustainable procurement solution. Countries should also be alerted that such donations can be a marketing strategy from pharmaceutical companies to penetrate markets and create habits for prescribers.

When defining their procurement strategy, countries will also need to define if they want to buy insulins and associated supplies separately from other health products or as part of the national procurement process for all medicines and health products. To ensure availability of all medical devices necessary to administer insulin and monitor its administration, they may also want to consider buying all products from a same supplier to avoid interruption of treatment due to the absence of one item. This decision will have an impact on which procurement method to be used and more particularly the analysis of the offers received.

[40] https://www.who.int/about/accountability/procurement

Procurement Methods and Contract Awards

When selecting a procurement method, the objective should be:

- To obtain the lowest possible price for quality assured products,
- To ensure suppliers' reliability, in terms of both quality and services,
- To maintain transparency in the process and minimise the opportunity for illicit influences on procurement decisions,
- To obtain the shortest lead time.

When buying insulin and associated supplies, procurement methods selected should encourage competition as a primary objective to reach lower prices. It is important for this purpose to regularly monitor the global insulin market to identify manufacturers that may offer lower prices.

As demonstrated for other categories of health products, the most efficient competition can be established across suppliers when the volumes purchased are increasing with guaranteed funds and when originator products are in competition with generic ones.[41] In the case of insulin, an option would be to incentivise competition between originators (from Novo Nordisk, Eli Lilly, and Sanofi) and quality-assured biosimilar insulins. An alternative option for LMICs is to check eligibility to insulin access initiatives proposed by some pharmaceutical companies. However, due diligence should always be carried out by countries to check if they can purchase human insulin at a lower price from a different supplier. Also, these initiatives should not be seen as a sustainable solution based on competition, but just a temporary solution totally dependent on the willingness of companies.

Procurement of insulin and associated supplies should be done according to national regulations. In some countries, public procurement should be carried out through annual tenders, particularly when the amount of procurement is above a specific threshold. Restricted tenders should be preferred to open tenders for medicines and associated supplies according to the WHO Operational Principles for Good Pharmaceutical Practices.[42]

Countries buying insulin and associated supplies may also consider establishing LTAs. LTAs will favour economies of scale, lower prices, and total purchase cost, eliminate the need for yearly restricted tenders, help the seller to know the delivery schedule well in advance to plan production and reduce distribution costs, assure the country a reliable supply, and protect against arbitrary and unjustified price increases.

Tenders with larger insulin volumes are more likely to generate offers with lower prices and more favorable contract terms since bigger markets stimulate suppliers' interest in bidding and encourage them to offer competitive prices to be awarded larger contracts. Higher volumes may be achieved through pooling of procurement volume either at a national level over one or two year forecasted needs, or through multi-country or global pooled procurement mechanisms described above in the section on procurement strategies.

Another procurement method which can drive prices down over time and reduce the likelihood of stock-outs is purchasing from multiple competitively priced suppliers, rather than purchasing only from the supplier offering the lowest price.[43] This approach can incentivise more manufacturers to stay in a particular market, though it will require having enough procurement volumes to justify

[41] WHO guideline on country pharmaceutical pricing policies
[42] who-edm-par-99-5.PDF
[43] Van Valen M, Jamieson D, Parvin L, Ramirez CL. Dispelling myths about drug procurement policy. The Lancet Global Health. Volume 6, No. 6, e609-e610, https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30190-6/fulltext?dgcid=raven_jbs_etoc_email

the split and guaranteed orders regularly placed to all selected manufacturers to maintain their incentive.

This method could also be beneficial for people living with diabetes as it can help avoid changing insulin or glucose meter and test strip brands too often. However, this requires obtaining from manufacturers small differences in prices.

