

What are pharma companies doing to expand access to insulin – and how can efforts be scaled up?

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Millions of people with diabetes worldwide, but especially those in low- and middle-income countries (LMICs), can neither access nor afford the insulin that they need. Although pharmaceutical companies are taking action to address affordability and have begun scaling up initiatives deemed successful, efforts remain confined to a few products, settings, and countries. As the rising burden of diabetes becomes a pressing issue for many healthcare systems in LMICs, and as new products and players enter the market, the biggest challenge will be to make progress at scale so that a genuine choice of insulin products is always available to people in these countries. This study examines companies' strategies to overcome barriers to access, highlights areas where progress has been made and identifies opportunities for future action.

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ACCESS TO MEDICINE FOUNDATION

The Access to Medicine Foundation is an independent non-profit organisation that seeks to transform the healthcare ecosystem by motivating and mobilising companies to expand access to their essential healthcare products in low- and middle-income countries.

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Table of contents

- 4 Executive summary**
Global insulin inequity is stark, and current access efforts fall short – but companies are now seeking sustainable ways to scale up access
- 6 The challenge**
Lack of access to insulin is a devastating problem for diabetes patients globally
- 12 Company profiles**
How are companies addressing access to insulin?
- 13 Eli Lilly
- 15 Novo Nordisk
- 18 Sanofi
- 20 Biocon
- 22 Industry analysis**
- 22 Lack of registration of essential insulins in LMICs is a barrier to expanding access
- 26 Companies are expanding access models, but system-level approaches to address chronic care are lacking
- 27 A patchwork of strategies to improve affordability
- 29 New strategies and partnership models are being used to tackle challenges in the insulin supply chain and the delivery of diabetes care
- 32 Spotlight**
Access to insulin for children and young people
- 34 Next steps**
How to meet the challenge of expanding access to insulin
- 36 References**
- 38 Appendix**

About this paper

How this paper was developed

The content in this paper has been drawn from data available in the public domain, peer-reviewed literature, and global health and policy reports. The paper was further informed by data collected for the 2022 Access to Medicine Index, as well as additional data collected specifically for the purpose of this publication and interviews held with partners and experts in the diabetes field. The content was supplemented with information provided by industry and global health stakeholders during the Expert Session ‘Closing the gaps in access to diabetes care in low- and middle-income countries’ hosted by the Foundation on 7 July 2022. A more detailed description of the methodology can be found in the appendix.

SCOPE OF THE RESEARCH

Companies

This study specifically analyses the actions of the three main insulin manufacturers: Eli Lilly, Novo Nordisk and Sanofi. One major manufacturer of biosimilar insulins, Biocon, is also in scope. The activities of other companies and organisations are also considered to provide context or support the information included in this study.

Products

This study is focused on insulins, which are essential products for many people living with diabetes mellitus. Data collected and analysed specifically includes human insulin (regular and isophane) and analogues including aspart, degludec, detemir, glargine and lispro. A full product list can be found in the appendix.

Countries

This study is focused on the context and actions taking place in 108 low- and middle-income countries (LMICs) that are home to over 80% of the world's population, using the same inclusion criteria as the 2022 Access to Medicine Index. A full country list can be found in the appendix.

EXECUTIVE SUMMARY

Global insulin inequity is stark, and current access efforts fall short – but companies are now seeking sustainable ways to scale up access

- ▶ Companies carry out a variety of initiatives to expand the reach of their products in LMICs, but often with limited scope, breadth and scale.
- ▶ By collaborating to solve access challenges, stakeholders in the global insulin ecosystem can take action to systematically and sustainably address the insulin access gap and increase treatment choice.

The number of people with diabetes worldwide is expected to reach 643 million by 2030, and 783 million by 2045, rising most rapidly in low- and middle-income countries (LMICs) as the burden of non-communicable diseases grows.¹ Yet, in LMICs, many people who need insulin currently do not have access to this essential, life-saving drug – and many more do not have the choice of products that all patients deserve. This is despite huge advances in diabetes treatments over recent decades, including products such as analogue insulins, which have already become well-established and preferred by patients and their healthcare practitioners in higher-income countries.

Pharmaceutical companies can play a major role in reversing this inequity by expanding access to their insulin products worldwide, including all the different types of insulin products in their portfolios. This paper looks at what companies are doing – or not doing – to address the core issues. Under the spotlight are the three companies that dominate the global insulin market: Eli Lilly, Novo Nordisk and Sanofi. Combined, these companies control over 90% of the global insulin market by value.² This paper also examines Biocon, a smaller company that markets biosimilar insulins, shedding light on the role played by such companies and their products (biosimilar insulins) in increasing access in LMICs.

Poorer populations miss out on access to insulin and treatment choice

No matter where they live in the world, every person deserves the medical treatment that would be best for them. The World Health Organization (WHO) recently added several analogue insulins to its Model List of Essential Medicines, with analogues joining the human insulins that were already listed – demonstrating an increasing recognition by global health stakeholders that both types of insulin are needed for patients in all countries.

Because registering a medicine is a necessary step that enables its sale in a country, data about registration can reveal a great deal about where a company is making a drug available (or has intentions to do so), and where it is not. Companies are taking steps to make their products available in LMICs, yet analysis by the Access to Medicine Foundation shows that poorer populations are being consistently overlooked when it comes to registration.

In some LMICs, the variety of types of insulins available is very limited. Only 29 of the 108 countries in scope have all the insulins classified as “essential medicines” by WHO registered, and only one of those is a low-income country. Worse, in 24 countries, no insulins were found to be registered at all. When even this initial step towards access has not been taken for any insulin products, the situation for those who need insulin to survive is very grave indeed.

Analogue insulins are widely registered in high-income countries, and most upper-middle income countries have at least one analogue insulin registered. However, at the bottom end of the country income scale, 15 of the 27 countries classed as low-income do not have a single analogue insulin registered. When no analogue insulins are registered, patients lose out on important treatment choices.

Addressing insulin affordability as a priority

The affordability of insulin remains a significant issue. Human insulins, while more broadly available than analogue insulins in LMICs, are still out of the reach of many people with diabetes. Analogue insulins are often priced significantly higher than human insulins, especially in LMICs, creating further barriers to access. In general, pharmaceutical companies have previously focused their attention primarily on expanding access to human insulins in LMICs, with analogues viewed as less of a priority – but this approach has started to shift, and could shift further in the future, as the importance of patients having access to both human and analogue insulins, and the need for competition from biosimilar products, is acknowledged.

Tapping into the potential of biosimilars

Expanding the number and type of insulins on the market in LMICs will have a positive impact on both availability and affordability. For this reason, quality-assured biosimilar insulins hold a great deal of potential, especially as several patents on long-acting insulins have recently expired – meaning biosimilar versions can now be launched as competitors. While the insulin market continues to be dominated by global insulin manufacturers, several biosimilars companies do already produce and market a significant quantity of insulin products in LMICs. However, companies have significant hurdles to overcome before their products' potential to expand access can be fully realised, including challenges in scaling up, competing with established brands, and satisfying complex regulatory requirements.

Seeking sustainable strategies to expand access

Over the last decade, as laid out in the company profiles on pages 12-21, insulin manufacturers have been building access programmes and exploring different strategies and initiatives in LMICs. They have tried a patchwork of approaches, often focused on a small number of countries, or based around particular types of products (e.g. human insulins) or specific patient populations (e.g. children). Most strategies are project-based and limited in scope, and do not yet guarantee sustained access for insulin-dependent patients requiring ongoing, life-long treatment.

However, companies are now starting to seek more sustainable, systemic approaches to expanding access to insulin in LMICs. This includes developing targeted approaches to address the needs of specific populations lacking effective access to healthcare, and engaging in partnerships to strengthen local health systems and supply chains. One particular consideration is that access to insulin must be paired with access to the monitoring devices (e.g. glucometers) and delivery devices (e.g. needles) that are needed to use insulin effectively and keep diabetes under control. As such, solving the major problems in access to insulin involves looking at insulin within the broader picture of patients' needs, and considering access to other essential products for managing diabetes.

To achieve long-term improvements and ensure that patients have access to the best available treatments, companies must step up efforts to ensure that successful access strategies are scaled up to reach more people, and strategies are expanded to include all insulin products. This paper identifies some of companies' existing efforts towards making sustainable access to insulin a reality in LMICs, as well as looking at where action is not currently being taken, and where gaps remain. While the challenges are complex, there is now real momentum towards overcoming those challenges and pursuing opportunities to sustainably expand access to insulin products in LMICs.

THE CHALLENGE

Lack of access to insulin is a devastating problem for diabetes patients globally

Insulin was discovered 100 years ago, transforming type 1 diabetes from a certain death sentence into a treatable long-term condition. Yet this transformation has been far from universal. Huge numbers of people living in low- and middle-income countries (LMICs) still do not have access to the diabetes products, including insulin, that they need to stay alive and healthy.

Daily access to insulin is essential for survival for patients with type 1 diabetes and many with type 2. Unfortunately, insulin products are often unavailable to those living in LMICs – and when they are available, they are often unaffordable. The stark reality is that without access to insulin, many more diabetic children and adults will suffer and die from this life-long, chronic disease.

This is certainly not a new problem; global gaps in access to insulin have been present ever since it was first discovered, manufactured and sold. But the problem is becoming more acute. The costs related to managing this condition represent a concerning global burden, as total health expenditure due to diabetes in adults amounted to USD 966 billion in 2021¹. The number of people with diabetes is expected to hit 643 million worldwide by 2030, and cases, mainly of type 2 diabetes, are rising most rapidly in LMICs. The situation is worsened by poverty, conflict and outbreaks of disease. Local and global disruptions threaten supply chains, damage fragile healthcare systems, and threaten both availability and affordability.