Restricted tenders among qualified suppliers

Procurement systems for health products, including insulin, should set up with restricted tenders where bids are only solicited from suppliers that have been qualified. Any supplier (*i.e.*, manufacturers or procurement agencies) should be considered as being either national, regional, or international. Some national regulations require business only through national suppliers (particularly wholesalers/distributors) which can lead to a negative impact on the prices offered that often include high mark-ups. Opening the restricted tenders to international suppliers can be helpful in encouraging national suppliers to reduce their prices to stay competitive. However, working with national suppliers (wholesalers/distributors) can have advantages as those suppliers tend to be more careful when dealing with the procurement and the importation process on behalf of their home country. Therefore, it is always important to compare offers on similar international commercial terms (IncoTerms) to allow a fair comparison of the offers received.

Setting up restrictive tenders will require defining criteria to qualify the suppliers based on their authorisation to sell the type of health products required, their QA/management systems and their past performance. One important element when qualifying the supplier for insulin is to ensure the QA requirements from the suppliers conform to national regulatory requirements. Qualification of procurement agencies can be done based on a questionnaire developed according to the WHO Model Quality Assurance Systems for Procurement Agencies. [44,45]

Qualification of manufacturers is based on their pharmaceutical license for production as well as confirmation of the Good Manufacturing Practice (GMP) status of the manufacturing site producing the required product according to national regulations. The existence of valid national marketing authorisations for insulins should also be considered whenever countries have functional regulatory agencies, as per the WHO Global Benchmarking Tool. [46] Countries that do not have functional regulatory agencies can rely on manufacturers having registered insulins with Stringent Regulatory Authorities (SRA) as defined by the WHO and, by 2022, those with prequalified insulins with the WHO Prequalification Programme (WHO PQP)[47].

When receiving offers from manufacturers/suppliers, it is key to compare the prices offered with prices available to neighbouring countries or other countries with similar procurement systems or economic situations. Regional procurement prices and/or online price databases can be useful but for the latter, it is often required to be a member or to pay to receive data.[48,49] The UNICEF SD catalogue[50] or catalogues may be shared upon request by some international distributors and could be useful.

Based on the outcome of the restricted tenders, it would be advised to establish a contract/LTA with suppliers for a certain period and a specific quantity (with some flexibility to cover potential extra-needs). Countries with large volumes can consider awarding contracts to two suppliers as it

[44] TRS986annex3.pdf (who.int)
[45] trs986-annex4-assessment-tool-based-on-the-model-quality-assurance-system.pdf (who.int)
[46] https://www.who.int/medicines/regulation/sras/en/
[47] https://www.who.int/medicines/regulation/prequalification/pq_human_insulin/en/
[48] PIEMEDS
[49] Pharma Price Information (PPI)
[50] Home page (unicef.org)

is always good practice to have a main supplier and a back-up supplier in case of production/performance issues with the main supplier. An 80/20 split of quantities can be considered.

Request for quotations from a limited number of suppliers (also known as competitive negotiation)

When allowed by national regulations, a small number of suppliers can be approached to get quotations. This may be applicable particularly if a country decides to buy all items (insulin and associated products) through a single supplier. This method is often used for small volume items, for emergency orders or when the number of manufacturers is reduced, which is particularly the case for insulin.

This procurement method requires a good market intelligence for insulin and associated products and particularly good knowledge of their prices in countries with similar economic level. All health products for diabetes care can also be purchased through international distributors with global footprint holding a pharmaceutical distributor licence in their country of origin. Several distributors with insulin and associated supplies in their catalogue can be contacted to compare their prices and contractual conditions.

In this case, customers can benefit from the economies of scale from international distributors operating in many countries, from their QA systems and often from long term agreements with transport companies, which may decrease the cost of transport and insurance.

A non-exhaustive list of international distributors offering insulin and associated supplies is accessible here.

Direct procurement through an international procurement agency, such as a UN agency

In many LMICs, some health products are procured through UN agencies as part of their programmatic support to governments for HIV/AIDS, TB, malaria, and reproductive health. This procurement is often funded by donors, but sometimes countries can also use their government budget to complete this procurement. Some agencies, such as UNICEF SD, UNDP or UNOPS, can also provide procurement services for health products to governments. UNICEF SD and UNDP have already started to support countries with procurement services for NCD medicines, including insulin and associated supplies (see box 2, page 12).

Direct procurement of any health products, such as insulin and associated supplies, through an international procurement agency should be authorised in the national regulations.

Where this is already the case for other categories of health products, this option may be covered by legislation. Otherwise, an adaptation in the national procurement regulations or an official waiver from the government will be needed.

Countries may also want to consider placing their order for insulin and associated supplies with other categories of health products to allow joint deliveries, particularly if all these products come from a stock available at the UN agency level.

One of the challenges to overcome when placing an order through UN agencies is prepayment conditions, as funds must be available upfront. Some UN agencies have put in place financing facilities that are accessible to countries to start the procurement before funds are transferred. Countries may want to explore this possibility when contacting any UN agency.

Buying through a UN agency can allow countries to benefit from Global LTAs for the health products purchased and take advantage of Global LTAs in place for transport and insurance. In addition, they benefit from the QA systems put in place by the UN agencies, compliant with WHO Model Quality Assurance Systems for Procurement Agencies. However, handling charges will need to be considered.

Direct procurement from pharmaceutical companies with access prices LMICs

Currently, Novo Nordisk is offering a ceiling price for human insulin of USD 3 a vial for 76 LMICs as part as Access to Insulin Commitment[51] to strengthen their efforts to reach the most vulnerable people with insulin at a reduced cost. Whenever countries are eligible for this offer, it is recommended to consult Novo Nordisk[52] directly and compare their offer with prices from other manufacturers supplying quality-assured insulins. When contacting Novo Nordisk, the eligibility of the country and IncoTerms should be confirmed (as no detailed list of eligible countries or IncoTerms are publicly available).

Procurement officers should also be encouraged to regularly monitor if new differential prices are offered by other manufacturers to LMICs. Countries with larger volumes should always keep in mind that, when doing tenders, they may often get lower prices than this ceiling price.

Budget and Availability of Funds at the Right Time in the Procurement Cycle

Potential sources of funds for insulin and associated products procurement can include those from the government or funds collected through user fees and/or health insurance. On rare occasions, procurement of insulin and associated supplies will be funded by donors (e.g, OCHA, European Commission).

To secure the necessary funding to cover the full quantity of insulins and associated supplies required nationally over a year or more, as per the schedule set for government procurement, all avenues should be explored, especially when developing Universal Health Coverage schemes.

If the available budget happens not to be enough to cover all the needs for insulin and associated supplies, a prioritisation exercise should be set up to classify all products grouped in the same procurement process in terms of vital, essential, and non-vital criteria. Within the group of insulin, arbitration could also be set up between human and analogue insulins, always considering specific needs of some groups of people with diabetes.[53]

Tender/Bidding Documents and Important Elements for Consideration When Doing Procurement

Management Science for Health[54] and associations of Central Medical Stores, such as the ACAME[55], provide advice on standard structure of bidding documents and even a standard dossier to be used to meet generic requirements when purchasing health products. These standard formats may need to be customised to legal requirements at national level when it comes to contractual agreements.

[51] Defeat diabetes (novonordisk.com)
[52] https://www.novonordisk.com/contact-us.html
[53] https://haiweb.org/wp-content/uploads/2016/04/ACCISS-Prices-report_FINAL-1.pdf
[54] https://www.msh.org/sites/default/files/mds3-jan2014.pdf
[55] https://www.acame.net/en/

Specifications

To ensure fair competition when doing procurement and to meet clinical outcomes anticipated in National Treatment Guidelines, it is important to define for each product purchased clear specifications.