About diabetes

Diabetes mellitus, also commonly known as diabetes, is a chronic condition in which the body is unable to produce or properly use insulin, an essential hormone that helps regulate blood glucose levels. When diabetes is left untreated, persistent high blood glucose levels cause devastating effects in body organs, including cardiovascular disease, kidney failure and nerve damage. Untreated or poorly controlled diabetes can lead to premature death in some cases and disabling conditions in others, such as lower-limb amputations and partial or complete vision loss.¹

The most common types of diabetes are known as type 1 and type 2 diabetes, with other types including gestational diabetes. Type 1 diabetes often has its onset during childhood or young adulthood. Because of the body's non-existent or very limited capacity to produce insulin, people living with type 1 diabetes need daily injections of insulin to survive. Type 2 diabetes is the most common type of the disease; it is generally diagnosed in adulthood, although onset in young people has been increasing in the past decades. Treatment of type 2 diabetes includes diverse interventions and medications, sometimes including insulin, which is an essential treatment for about 15% (approximately 63 million) of people living with type 2 diabetes worldwide.³

Momentum for change

This is a key moment to make a leap forward and address the chronic lack of equity in access to diabetes treatment, because several developments have coalesced that are potentially game-changing.

For one thing, the last three decades have seen significant innovation. Products have been launched that can significantly improve the lives of people living with diabetes, such as analogue insulins (see box, page 7), which can allow for improved

Diabetes by numbers:^{1,3}

- ▶ Over half a billion adults worldwide currently have diabetes.
- ▶ Three out of four adults with diabetes worldwide live in LMICs.
- ▶ Around 45% of people with diabetes are undiagnosed and unaware of their condition.
- ▶ Worldwide, 6.7 million deaths per year were attributed to diabetes in 2021.
- ▶ Insulin is estimated to be needed by over 72 million people, including 9 million people living with type 1 diabetes.
- ▶ Approximately half of the people living with type 2 diabetes who need insulin worldwide are actually receiving treatment.
- ▶ An estimated 94% of the global increase in diabetes by 2045 will occur in LMICs. The number of people living with diabetes is projected to grow 129% in Africa by 2045, in comparison to an estimated growth of 13% in the European region.

control of blood sugar levels after meals and overnight - making patients' lives easier, cutting the risk of hypoglycaemia (low blood glucose levels), and potentially increasing adherence to treatment. Alongside this, some insulin products now allow more storage flexibility by decreasing the need for refrigeration – an advantage in many low-resource settings –, and more user-friendly delivery and monitoring devices have been developed, including pens and insulin pumps.

For another thing, WHO recently made a landmark decision about analogue insulins. Human insulins have been recognised as essential products and have been included in the WHO Model List of Essential Medicines (EML) since its very first edition in 1977; but in 2021, WHO made the landmark decision to add long-acting analogue insulins degludec, detemir and glargine – and their biosimilars – to the list.

The addition of several analogue insulins to the EML is a recognition of the importance of these products to diabetes patients in every country, and the need for more competition in the market, and could be a catalyst that changes the way companies and governments consider the role of analogues in LMICs. However, as things stand, analogues are significantly more expensive than human insulin⁴ and still represent the minority of overall insulin volumes used in LMICs.⁵ A concerted approach is urgently needed to expand access to all types of insulins so that health-care practitioners are able to offer their patients a genuine choice and prescribe the best treatment for each person and their circumstances.

The fact that patents on certain analogue insulins have recently expired could also have positive implications for access. This could lead to healthy competition from biosimilar versions (see page 9), and therefore more competitive prices in LMICs. Biosimilars face many challenges in the global diabetes market, as this paper will explore – but there is a real opportunity to expand access to analogues now that off-patent versions are possible.

With the launch of WHO's Global Diabetes Compact in 2021, there is renewed impetus towards bridging the gaps in access to diabetes care worldwide, as well as clear goals and a framework for change (see box, page 8). The first-ever global targets for diabetes were ratified by the World Health Assembly in 2022, including the

Types of insulins

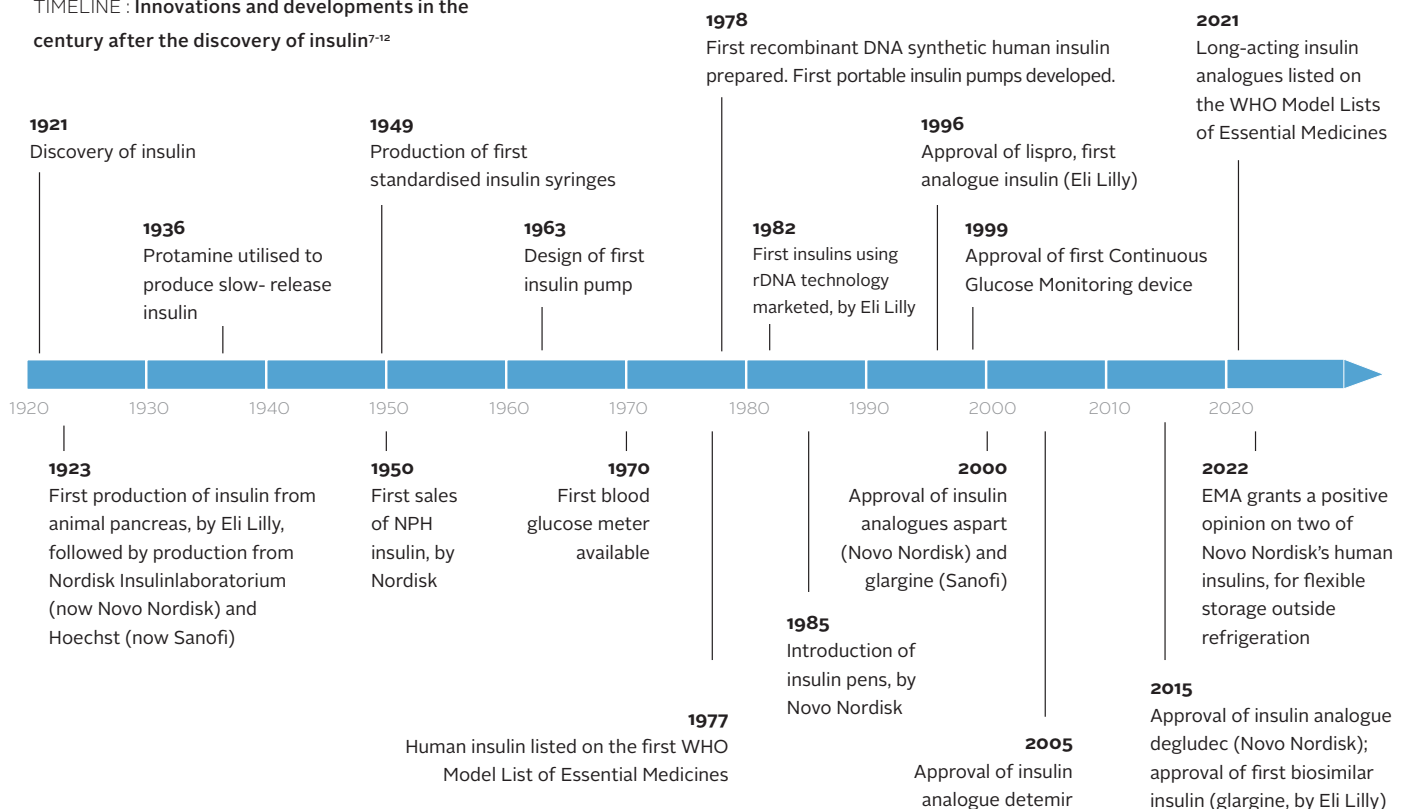
Insulin production began in the 1920s from animal pancreases. Currently, biosynthetically produced insulin has almost fully replaced the global use of animal insulin. Two types are available on the market: human insulins and analogue insulins.

Human insulins have been available for over 40 years. This type of insulin includes human regular insulin, which has a relatively short onset and duration of action, and isophane or Neutral Protamine Hagedorn (NPH) insulin, which has an intermediate range of action.

Analogue insulins are newer products with a targeted onset and duration of action, which facilitates a more specific blood sugar control. Rapid-acting products include aspart and lispro, and long-acting products include glargine and detemir. These were introduced in previous decades, but recent years have seen the introduction of products with ultra-long range of action, such as degludec.

In addition to insulin, patients sometimes need **glucagon** injections to increase blood sugar levels and counter the adverse effect of an excessive dose of insulin.

TIMELINE : Innovations and developments in the century after the discovery of insulin⁷⁻¹²



goal that 100% of people with type 1 diabetes have access to affordable insulin and blood glucose self-monitoring by 2030.⁶

Given these advancements and the pressing need to address the global diabetes burden, the momentum for change must not be lost. A century on from the discovery of insulin, efforts to expand access to insulin must be scaled up so that the millions of people living with diabetes worldwide can have full access to insulin, including human and analogues, and all the long-term care they need to live full and healthy lives.

This paper seeks to inform and inspire more collaborations and actions from companies involved in the global insulin market, as well as from policymakers, investors, local governments and global organisations. It is published by the Access to Medicine Foundation, which has been tracking pharmaceutical companies' actions on access to their diabetes products in LMICs for more than a decade. By identifying opportunities for improvement, and by engaging with key stakeholders in access, the Foundation stimulates companies to improve access to their products across the world.

The analysis in this report builds on data collected by the Foundation's Access to Medicine Index, which – since 2008 – has been measuring and analysing how of some of the world's largest pharmaceutical companies perform on access to medicine. The main global insulin manufacturers – Eli Lilly, Novo Nordisk and Sanofi – were also given the opportunity to submit further data on their insulin products for analysis in this report. Data was also collected from Biocon, an Indian company which is one of the largest producers of biosimilar insulin.

The global insulin market is dominated by three companies

The insulin market is currently dominated by three pharmaceutical manufacturers. Together, Eli Lilly, Novo Nordisk and Sanofi control over 90% of the global insulin market by value.^{2,13} These three manufacturers produce 83% of the insulin sold in LMICs, where they also hold around 95% of the market share.⁵ In 2021, these three companies' yearly combined global revenue from insulin was approximately USD 18 billion.^{14–16 *}

Yet, these companies – and the handful of smaller companies that make up the remaining share of the market – do not make all of their products available in every country in the world. Many people living in LMICs have access only to a limited selection of insulin products, because – for example – a company may not see the commercial value of registering and launching its product in a particular market. Even though companies have made commitments to increase insulin access, products remain out of the reach of health systems – and therefore patients – in many LMICs.