Insulin specifications should include several parameters:

- INN of the insulin purchased: INN are created by WHO and the list of updated INN for insulin is available under the INN School website.[56]
- Specify if human or analogue insulin.
- Specify the timing of their action: rapid-acting, short-acting, intermediate-acting, or bi-phasic (a mix of short acting and intermediate acting), long-acting.
- Add the strength: described in international units IU/ml (40, 100 or 300).
- Add the presentation required: vials, prefilled pens, cartridges, and the volumes (*e.g.*, 10ml vials, 3ml pens, etc…).

Whenever insulin specifications are not detailed in the national standard list for procurement (catalogue), they should be set based on National Treatment Guidelines and nEML by an expert committee in which members should demonstrate their freedom from any vested interest towards the pharmaceutical industry.

Those insulin specifications should be strictly reported into bidding documents.

Specifications for insulin syringes, blood glucose meters and test strips should be generic enough to allow more competition across suppliers. WHO is currently working on specifications for blood glucose meters and hopefully these specifications will be soon available on their website. Target product profiles describing the main characteristics for blood glucose meters for self-monitoring are also under development to guide manufacturers to propose blood glucose meters more adapted to the needs of people living with diabetes.[57] Countries could also rely on specifications available on UNICEF SD catalogue for insulin syringes.[58]

Manufacturers frequently give blood glucose meters for free to impose a brand and the regular purchase of test strips for this specific brand. It is preferable for countries to define the type of blood glucose meters they need taking into consideration the cost of the test strips.

Buying all products as a lot or within a bundle

Before launching a procurement process, and to avoid having insulin vials without insulin syringes for instance, countries may consider purchasing all necessary products for diabetes care in a lot for procurement. WHO, in collaboration with PATH, is working on a prototype to bundle insulin with associated products necessary for delivering insulin and self-monitoring blood glucose levels[59]. This option should be considered carefully by countries and lessons should be learnt from the experience of countries receiving kits.[60] Countries should balance the advantages of guaranteeing the availability of all items with the risks if the prototypes proposed are not well designed. This approach may indeed lead to more expired products and a waste of resources.

[56] https://extranet.who.int/soinn/
[57] World Diabetes Day 2020 - FIND (finddx.org)
[58] Syringe,insulin,1ml,U-100,30-31G/BOX-100 (unicef.org)
[59] https://www.path.org/media-center/path-and-helmsley-charitable-trust-partner-improve-access-safe-administration-insulin-and-self-care-people-living-diabetes/
[60] JSI_LogisticHandbookAddendum_2_2020.pdf

Quality Assurance requirements

For suppliers

Procurement agencies or wholesalers contracted out to procure health products, including insulins and associated supplies, should comply with the WHO Model of Quality Assurance system for procurement agencies[61]. Compliance to this standard ensures customers that these suppliers have a quality manual, qualification procedures of manufacturers, procurement strategies and methods, purchasing, storage and distribution capacities in line with WHO standards.

Any supplier of health products (i.e., manufacturers or procurement agencies), including insulin and associated supplies, should comply with the WHO Good Distribution and Storage Practices[62]. Compliance to these standards ensures that the quality of health products handled by suppliers is maintained throughout the numerous activities that occur during the trade and distribution process. It also prevents their distribution system from supplying falsified, unapproved, illegally imported, stolen, substandard, adulterated and/or misbranded medical products. Finally, it also guarantees that the quality of health products they procure is maintained by means of adequate control throughout their storage.

For insulin

The QA criteria for approving insulin supplied by a manufacturer/supplier are based on national regulations and/or WHO norms and standards for medicines (more particularly if there is no national registration in place in country).