While in some countries there is limited choice, in other countries there are no options to choose from whatsoever. In these countries, which are among some of the poorest in the world, none of these companies' products are made available – meaning that diabetics simply cannot get the insulin they need.

Affordability remains a barrier to accessing insulin

The challenges impacting affordable access to insulin are complex and multifaceted. While the public sector covers the cost of insulin in some LMICs, either directly or via reimbursement, many patients in LMICs pay out-of-pocket.¹⁷ Overall, the percentage of patients paying out-of-pocket for healthcare is 35% in LMICs, compared to 13.6% in high-income countries, where the public sector is more likely to be involved.¹⁸ Unfortunately, higher insulin prices are usually found in the private market – further compounding the issue for patients living in LMICs.¹⁹

Individual buyers and governments across different LMICs pay highly variable prices for insulins.⁵ The same insulin can cost ten times the price depending on

WHO Global Diabetes Compact

The Sustainable Development Goals, set in 2015 by the United Nations General Assembly, include the reduction of premature mortality from non-communicable diseases (NCDs) by one third. The deadline for this goal is 2030, but the mortality figures for diabetes are one of the main factors making the goal difficult to attain.²³ In response to this, WHO launched the Global Diabetes Compact in 2021. 'Key asks' have been formulated as priority areas for action for different stakeholders, including the private sector, such as to "Improve access to diabetes diagnostics, medicines and health products, particularly insulin, in low- and middle-income countries".²³

WHO prequalification programme

To address the market concentration issue, and to increase supply and affordability, it is critical for more manufacturers to enter the market and produce quality-assured insulin. In 2019, WHO launched a pilot programme for the prequalification of biotherapeutic medicines, including human insulin; and in 2022, the programme was expanded to include long-acting analogue insulins.²⁴ Product prequalification can reduce the regulatory burden on pharmaceutical companies – therefore making it more attractive to launch their products in these countries. The overall prequalification programme started in 2001 for HIV/AIDS medicines. WHO has since been expanding the scope of the products, working in cooperation with national regulatory agencies and international organisations to apply standards of quality, safety and efficacy of essential products. The inclusion of human and long-acting analogue insulins in the programme has the potential to help create a secure supply of quality-assured insulin, including of biosimilar products, in LMICs.

* Uncorrected USD figures.

location, as one study found⁴ – and the highest median insulin prices have been found in low-income and lower-middle income countries.²⁰

The reasons for high costs are various; the manufacturer's selling price, wholesale and retail mark-ups, taxes and other tariffs also have an influence on insulin's final price.²¹ A lack of affordability can lead patients to not being able to access insulin at all, or to patients rationing their insulin if they cannot afford the quantity they need. Indeed, discontinuation of insulin treatment has been identified as a common issue in LMICs, with the cost of insulin and monitoring tools being one of the main reasons.²²

People with diabetes in LMICs face persistent challenges in accessing a continuous, reliable, affordable supply of insulin – a problem that applies to all types of insulins. Many people still struggle to access human insulin, as it is not always available and is often unaffordable, especially in low-resource settings. Access to insulin analogues is even more limited. Even when these products are available, they are often unaffordable. Prices are two to six times higher than those of human insulins, with affordability varying significantly between countries.^{4,20}

While analogues are consistently priced higher than human insulin, the difference in production costs between these products does not reflect the price differential at which they are sold. According to figures from 2018, the estimated cost of production was only slightly higher for analogues compared to human insulins, primarily due to higher prices of Active Pharmaceutical Ingredients (APIs).²⁵

Having access to analogue insulins can bring important advantages to people living with diabetes. In terms of controlling blood glucose levels, analogue insulins provide equal effectiveness in comparison to human insulins, while having the potential to decrease adverse effects.^{26,27} Analogues can also be administered more conveniently and increase patients' adherence to treatment.^{28,29}

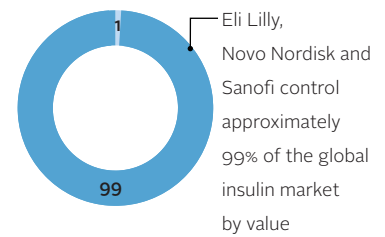
However, the current reality is that most people living in LMICs do not have access to analogues or more convenient delivery methods. Analogues are still not listed on many LMICs' National Essential Medicines Lists, and consequently not supplied in the public sector, as is the case in countries including Senegal and Myanmar. Even when analogue insulins are listed on a country's National Essential Medicines List, this does not always mean that patients have access to such products via the public sector, as is the case in Kenya.^{4,30,31} Nonetheless, the inclusion of analogues in countries' National Essential Medicines Lists, alongside the entrance of more analogue insulins in more LMIC markets and the resulting increase in competition, may soon lead to broader access to these products.³²

Opportunity for biosimilars companies to expand access to insulins

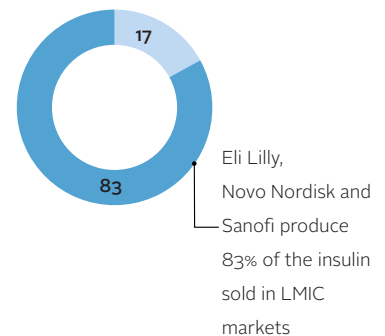
Biosimilar insulins, products that are highly similar to reference insulins, have been on the market since 2015*. Biosimilar companies, for example Biocon, Gan & Lee and Wockhardt, focus specifically on manufacturing and marketing biosimilar versions of insulin products, both human and analogue.⁵ Though they are much smaller manufacturers than Eli Lilly, Novo Nordisk and Sanofi, these biosimilar companies could play a big role in access. While the main three insulin manufacturers still hold most of the market globally, several biosimilar manufacturers produce and market a significant amount of insulin products in LMICs.⁵

Biosimilars have a meaningful share of the human insulin market in LMICs. Since several patents on analogue insulins have recently lifted, they have also had the option to manufacture biosimilars of analogue insulins. There is hope that analogue insulins can reach people in LMICs via biosimilar versions. However, this development has yet to be fully realised. In one study of insulin use in 32 LMICs, biosimilar products (manufactured by all company types) accounted for 29% of the volume of human insulin used by patients, but a mere 8% of the analogue insulin used by patients.⁵

Share of the global insulin market (%)¹³



Insulins sold in LMICs (%)⁵



Biosimilar insulins

Insulin is classified as a biological drug, i.e., a complex molecule made from living cells or organisms. A 'biosimilar' is a drug that is highly similar to a biological drug (the 'reference product' manufactured by originator company) that is already on the market.

Because insulin is a biological product, its structure is much more complex than that of simple chemical molecules which can be copied to create almost exact replicas of an originator product. Biosimilar drugs are copies of a biopharmaceutical product; but because of the inherent nature of biological products, the process is more complex and while they are produced in the same way and can have a similar clinical effect, exact replicas cannot be obtained.³⁵

Several biosimilar insulins have been launched in recent years, including regular and isophane human insulin and analogues such as glargine.

* Biosimilar products are manufactured by both big global companies that also manufacture originator products and by smaller manufacturers. For the purpose of this study, the term 'biosimilar insulin'

is used to define all insulins produced by smaller manufacturers (other than Eli Lilly, Novo Nordisk or Sanofi).

The introduction of biosimilar insulins in LMICs has the potential to lower prices for governments and patients. In general, biosimilar products can be introduced at lower prices, which is particularly seen when several biosimilars of the same medication exist in a certain market. For example, the availability of several insulin biosimilar versions has led to significantly lower prices than for originator brands in Bangladesh.³² After the introduction of biosimilars, originator companies typically respond by lowering prices. Such price cuts of originator products have been seen for the analogue lispro after the introduction of a biosimilar competitor.³³

However, significant price changes have not always been noted after the introduction of a biosimilar into the market.^{5,34} If biosimilar products are not significantly cheaper than the originator insulins in LMICs, patients may not see the case for changing their treatment plan, making it difficult for biosimilar companies to increase uptake of – and trust in – their products among prescribers and users.^{4,34}

Reasons for the low availability of biosimilars may be related to various hurdles that manufacturers of these products face, including regulatory challenges, lack of trust from the government and prescribers and – in some cases – uncertainty about the patent status of the originator product.³⁵ Even though there is no evidence for reduced efficacy or a higher rate of adverse events when using biosimilar insulin, there is little knowledge and guidance available for prescribers and very often these are not included in LMICs' National Essential Medicines Lists.^{33,34}

While the focus of this paper is primarily on access to insulin in LMICs, it is crucial to bear in mind that delivery methods and monitoring tools are an integral part of diabetes care and also affect doctors' and patients' decisions about which insulin products to prescribe and use. However, for many people with diabetes in LMICs, most of these products remain unaffordable.³⁶

Delivery methods

To control blood glucose levels, insulin needs to be injected subcutaneously (under the skin), which can be done in several ways:



A needle and a syringe: Human insulin is mostly sold in vials, and the patient or their carer must prepare the appropriate dose and inject it. This can be challenging for many people, including children and the elderly.



Insulin pens: This is the main delivery method for analogue insulins. Pens can be prefilled with insulin or fitted with a replaceable insulin cartridge. Pens allow for a more convenient and accurate delivery of the required insulin dose.



Insulin pumps: These are small electronic devices that deliver insulin following a pre-programmed schedule or automatically according to blood sugar levels. Even though these are more convenient, insulin pumps are still expensive and difficult to access for many patients.