- When limited regulatory capacity exists in country, it is strongly recommended to rely on approvals granted by Stringent Regulatory Authorities[63], WHO Prequalification Programme (WHO PQP)[64] (currently assessing human insulins[65]) or UN agencies, more particularly for biological products, such as insulins.
- Biosimilar insulins are available on the international market. It is strongly recommended to accept only those which were granted marketing authorisation/registration by a Stringent Regulatory Authorities as the assessment of biological products requires specific expertise which is not yet available in all LMICs. Considering the WHO PQ Programme has recently included human insulin in their scope, countries should regularly monitor the medicines WHO PQP website[66] to see if biosimilar human insulins have been listed. To find out more about biosimilars and biosimilar insulins, the ACCISS toolkit is a useful resource.[67]

Biosimilars are just as they sound: a “similar” version of a biological medicine. As with generic medicines, biosimilars can only be produced once a patent for the original biological medicine has expired or if a voluntary license is signed between the innovator and the biosimilar company

[61] https://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS986annex3.pdf?ua=1
[62] https://www.who.int/publications/m/item/trs-1025-annex-7-gdp-medical-products
[63] List of Stringent Regulatory Authorities (who.int)
[64] WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control) | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)
[65] https://www.who.int/medicines/regulation/prequalification/pq_human_insulin/en/
[66] Welcome to Medicines Prequalification | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)
[67] Biosimilar Insulin FAQ - Haiweb - Acciss Toolkit

For associated products

QA criteria for approving insulin syringes, blood glucose meters and test strips should be based on national regulations for medical devices, if available, as well as on WHO norms and standards for health products.

When limited regulatory capacities exist in countries, it is strongly recommended to rely on regulatory approvals given in countries being founders of the International Medical Device Regulators Forum (IMDRF), being European Union, United States, Canada, Australia, and Japan[68] or approved sources by UN agencies.

IncoTerms

When selecting the IncoTerms for procurement of insulin and associated supplies, countries should take into consideration their capacity to handle transport, customs clearance, and insurance of goods in transit. For countries having limited capacity or buying small volumes, it might be easier to consider Carriage and Insurance Paid To (CIP) or Delivered A=at Place (DAP) IncoTerms.

When comparing offers from different suppliers (either national, or regional or global), it is important to compare prices with similar IncoTerms. The same should be considered when doing direct procurement from UN agencies or directly from manufacturers. Small countries having limited capacities to handle transport or countries logistically difficult to reach, such as island nations, should always favour IncoTerms including transport and insurance.

Payment terms

As with the purchase of any health product, payment terms will be important to define (partial pre/post-delivery, following delivery or prepayment needed).

When initiating the procurement process, it will be important to ensure funds are made available when payment is required.

Delivery conditions (split deliveries, specific conditions)

When doing annual procurement, for countries purchasing large volumes, there is a need to specify if deliveries should be split to get better expiry dates. Careful attention paid to the total shelf-life of products is needed to avoid product loss due to expiry, as well as to the remaining shelf-life required for products at delivery in country.

It is also important to highlight the storage conditions for insulin and some glucose test strips and to ensure delivery of insulin is done under appropriate conditions (2 to 8°C). Data-loggers should be required in consignments for insulins and other cold chain products during transport and in all transit storage premises.

[68] GHTF Archives (imdrf.org)

DISTRIBUTION AND STORAGE

The procurement strategy used should consider the distribution and storage capacities at national level.

Insulin and associated products, like other products, should be distributed and stored according to WHO Good Practices for Storage and Distribution.

As a standard practice, all shipments from suppliers should be physically checked on receipt. Regular distribution to health facilities should be done according to the needs defined based on an order form (paper based or electronic) and storage capacity in health facilities taking into consideration a buffer stock to avoid stock outs.

If transport is subcontracted to an independent company, clear requirements should be stated in the contract and the application of these requirements should be monitored. Insulin is required to be stored between 2°C and 8°C, therefore a cold chain should be in place at the central level but also at regional/provincial levels and in health facilities receiving the products. At reception, it is important to check data-loggers included in the shipment, if any, and to download the data to check if there was any temperature excursion during transport. In case of any excursion, the information must be forwarded to the supplier QA department for them to confirm if the product could still be used or not.

Before delivering insulin to health facilities, confirmation should be made that they have a functional refrigerator to keep insulin and to regularly monitor and keep record of the temperature inside the refrigerator at least twice a day. It is also important to record batch numbers of products delivered and to accompany deliveries with key documents (delivery note) to be signed by health facilities.

Adequate storage capacity should also be in place to keep the insulin syringes and the blood glucose meters and test strips. Storage conditions for glucose tests strips are usually between 4°C and 30°C but they should not be stored or transported under cold chain conditions.

USE

Clear instructions on storage and use of insulin, consistent with the regulator-approved information, should be given to health workers and people using insulin, as well as guidance on how to use blood glucose meters and test strips.

It could be useful for pharmacists to develop a short leaflet to be given to people using insulin, and to have available in-person counselling on use, in addition to the advice given by health workers. This leaflet should include guidance related to storage conditions for insulin and associated products such as test strips as well as contact details in case of a problem with the product. It could also include guidance on the administration of insulin and the necessary monitoring to be performed by people living with diabetes.

Guidelines are also developed in some countries[69] and user guidelines are also available from ISPAD[70]. Advice should be provided to people on the possibility to keep insulin outside of cold chain at user level for a maximum of four weeks at below 25 °C and protected from light. Blood glucose test strips, after opening the container, have a limited shelf-life (between three to six months depending on the brand) and should be kept between 4°C and 30°C, but not in a refrigerator or freezer. Depending on the brand procured, clear instructions should be given to people living with diabetes.

[69] http://med.kg/images/MyFiles/KP/2019/endokrinology/kp_SD1_tipa_diagnostika_i_vedeniye.pdf
[70] https://www.ispad.org/page/ISPADGuidelines2018

In countries where biosimilar insulins are approved and procured, clear instructions should be given to prescribers on switching between originators and biosimilars and the advice should be developed with the support of National Regulatory Authorities.[71] At the time of writing, even in countries with Stringent Regulatory Authorities, no guidance is available describing how to switch between different biosimilars.

As adherence to treatment being key in diabetes care, it would be important to regularly get feedback from users on their use of the products received. They should also be encouraged to notify to health workers and pharmacists of any issue faced with health products supplied to them.

Clear instructions should be provided on safe waste management of insulin syringes and empty vials/pens according to national regulations for health products. If necessary, countries could also refer to the WHO guidelines for waste management.[72]

MONITORING AND EVALUATION

Procurement Performance

At least once a year, standard indicators should be reassessed within the national procurement system of medicines, including insulin, to optimise over time availability and affordability criteria.

These indicators could include:

- planned versus actual types (including strengths and presentations) of insulin purchased and in what quantities compared to forecasted needs,
- prices obtained locally in comparison to international prices for insulins,
- supplier performances based on delivery lead-time, compliance with contract terms, partial shipments, quality alerts, remaining shelf-life at delivery, compliance with packaging and labelling instructions based on valid local marketing authorisations,
- percentage of insulin in stock at various levels of the supply system,
- report on stock-outs and sub-standard quality of insulins.

Quality Issues

A formal system should be established which encourages health workers, pharmacists, and insulin users to report potential problems (*e.g.*, toward side effects, lack of efficacy as well as frosted or discolored insulin liquid, or insulin that has threads or clumps). Poor product quality needs to be reported to the National Regulatory Agency and the Central Medical Store when it exists.

Price monitoring and transparency on prices

For insulin in particular, it is important to regularly monitor prices obtained by other countries with a similar economic level. This will help countries to check the procurement strategy used is allowing them to get the best possible prices. As suggested by WHO in its recent WHO guideline on country pharmaceutical pricing policies[73], it is also important for countries to be transparent on prices obtained from procurement and to make this information available in the public domain. Often pharmaceutical companies may resist to the publication of their sales prices to a particular country and will add confidentiality clauses in agreements/contracts signed with procurers at national or global level.

[71] InterchangeabilitFINAL28aug.pdf (haiweb.org)
[72] WHO | Safe management of wastes from health-care activities
[73] WHO guideline on country pharmaceutical pricing policies

HEALTH ACTION INTERNATIONAL

WWW.HAIWEB.ORG