Monitoring tools

To keep diabetes under control and avoid complications, patients need to frequently monitor their blood sugar levels, using one of these devices:



Glucometers: These are small portable devices. The patient uses a needle or a lancet to prick their finger, and a test strip to capture a drop of blood, so that the device can measure the blood sugar level. Even though the device itself can last for a long time, needles or lancets and test strips need to be replaced for every measurement. These devices have been included by the WHO in its Model List of Essential In Vitro Diagnostics.³⁷



Continuous Glucose Monitoring devices (CGMs): These are devices that track blood glucose continuously throughout the day. A CGM includes a disposable sensor that is placed under the skin which conducts readings every few minutes and sends this information to an attached transmitter and, usually, to a separate receiving device, such as a smartphone. CGMs provide a convenient way of keeping oversight of one's blood glucose levels, but remain largely out of reach in LMICs due to various factors, including the reduced number of manufacturers, the lack of reimbursement and the cost of the sensors.³⁸

Securing a sustainable supply of insulins

People living with diabetes require a secure and uninterrupted supply of insulin. However, many LMICs lack an adequate infrastructure for the manufacture or importation of insulin, or for its storage and distribution – impacting availability in both the public and private sectors. Some countries also only import insulin from one source, making them more vulnerable to shortages.^{20,39} The fragility of global supply chains for essential health products has been made abundantly clear during the COVID-19 pandemic,⁴⁰ which also disproportionately affected people living with chronic conditions such as diabetes. There is now an opportunity to improve global health security, including by strengthening health systems and supply chains, and to increase preparedness for other crises, such as future pandemics and climate change-related disasters.

Under-importation of insulin appears to be an issue in many countries, as a mismatch has been identified between the amount of insulin supplied and the amount needed to treat people living with diabetes, with health systems being often unaware of actual demand. Reasons for this might include weak forecasting systems and systemic barriers preventing people from accessing treatment.³⁹ For instance, poor capacity to properly forecast insulin needs has led to countries such as Mozambique and Kyrgyzstan not having the right quantity of insulin in local health care facilities.⁴¹

For insulin, one particular challenge is that it must be kept in continuous cold storage until it is administered. Breaking the cold chain can have consequences on safety and insulin potency, which, once lost, cannot be regained. Maintaining a proper cold chain can be a challenge in many LMICs, particularly in rural areas, which are more likely to lack infrastructure such as a continuous electricity supply, cold chain transportation vehicles, or refrigerated storage.

This issue has gained more widespread attention since the launch of COVID-19 vaccines requiring cold or ultra-cold storage in late 2020. Those cold chain requirements posed a challenge for many countries, and affected procurement choices and the speed of the vaccine roll-out in LMICs.⁴² However, investment in strengthening countries' cold chain infrastructure for COVID-19 vaccines could now have a positive benefit for insulin products (see page 29), while advancements in knowledge about insulins' heat-stability can also reduce the reliance on cold storage at the end of the supply chain.

COMPANY PROFILES

How are companies addressing access to insulin?

Eli Lilly, Novo Nordisk and Sanofi

The three largest manufacturers of insulin – Eli Lilly, Novo Nordisk and Sanofi – have been involved in the insulin market since its earliest days, with all three companies or their predecessors starting to produce and market insulins in 1923. Over time, these companies have developed differing portfolios of diabetes products, including different types of insulin products and other diabetes medicines.

While all three companies have both human and analogue insulins in their product portfolios, their approach to the insulin market in low- and middle-income countries (LMICs) varies, including each company's choice of which products to prioritise for patients in these countries. Over recent years, the companies have also explored a range of access strategies targeted at expanding access to insulin in LMICs, including paediatric diabetes programmes, training programmes, and pricing strategies.

Details of the three companies' approaches are laid out in the following pages. These profiles, which are not comprehensive, set out some of the main examples of each company's strategies to improve access in LMICs, and provide an overview of what key actions are currently being taken.

Biocon

A number of smaller manufacturers of biosimilar insulins have entered the market more recently and are starting to implement strategies to improve access to their products in LMICs. Their portfolios can include biosimilar versions of human and analogue insulins. One such company, Biocon, is profiled on page 20.

COMPANY PROFILE

Eli Lilly

Eli Lilly's approach to expanding access to its insulins in LMICs sits within a wider access strategy covering healthcare more generally. As part of this, the company has a significant paediatric programme for children and young people with diabetes. Eli Lilly also pursues partnerships and takes part in initiatives at the country level. Of the other company initiatives to increase access to diabetes care, most are focused within the United States, which is not in scope of this paper. (A full list of countries in scope can be found in the appendix).

How diabetes products fit into Eli Lilly's overall approach to access

Eli Lilly approaches access via its Lilly 30x30 programme, which aims to deliver access to high-quality healthcare for 30 million people in resource-limited settings annually by 2030 – including, but not exclusively, people living in LMICs. This strategy covers diabetes, cancer and COVID-19 among other disease areas and includes efforts to explore and expand alternative business models, access strategies and patient support programmes. In 2021, the estimated reach of the programme was 11.6 million people across all disease areas, an increase of approximately 6.6 million since 2015. This programme aims to cover a wide spectrum of treatment areas and geographies. The company has not disclosed specific outcomes or the number of patients reached through individual programmes within 30x30.

In 1968, the company established Eli Lilly and Company Foundation, Inc., a U.S.-based tax-exempt organisation commonly known as The Lilly Foundation. The Foundation's grant activities are focused within the United States, but it also provides some financial grants to organisations working internationally.

Focus on paediatric programme

The company has supported the Life for a Child programme since 2009, and this now forms part of its approach to achieving the Lilly 30x30 goal. Life for a Child is a collaborative initiative, established in 2000 and administered by the organisation Diabetes NSW & ACT, that supports the delivery of healthcare to children and youths with type 1 diabetes living in low-resource settings. It covers diagnosis, monitoring, diabetes education and access to diabetes products including insulin. Through its support to the Life for a Child programme, the company donated over 3.2 million vials and cartridges of insulin, including insulin analogues such as glargine (Basaglar®), to children and youths in LMICs between 2009 and 2021. Notably, this programme also provides delivery devices (e.g. syringes), blood glucose monitoring devices and test strips.

In 2022, Eli Lilly announced a commitment to support UNICEF's work with funding of USD 14.4 million up until 2025. The contribution will be directed towards improving prevention, care and treatment of non-communicable diseases (NCDs), including diabetes, at different levels of care. Focuses will include strengthening data and health information systems and building capacity among local health care providers. The initiative aims to improve health outcomes of 10 million children and adolescents and will cover Bangladesh, Malawi, Nepal, the Philippines and Zimbabwe.

Donations of insulin via humanitarian partners

Eli Lilly provides donations of insulin via humanitarian partners. For example, in 2022 the company donated over 1.3 million insulin vials and pens through Direct Relief and Project HOPE for hospitals and patients in Ukraine.

* Glucagon is used by insulin-dependent patients to counter the adverse effect of an excessive dose of insulin, i.e. severe hypoglycaemia.

Eli Lilly & Co

Headquarters

Indianapolis, United States

Company focus

Research-based pharmaceutical company with a focus on non-communicable diseases.

Profile

Eli Lilly was the first company to commercialise insulin worldwide. In addition to insulins, its portfolio includes several other diabetes treatments, as well as oncology products and medicines to treat inflammatory diseases. Insulin lispro (Humalog®) is one of the company's blockbuster products and represents its second largest source of revenue.

Products for insulin-dependent patients

3 human insulins (vials)

- Insulin human, rdna origin (Humulin®) ★
- Isophane human insulin (Humulin N®) ★
- Isophane human insulin / human insulin (recombinant) (Humulin 70/30®) ★

3 analogue insulins (vials and pens)

- Insulin lispro (Humalog® and Lyumjev®)
- Insulin lispro/insulin lispro protamine (Humalog Mix®)
- Insulin glargine (Basaglar®) ★

2 glucagons*

- Glucagon for injection (Glucagon) ★
- Nasal glucagon (Baqsimi®)

★ *This product is on the WHO Model List of Essential Medicines*

Country-specific strategies to improve access to insulin and diabetes care

The company participates in initiatives aimed at strengthening the continuum of diabetes care. As an example, Eli Lilly has been collaborating with the global network Academic Model Providing Access to Healthcare (AMPATH) since 2002. In western Kenya, working alongside the Ministry of Health, the partnership implemented a chronic disease management programme. Eli Lilly has made product donations and provided financial support to several of AMPATH's initiatives. Since the beginning of the programme, the company has reported donating over USD 215 million worth of medications, including insulin. With the support of Eli Lilly, AMPATH has put in place a home glucose monitoring programme in Kenya. Over 3,000 people living with diabetes are enrolled in the programme, which covers care, education and medications, including insulin. Of these, 469 are enrolled in the home glucose monitoring programme, through which they access facilities for self-monitoring of their blood glucose, helping achieve better control of their condition. In February 2022, AMPATH announced new partnerships in Ghana and Mexico with the support of Eli Lilly and the Lilly Foundation, aiming to strengthen more health systems.

Through the Lilly Global Health Partnership, a component of the company's Lilly 30x30 programme, the company is supporting the Tshwane Insulin Project (TIP). TIP is a five-year research programme launched in 2019 in South Africa as a public-private partnership with academia and the government. The project consists of a digital health intervention aiming to improve diabetes care through a variety of activities, including training for primary healthcare providers, patient education, and the use of an app to assist with initiation of insulin treatment and its subsequent management.

Eli Lilly has also partnered with Mexico's General Health Council and The United States-Mexico Foundation for Science (FUMEC) to develop and implement digital health tools. By optimising public health information systems, the aim is to improve engagement between healthcare providers and users and foster a more effective decision-making process for providers and policymakers and benefit more than 5.7 million people by 2030. As part of this partnership, Eli Lilly is taking part in the development of an epidemiological surveillance system, SANENT (National System for Analysis of Non-Communicable Diseases), to support the treatment of people living with type 2 diabetes in Mexico, a country with one of the world's highest burdens of diabetes.

At present, Eli Lilly does not publicly disclose detailed information regarding registration of products and access strategies for diabetes care in LMICs, and has provided limited data to the Access to Medicine Foundation for this analysis



Manuel, who lives in Bolivia and was diagnosed with type 1 diabetes at two years old, measures his blood glucose levels - credit: Eli Lilly, *Life for a Child*



Dr Nicholas Kirui and Dr Sonak D Pastakia take part in a retrospective assessment of the quality of diabetes care in a rural diabetes clinic in Western Kenya - credit: Eli Lilly, AMPATH Kenya

COMPANY PROFILE

Novo Nordisk

Novo Nordisk takes a wide range of approaches to expanding access to diabetes care, including a paediatric programme, pricing commitments, and taking steps to evaluate the heat stability of its insulin products in order to reduce cold storage requirements. In LMICs, Novo Nordisk focuses its access strategies primarily on its human insulin products.

Diverse access strategies, with a focus on human insulins

Novo Nordisk has launched a social responsibility strategy, Defeat Diabetes, which sets long-term goals in the areas of prevention, provision of affordable care and innovation in diabetes. To work toward these goals, the company has prioritised three areas of work: reaching more children with type 1 diabetes, reducing the price of human insulin and committing to donations for relief efforts.

The company has a range of strategies in place that tackle different areas of healthcare in line with its Defeat Diabetes strategy. Among Novo Nordisk's various strategies are its Changing Diabetes in Children programme (CDiC), which works to provide care for children with type 1 diabetes in LMICs; a programme focused on prevention of chronic disease, aiming to tackle the rise of diabetes type 2 in urban settings; and the Novo Nordisk and Novo Nordisk Foundation co-funded Diabetes Compass initiative, run by the World Diabetes Foundation, which helps build healthcare capacity in LMICs. More recently, the company has started to roll out its new iCARE model, described below.

Exploring a partnership-based model via Base of the Pyramid

In addition to these strategies, Novo Nordisk carries out multi-country strategies to tackle different challenges across the continuum of diabetes care. In 2012, the company established the Base of the Pyramid programme, a partnership model aiming to enhance access to diagnosis, treatment, and management of diabetes for people living with diabetes at the base of the economic pyramid. The programme covers capacity building, tackling supply challenges, patient education, and provision of human insulin at a lower price. For example, in collaboration with local partners in Kenya, gaps related to inadequate demand forecasting and insufficient capacity for storage and cold chain management were identified and addressed, achieving a regulation of cost structures and a more stable insulin supply.

Pursuing a comprehensive approach via iCARE

Novo Nordisk is now expanding its strategies through a comprehensive approach to access in LMICs. The iCARE initiative was launched in 2021 as a business-integrated model aimed to improve access to diabetes treatment in 49 countries in sub-Saharan Africa through four areas of work (Capacity, Affordability, Reach and Empowerment). The initiative aims to substantially increase the number of people with diabetes accessing insulin in sub-Saharan Africa (excluding South Africa) by 2025. iCARE has been launched in seven pilot countries so far: Ethiopia, Ghana, Côte d'Ivoire, Kenya, Nigeria, Sudan and Tanzania. This initiative targets challenges such as affordability barriers impeding access to care for vulnerable patients, hurdles in procurement and supply chains (including last-mile distribution), mark-ups, inadequate forecasting, healthcare practitioners' capacity, knowledge gaps in diabetes management, and patient education. In these pilot countries, it has engaged with local governments and local partners to carry out localised strategies and track the impact of the approach. The initiative also aims to achieve both affordability and financial sustainability, as

* Glucagon is used by insulin-dependent patients to counter the adverse effect of an excessive dose of insulin, i.e. severe hypoglycaemia.

Novo Nordisk A/S

Headquarters

Bagsværd, Denmark

Company focus

Research-based pharmaceutical company with a primary business focus on diabetes.

Profile

Novo Nordisk leads the insulin market, holding almost half of the share of the total insulin market globally in 2021. In a smaller proportion, the company portfolio also includes products targeting other endocrine disorders, haemophilia, and obesity, as well as hormone replacement therapies.

Products for insulin-dependent patients

3 human insulins (vials and pens)

- Insulin human (rdna) (Actrapid®) ★
- Isophane human insulin (Insulatard®) ★
- Biphasic human insulin (Mixtard®) ★

7 analogue insulins (vials and pens)

- Insulin aspart (l-arginine) (NovoRapid®)
- Insulin aspart (niacinamide) (Fiasp®)
- Biphasic insulin aspart (NovoMix®)
- Insulin degludec (Tresiba®) ★
- Insulin degludec/insulin aspart (Ryzodeg®)
- Insulin detemir (Levemir®) ★
- Insulin degludec/liraglutide (Xultophy®)

1 glucagon* (injections)

- Glucagon (GlucaGen HypoKit) ★

★ *This product is on the WHO Model List of Essential Medicines*

increased sales volumes will enable lower costs and thereby lower prices.

Other company initiatives have focused on strengthening health systems to improve diabetes care. For example, since 2021 Novo Nordisk has supported a programme for integrating type 1 diabetes care into the health systems of eight countries in eastern Africa and the Middle East, including six countries in scope: Ethiopia, Kenya, Malawi, Mozambique, Rwanda and Tanzania. The Programme covers aspects of health system planning, awareness-raising campaigns, diagnosis, treatment, provision of medical supplies, and patient support and education. The eight countries were selected based on their level of commitment to strengthening diabetes care as part of their broader approach to non-communicable diseases. The programme is carried out through a partnership between the World Diabetes Foundation and local partners, including the participating countries' ministries of health and healthcare institutions.

Pricing and affordability strategies

Novo Nordisk has focused its affordability strategies primarily on its human insulin products, via such initiatives as Base of the Pyramid and iCARE, but also more broadly. As part of the Defeat Diabetes strategy, the company has an "Access to Insulin Commitment", which includes a price ceiling commitment. Since 2020, the price ceiling has been lowered to 3 USD per human insulin vial for 76 LMICs. These include all Least Developed Countries, other low-income countries, and a selection of middle-income countries where large low-income populations lack sufficient health coverage. The Commitment is an offer to 76 governments (i.e. to the public health system), although it has not been taken up by all countries.

Concerning analogue insulins, Novo Nordisk has limited strategies in place. In the private market, the company provides patient assistance programmes in countries including Mexico and Egypt, where insulin degludec (Tresiba®) is offered at discounted prices for some patients. No information regarding access strategies involving analogues in low-income countries has been provided by the company.

Paediatric programme

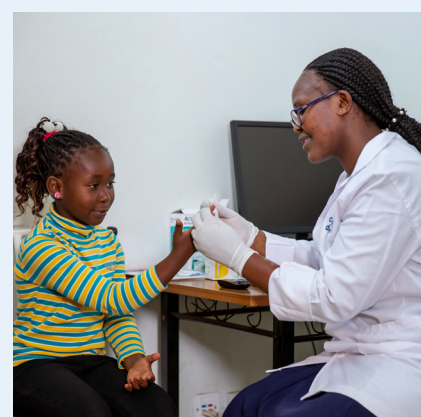
The Changing Diabetes in Children (CDiC) programme was established by Novo Nordisk in 2009 with the objective of improving access to care for children with type 1 diabetes in LMICs. CDiC works to raise public awareness of diabetes, strengthen healthcare capacity and increase access to human insulin through the donation of these products and other necessary commodities. The company has donated around 2.9 million vials and 245,000 pens of human insulin via the programme. More recently, CDiC has been making efforts to strengthen digital innovations and local data systems, aimed at increasing evidence-based policy making. The programme is carried out through public-private partnerships in 24 countries, including Cambodia, Guinea, Senegal and Peru, and has reached over 34,000 young people since its start.

Strengthening the supply chain

Novo Nordisk has worked alongside various partners to tackle issues affecting the insulin supply chain. For instance, it is part of the multisectoral Coalition for Access to NCD Medicines & Products, which is working to implement a forecasting tool to be used for estimating annual quantities and costs of products for diabetes care. This initiative, carried out in collaboration with PATH and several local ministries of health, is providing technical guidance to communicate with key country stakeholders and make better use of forecasting results to inform financing and procurement processes. The programme currently covers Kenya and Uganda, and an evaluation of the initiative is taking place during 2022, with the aim of later expanding it to Tanzania and the rest of the East Africa region.



Healthcare workers at a clinic examine the foot of a man with diabetes - credit: Sala Lewis



A child taking part in a Novo Nordisk programme in Kenya in 2019 has her blood sugar level tested by a healthcare worker - credit: Sala Lewis

To address issues affecting the cold chain for insulin, the company has also supported partners and institutions by providing fridges and training healthcare personnel in several countries in sub-Saharan Africa, as part of its iCARE model.

Donations of insulin in humanitarian and emergency settings

Novo Nordisk donates insulins and other products by partnering with humanitarian organisations such as Direct Relief and the Red Cross. Through these programmes, Novo Nordisk provided people living in conflict situations in Ethiopia, Yemen and Ukraine with over 227,000 vials of human insulin between 2021 and 2022. To alleviate the impact of the COVID-19 pandemic, the company also donated approximately 1.3 million vials of human insulin to humanitarian organisations. Although in lower volume, the company has also included needles and different types of pens in its donations.

Advances in heat-stable insulins

Following the EMA positive opinion, two of Novo Nordisk's human insulins, Actrapid® and Insulatard®, are undergoing national submissions to authorise an additional flexible storage option outside of refrigeration at temperatures up to 30°C, for up to four weeks before opening.^{11,12} This has the potential to facilitate insulin distribution and diabetes management in contexts with hot climates and where maintaining continuous cold storage represents a challenge, such as rural areas without electricity.

COMPANY PROFILE

Sanofi

Sanofi's approach to expanding access to diabetes care and its insulins in LMICs includes pricing strategies to increase the affordability of analogue insulins, programmes to train healthcare professionals, and multiple localised country-based initiatives. The company has recently made new commitments and announced a new approach aimed at improving access to prevention, treatment and care for people living with diabetes in many LMICs. The focus of Sanofi's insulin portfolio is on analogue insulins.

New Global Health Unit aims at sustainable access

In 2021, Sanofi launched its Global Health Unit, which will continue and expand the company's work with local governments and stakeholders, intergovernmental agencies and non-governmental organisations to increase access to its medicines. Sanofi plans for this unit's remit to cover 40 LMICs, which include countries that currently have severely limited access to insulin, such as Tuvalu, Haiti and Guinea-Bissau. The unit will seek to improve access to 30 medicines for communicable and non-communicable diseases (NCDs), most of them listed on the WHO Model List of Essential Medicines (EML). The medicines will include insulin glargine, a long-acting analogue recently added to the EML, and glulisine, a rapid-acting analogue. Through the Global Health Unit, Sanofi has shared a commitment to expand access to analogue insulins, with the target to reach 300,000 insulin-dependent patients by 2030, in comparison to its 2021 reach of 15,000 patients. Sanofi aims for the unit to be self-financed by charging just enough to cover the cost of treatment. This will be implemented through the sale of products under a new brand ('Impact') at a lower price. The unit also aims to strengthen health systems by establishing an impact fund to support start-up companies and other innovators involved in the development of sustainable healthcare in the 40 LMICs within the unit's remit.

Analogues are central to Sanofi's affordability initiatives

Before including analogue insulins within the scope of its Global Health Unit, Sanofi had also put in place specific strategies to increase the affordability of these products. For example, since 2021, Sanofi has listed insulin glargine (Lantus®) in the National Health Insurance Scheme and State Health Insurance Scheme of two of Nigeria's 36 states at a price on par with human insulins. The company also plans an expansion of this strategy to two more states in 2022, aiming to reach 3,000 patients.

As another example, in Kenya, Sanofi tailors its pricing strategies to both the public sector and private sector markets. The company offers a price for its insulin glargine (Lantus®) in the public sector that is low enough to ensure it can be listed for complete reimbursement. For patients paying out of pocket, there is a state partnership and patient support programme which provides a free cartridge of insulin glargine (Lantus®) for every two cartridges purchased by new patients. This product is also available in Kenya via a private health insurance, which Sanofi made possible by signing a commercial agreement.

For people paying out of pocket, Sanofi also pursues strategies such as patient assistance programmes to provide discounts for certain products in different countries, as is the case in Brazil for insulin glargine (Lantus® and Toujeo®).

Sanofi
Headquarters Paris, France
Company focus Research-based pharmaceutical company with a large and varied portfolio, including products for communicable and non-communicable diseases.
Profile Sanofi's diabetes products sit within a wide-ranging portfolio that encompasses many different therapeutic areas and product types, from antibiotics and vaccines to immunotherapy and innovative oncology treatments. Insulin glargine (Lantus® and Toujeo®) is one of the company's best-selling products worldwide.
Products for insulin-dependent patients 1 human insulin (vials) <ul style="list-style-type: none"> • Human recombinant insulin (Insuman®) ★ 5 analogue insulins (vials and pens) <ul style="list-style-type: none"> • Insulin aspart (Insulin aspart Sanofi) • Insulin glargine (Lantus® and Toujeo®) ★ • Insulin lispro (Admelog®) • Insulin glulisin (Apidra®) • Insulin glargine / lixisenatide (Suliqua® / Soliqua®) ★ <i>This product is on the WHO Model List of Essential Medicines</i>

Building capacity for supply chain management

Sanofi has been tackling some long-term challenges related to the cold chain management of insulin. The company has a programme in place which aims to improve the transport and cold chain management of vaccines and insulins. This programme targets gaps in the capability of cold chain management and provides training to pharmacists in hospitals and other key institutions in India to improve good pharmacy practice and cold chain monitoring and management. In 2021, approximately 150 pharmacists were trained through this initiative across 10 institutes in India.

Piloting new approaches to assess potential

To tackle challenges in the provision of care for NCDs, Sanofi launched a pilot project in Kenya in 2018 called 'Ngao Ya Afya'. The initiative, which was implemented in partnership with international and local stakeholders, encompassed digital and non-digital interventions to improve access to care for patients with diabetes and hypertension. It included giving access to discounted consultations, medical tests and discounted Sanofi medicines such as glargine (Lantus®), as well as some non-Sanofi medicines. The initiative also provided tools for monitoring glucose, alongside a digital platform patients could use to aid self-management. In 2019, 675 patients had access to discounted prices through the digital health wallet for diabetes and/or hypertension treatments.

Youth programme with a focus on education

The KiDS project is an educational programme co-created by Sanofi and the International Diabetes Federation in 2013, in collaboration with the International Society for Paediatric and Adolescent Diabetes and local partners such as the Public Health Foundation of India, the Brazilian Diabetes Society and the Associação de Diabetes Juvenil (ADJ) in Brazil. This programme targets school-teachers, nurses, policymakers and families, and aims to provide education about diabetes and decrease stigma and discrimination against children with this condition. The programme also aims to promote healthy lifestyles for the prevention of type 2 diabetes among children. By the end of 2021, the trainings provided by the programme had reached around 340,000 children, 19,800 school staff and more than 15,000 parents in 10 countries, including five of the countries in scope of this paper.

Donations of insulin

Sanofi has engaged in short-term insulin donation initiatives. For instance, the company has donated around 30,000 units of insulin to people in Ukraine, including not only human insulin but also the analogues aspart, glargine, lispro and glulisine.



A child takes part in Sanofi / International Diabetes Federation's KiDS programme in India
- credit: Govt High School, Fatorpa



A child takes part in Sanofi / International Diabetes Federation's KiDS programme in India
- credit: Janta High School, Mapura

COMPANY PROFILE

Biocon

Biocon has ambitious goals to improve access to its insulins in LMICs by lowering prices and boosting affordability, although the company is only in the early stages of taking steps towards achieving these goals. Biocon has also recently begun pursuing other strategies involving education and donations.

The role of biosimilars in expanding access

Biosimilars companies could play a key role in expanding access to insulins in LMICs (for more on biosimilars, see pages 9-10). As one of the world's largest manufacturers of biosimilar insulins, Biocon was invited to contribute data for analysis in this paper, which will look at what actions the company is taking – and what strategies it is planning to pursue – to expand access to its insulin products.

Through its Biocon Biologics subsidiary, the company manufactures and sells seven biosimilars and novel biologic products, including four insulin products (see box, right). Since 2004, Biocon has supplied over 2.75 billion doses of human insulin globally. Its biosimilar insulins Semglee® (branded insulin glargine) and insulin glargine (unbranded), co-developed alongside the US-based generic medicine manufacturer Viartis, were approved by the US Food and Drug Administration (FDA) in 2020 and, in 2021, Semglee® was given the first-ever interchangeable label for a biosimilar in the US, i.e., pharmacies are authorised to dispense Biocon's insulin glargine (Semglee®) as a substitution for the reference product, Sanofi's insulin glargine (Lantus®). In February 2022, Biocon announced it had entered into an agreement to fully acquire Viartis's biosimilars business.

Ambitious aims and small first steps on pricing and affordability

Biocon's stated aim is that its biosimilar insulins should reach one in five insulin-dependent people with diabetes globally, though no date has been publicly set for this goal. As part of its approach to achieving this, in 2019 the company launched its strategy 'Mission 10 cents', committing to offering its human insulins for less than USD 10 cents per day from vials directly sourced from Biocon Biologics by governments in LMICs.

The programme has been launched in the Philippines, where the company signed a memorandum of understanding (MoU) with two municipalities and the social enterprise reach52, covering programme implementation and the logistics required to provide last-mile delivery of insulins at a price aligned to Biocon's Mission 10 cents. In 2020, Biocon signed an agreement with the organisation Christian Social Services Commission (CSSC) in Tanzania to help implement its Mission 10 cents initiative. Even though the company has reported that it has not yet received any firm orders from CSSC, in 2022, Biocon Biologics signed a procurement agreement with the Tanzanian Ministry of Health to supply insulin for under USD 10 cents per day. The company also reports that it has supplied its human insulin to the public sectors in Ghana since 2020 and in Mozambique since 2021, keeping the 10 cents mark as the price ceiling for end users in these countries. So far, Biocon has not reported specific outcomes or patient reach data for the implementation of this strategy in the aforementioned countries.

Education initiative for healthcare providers, coupled with insulin donations

In 2021, Biocon entered a partnership with the Research Society for the Study of Diabetes in India (RSSDI) to launch the Biocon & RSSDI Initiative for Diabetes Knowledge in Type 1 Patients (BRIDGE-1). RSSDI will provide training for

* This product has yet to be registered or marketed in countries in scope.

Biocon Limited

Headquarters

Bengaluru, India

Company focus

Biopharmaceutical company with a sizeable global footprint. Its biosimilar products, including oncological products and insulins, are manufactured by the company's Biocon Biologics subsidiary.

Profile

Biocon is dedicated to the manufacturing of APIs, generic products and biosimilars across disease areas including immunology, oncology and diabetes. The company was founded in 1978 and has since expanded into biosimilars, with its biosimilars business now forming Biocon's largest segment in terms of revenue.

Products for insulin-dependent patients

- 3 human insulins (vials)
- Rh-insulin (30% as soluble insulin injection and 70% as isophane insulin injection) ★
 - Rh-insulin (NPH / isophane insulin) ★
 - Rh-insulin (50% as soluble insulin injection and 50% as isophane insulin injection) ★

2 analogue insulins (vials and pens)

- Insulin glargine ★
- Insulin aspart *

★ *This product is on the WHO Model List of Essential Medicines*

approximately 400 healthcare providers regarding the management of type 1 diabetes, with Biocon contributing educational materials and also providing free-of-charge human (Rh-insulin) and analogue (insulin glargine) insulins for type 1 diabetes patients of these providers, for up to three years. This is expected to cover the insulin needs of approximately 1,000 young patients.

Strengthening diabetes care services

The Biocon Foundation, the Corporate Social Responsibility arm of the company, is putting in place some initiatives to strengthen diabetes care services in India. The Foundation operates NCD 'specialist clinics' that provide free-of-charge services in three locations in India. The clinics address a range of issues, including screening, diagnosis and management of type 2 diabetes. Biocon has reported that around 1,400 patients have benefited from services offered at these clinics.



A man has a blood sample taken to measure his blood glucose level - credit: Biocon



A woman has her blood sugar levels checked at a clinic - credit: Biocon, reach52

INDUSTRY ANALYSIS

Lack of registration of essential insulins in LMICs is a barrier to expanding access

Making sure insulins are registered in low- and middle-income countries (LMICs) is an important step in securing access to these medicines for people with diabetes. Outside of certain exceptional circumstances, registration with a country's national regulatory authority is the only way to enable distribution and marketing of a product in that country. It does not guarantee that the product will actually be made available, but it is a precondition for ensuring access.

Human insulins are widely registered, but inconsistently

Human insulins* are the most widely registered** type of insulin in LMICs. For example, Novo Nordisk is the largest seller of human insulin worldwide, and has registered at least one of its human insulins in more than three quarters of the LMICs in scope of this paper.***

However, in several low-income countries, very few (or in some cases, none) of Novo Nordisk's human insulins have been registered – and nor have human insulins from the other companies in scope, according to the data available. Biocon, another company with an important footprint in LMICs, has registered at least one of its human insulins in approximately two fifths of upper middle-income countries, but only in approximately one fifth of low-income countries in scope.

Companies lag on registering analogue insulins, with wide gaps

Analogue insulins* are registered in a smaller number of LMICs overall, compared to human insulins. Registration of these products was not reported in almost one third of countries in scope.

Where analogues are registered, they are most likely to be insulin detemir (Levemir®) or insulin degludec (Tresiba®). These two long-acting analogue insulins, both from Novo Nordisk, were recently listed on the WHO's Model List of Essential Medicines (EML) and are the most widely registered analogues in LMICs, registered in 71 and 48 out of the 108 countries respectively.

Among LMICs, companies prioritise registration of their insulins in countries classed as upper middle-income, which usually represent larger and more stable markets compared to lower-middle and low-income countries. This is true for all types of insulin, but the situation becomes particularly stark when looking at analogue insulins. While there is at least one analogue registered in the majority of upper middle-income countries, this is the case for less than half of the low-income countries in scope.

A prime example would be insulin glargine, a long-acting analogue insulin recently included in the EML. Out of the countries included in this analysis, insulin glargine (from either Sanofi or Biocon) is registered in 57.7% of upper-middle income countries, 41.8% of lower-middle income countries and only 7.4% of low-income countries. Biocon's insulin glargine is registered in 28 of the 108 countries in scope, while Eli Lilly and Sanofi do not publicly disclose individual registration data for their insulin glargine (Basaglar® and Toujeo®, respectively).

* See page 39 for a full list of products assessed for registration in this analysis.

** For this analysis, a product is considered to have been registered if it has been either a) filed for registration by the company, or b) has been registered by the regulatory authority.

*** See page 40-41 for more information on the 108 countries in scope of this analysis.

FIGURE 1. Stark differences in insulin registration between countries

Out of the 108 low- and middle-income countries analysed, 74 countries have at least one human insulin and at least one analogue insulin registered; 10 countries only have human insulin registered; and 24 countries have no insulins registered, according to the data available. This graph divides that data between upper-middle income countries (UMICs), lower-middle income countries (LMICs), and low-income countries (LICs).

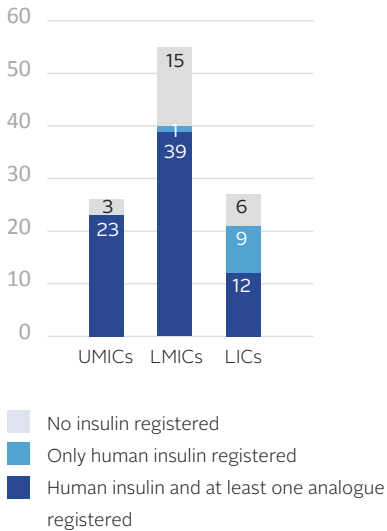
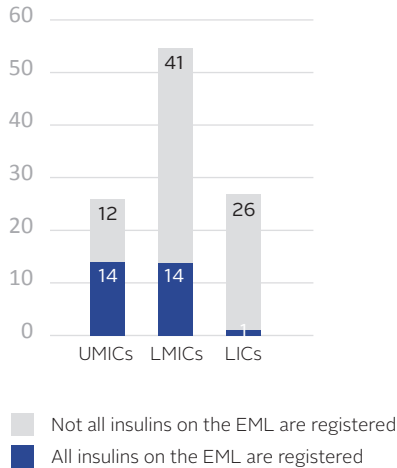


FIGURE 2. 79 countries do not have all essential insulins registered

Out of the 108 low- and middle-income countries analysed, only 29 countries (27%) have all insulins from WHO's Model List of Essential Medicines registered – and as this figure shows, low-income countries are most likely to not have all essential medicines registered.



The countries left furthest behind

While in some countries only human insulins are registered, there are 24 countries in scope where none of the four companies examined by this paper are known to have registered their insulins*. These include politically unstable countries and those affected by conflict, e.g., Somalia and South Sudan, or countries with small populations such as Kiribati and Tuvalu.

Lack of registration can have a severe impact on access and ultimately on the health outcomes of patients living in those countries. Lack of access can be particularly detrimental in those countries as many of the countries without reported registration of insulin are also affected with a very high burden of diabetes.

Opportunities for expanding registration can be pursued more widely

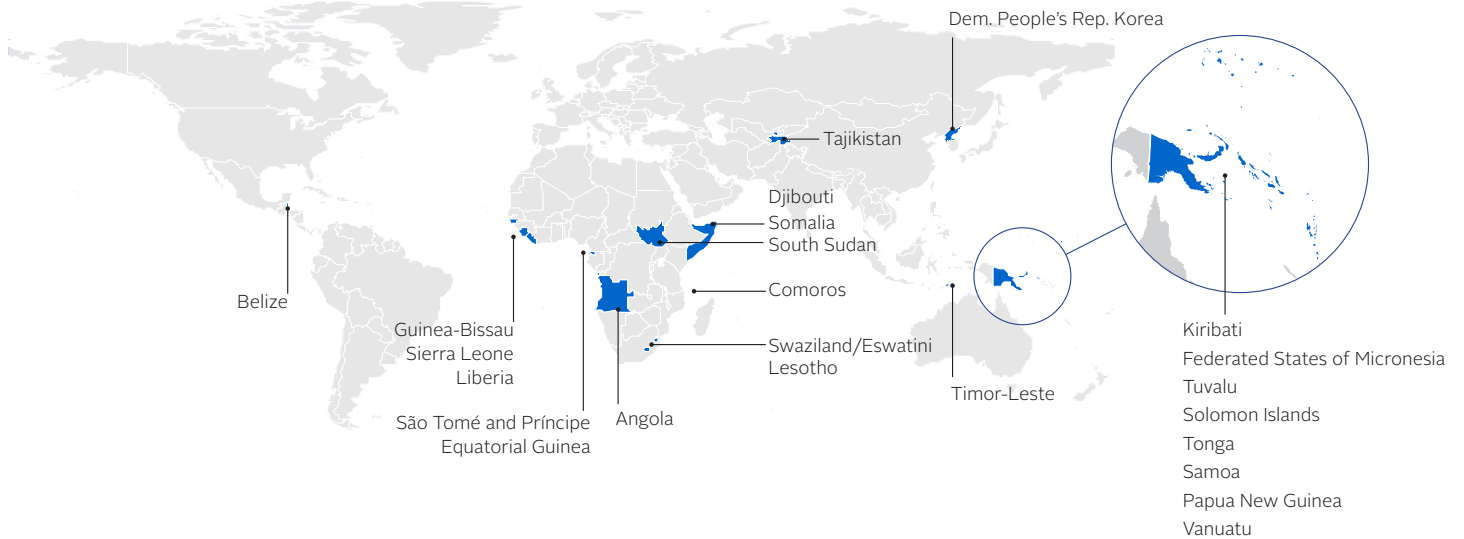
Insulin manufacturers can pursue registration in countries where very few or no insulins are registered (as highlighted above), as well as countries with a high burden of diabetes that struggle with availability of insulin, such as many in the West Pacific region.

There are mechanisms that can facilitate registration of companies' products in LMICs, including insulins, and the main global insulin companies do pursue some of these opportunities. Companies can register their products with National Regulatory Authorities (NRAs) that are classed by the World Health Organization (WHO) as Stringent Regulatory Authorities (SRAs), such as NRAs in the US, UK or Japan. Once the product is approved by an SRA, then countries with non-SRA drug

* As data may not be complete, this does not necessarily represent complete absence of insulin; however, it does indicate competition between manufacturers and access to insulins may be very limited in these countries.

FIGURE 3. In 24 countries, no insulins were found to be registered

Countries highlighted blue on the map do not have any insulins registered, according to the data available. No insulins were found to be registered in 10 of the top 15 countries with the highest burden of diabetes (by DALY rate),⁴⁴ among the countries in scope. The Western Pacific region has the highest estimated number of deaths related to diabetes among adults, accounting for approximately 2.3 million deaths in 2021.¹



authorities can use an accelerated and streamlined regulatory process to facilitate approval.

Recently, some companies have also taken steps towards using international mechanisms such as the European Medicines Agency (EMA)'s 'EU-M4all' procedure (EU-M4all). In April 2022, the EMA, in cooperation with WHO, granted a positive scientific opinion for a proposed update to the storage conditions without refrigeration of two human insulin products. The update is exclusively for non-EU markets.^{11,12} In August 2022, Novo Nordisk received the first country approval, in Lebanon (not in the scope of this paper), for the additional storage option. Following the obtained positive opinion from the EMA, Novo Nordisk also submitted applications to WHO for prequalification of the human insulin products Actrapid® and Insulatard®, including the flexible storage options. A positive outcome from mechanisms such as WHO prequalification and EU-M4all can facilitate regional and national approvals in LMICs.⁴⁵

In 2022, Sanofi made a public commitment to make its glargine the first analogue insulin to be submitted for WHO prequalification (see page 8). This could represent an important step in expanding access to this essential product and could encourage others to pursue this route with their analogue insulins.

Registering biosimilar insulins in LMICs

The registration of biosimilar insulins in more LMICs represents an opportunity to increase access to these products, especially in settings where few or no insulins are currently available.

There are specific challenges to overcome; the registration of biological products such as insulin can be complex due to complex regulatory requirements, which often represent a high financial burden for smaller manufacturers.^{35,46} In addition, registration of insulin may be more difficult in many LMICs due to limited local expertise in regulatory evaluation processes for biological products.⁴⁷

To tackle these challenges, a key strategy for biosimilar manufacturers is to engage in WHO's prequalification procedure and in other collaborative procedures. The WHO prequalification programme has potential to facilitate the work of regulatory authorities and increase trust among procurers, prescribers and patients in LMICs. The programme can also facilitate the sale of insulin products via international non-profit procurement mechanisms and organisations. However, at the time of publication, no biosimilar companies have applied to the prequalification programme for insulin products.

Biosimilar manufacturers could also invest in more studies that assess the efficacy and safety of their products (also called 'switching' studies) and help disseminate study results. This may help increase approval, uptake and trust for quality-assured biosimilar insulin.

INDUSTRY ANALYSIS

Companies are expanding access models, but system-level approaches to address chronic care are lacking

Building on insights from longer-term programmes and initiatives, the main global insulin manufacturers are now exploring strategies to widen the reach of their products in LMICs. A shift towards more systemic business approaches to expand access to insulins can be observed, although this has not yet had a widespread effect and is not supported by independently verified data. As the global demand for insulin rises, all manufacturers will need to adapt and move towards global and sustainable approaches for access to all insulin products.

A higher-level public commitment to increase access to diabetes care can be an important step in fostering integration of access strategies at every level of a company's insulin business. As of today, only Novo Nordisk – a company with a portfolio primarily focused on diabetes products – has established a global corporate strategy targeted at improving access specifically to diabetes care, with its "Defeat Diabetes" strategy. However, other companies, such as Sanofi, have now taken significant steps to establish commitments for expanding access to insulin products in LMICs.

More generalised access strategies may also have an impact in advancing access to diabetes care in LMICs. For example, Eli Lilly's 30x30 encompasses diabetes and seeks to expand access to insulin and other diabetes products in low-resource settings. However, this strategy covers several disease areas, and outcomes specific for diabetes-related activities have not been disclosed.

Some companies aim to integrate access, but impact evaluation needed for sustainability

Over the last few years, both Novo Nordisk and Sanofi have demonstrated a shift towards more integrated business approaches to insulin. Novo Nordisk has begun to implement its new business model iCARE in sub-Saharan Africa, and Sanofi recently launched its Global Health Unit. An integrated approach involves centring financial sustainability from the beginning and integrating initiatives into countries' health systems, as well as other elements such as strengthening diabetes care.

Regular monitoring and evaluation and public disclosure of the impact of access strategies is necessary to make progress toward more integrated approaches to access. This should include tracking and sharing information about patient reach, volumes of insulin sold and impact on outcomes for patients in both the short- and long-term. This data can provide valuable insights that can improve ongoing projects and inform future strategies. Companies can strengthen their evaluation processes either by developing monitoring and evaluation frameworks in-house or working with academic partners and other third parties.

For example, a 2017 assessment of the Base of the Pyramid programme by Novo Nordisk's academic partner University College London provided useful information for the future. This assessment showed that the strategy had succeeded in lowering the final insulin price, but that many people still battled with the costs of travel and necessary commodities such as monitoring tools.⁴⁸ Similarly, Sanofi's Ngao Ya Afya initiative was co-led and assessed by its partner on the project, PharmAccess Foundation, revealing challenges concerning patients' adherence to care.⁴⁹

To date, limited data exists on the impact and reach of companies' access initiatives. More systematic monitoring, evaluation and public sharing of learnings and progress will be fundamental to advance and scale-up such strategies in a sustainable way. In this way, successful factors to improve the availability and affordability of insulins can be better understood and replicated to reach more people with diabetes in more LMICs.

INDUSTRY ANALYSIS

A patchwork of strategies to improve affordability

The data shows that companies vary their approach to affordability depending on the type of insulin (e.g. human or analogue) and the context in particular countries (e.g. the role and structure of public sector healthcare, or the country's income level).

Some of the companies' access models analysed in this paper so far include aspects that are intended to increase affordability of insulin. This section looks more specifically at what actions companies are taking on pricing, whether they are participating in tenders, and the use of patient assistance programmes.

Affordability strategies for human insulins: opportunities to expand access

Price ceilings are one approach companies are exploring as an affordability strategy, with a specific focus on human insulins. For example, Novo Nordisk has established a price ceiling in 76 countries (see page 16), and Biocon has launched Mission 10 cents (see page 20) – with both companies setting their price ceiling at a similar level. These affordability strategies can reduce the costs for governments and patients.

However, implementing a price ceiling as a blanket approach may not consider the diversity of contexts in different LMICs, and it is important for companies to consider differences in how health systems function and what the ability to pay is for the different payers and patients across different levels of the income pyramid.

Companies can also increase access by participating in public sector procurement, via tenders and through international pooled procurement mechanisms, such as via non-profit international medicine suppliers including by UNICEF and IDA Foundation. When companies enter such contracts, the availability and affordability of insulin can improve locally for a large number of patients at a time. Engaging in these strategies is key to expanding access to all types of insulin, but is especially vital to expanding access to human insulin – which can generally be procured at a lower price than analogue insulin – in countries where access to this essential product is still limited, including many countries in which there is a high burden of diabetes.

Some strategies pursued for analogue insulins, but affordability a challenge

Most of companies' affordability strategies are focused on human insulins. This is important, as due to their lower prices, human insulins continue to be the most cost-effective option for many patients living in LMICs. However, this also contributes to the fact that analogue insulins remain much more expensive products than human insulins in most countries. If prices are high, demand is likely to be lower – contributing to a self-perpetuating cycle.

Of the analogues assessed in this paper, equitable pricing access strategies were only identified for Sanofi's insulin glargine (Lantus® and Toujeo®). The company implements pricing strategies targeted at different payers including public entities, patients paying out of pocket, and those covered by private insurance. For instance, the company offers a reduced price for its products in countries including Kenya and Nigeria. However, the number of patients receiving analogues in the aforementioned countries seems to be limited. By incorporating analogues within the remit of its new Global Health Unit, Sanofi shows potential to increase access to these products in LMICs. To understand the impact of this new strategy and the potential increase in access to these products, tracking patient reach will be fundamental.

Other industry initiatives for analogue insulins have focused on providing discounts via patient assistance programmes for patients paying out of pocket. While

these initiatives can be an effective tool for improving the affordability of these products, they often do not result in sustained access and affordable pricing, as they are usually limited in terms of eligibility criteria and cover a relatively small number of individuals.

Analogue insulins remain out of reach for most patients accessing care through both public and private sectors. For example, in the second-largest hospital in Kenya, long-acting analogues, now categorised as essential medicines on the EML, represented less than 4% of total insulin utilisation in 2020.³² Furthermore, Sanofi reported the number of patients reached with insulin glargine (Lantus®) in the whole country in 2020 was less than 300.

The future of pricing and affordability

Insulin manufacturers, including biosimilars companies, can continue to expand pricing and affordability strategies to cover more countries and more products. One key way they can do this is by pursuing intra-country pricing strategies. This involves setting different prices for different payers and population segments within a country, such as national health authorities, public and private institutions and individual patients paying partially or totally out of pocket. It is important that companies share information about how and where pricing strategies are being applied, the criteria considered to establish price conditions, and the financial outcome for patients accessing care through both public and private sectors.

In addition, companies can expand affordability strategies to include not only human insulins, but also essential analogue insulins. This will help to expand access to these products, so that people living with diabetes in LMICs have the same treatment options that people living in high-income countries have had for decades. This could include, for example, engaging with local governments to establish demand, participating in more tenders, and offering lower prices. In addition, biosimilars manufacturers can increase the affordability of analogue insulins by launching quality-assured products in LMIC markets.

Reaching the most vulnerable patients via donations

For many years, companies have engaged in donations of their products, including insulins, to people with diabetes living in low-resource and/or conflict areas. Some donations are short-term, often in response to a natural disaster or crisis situation, while other donation programmes are long-term. Such donations can be fundamental for the survival of people with diabetes who otherwise would not have any options to access treatment.

The impact of insulin donations has previously been identified by international stakeholders as beneficial, and in some cases, outcome studies have shown that programmes correlate with reduction of related mortality and improvements in patients' blood glucose control.⁵⁰ Nonetheless, concerns over the sustainability of donation programmes have been raised, as access to treatment may become fully dependent on industry presence.⁵⁰ In some cases, long-term programmes do cover elements of addressing health system needs, but as companies move forward their donation programmes should systematically incorporate plans for transitioning towards sustainable strategies to ensure continued access.

In addition to insulin, patients need access to products including syringes, injection pens, monitoring devices and test strips. These are vital tools for administering insulin and for managing diabetes. As many countries still rely on donations to provide access to these necessary commodities, it is essential for all companies to systematically include these products in their donations and access strategies, for instance by working in partnership with companies producing diagnostics and medical equipment. To increase the understanding of current global gaps, it is important that companies disclose information regarding what products are being donated and where.

INDUSTRY ANALYSIS

New strategies and partnership models are being used to tackle challenges in the insulin supply chain and the delivery of diabetes care

A range of challenges across the supply chain and within health systems can ultimately affect the availability and affordability of insulin, as well impacting the supply of other essential diabetes commodities, such as devices and diagnostics, for people with diabetes. Pharmaceutical companies cannot solve these issues alone, but they can play an important role by working with other global and local stakeholders to address some of the problems that prevent people with diabetes from getting access to the treatment they need.

Helping to solve issues in the supply chain

Securing a sustainable and affordable supply of insulin requires action across the supply chain, from the manufacturing facility up to the last mile. But for many LMICs with limited resources, the infrastructure required for the proper procurement, delivery, logistics and cold storage of medicine is often lacking.

Because pharmaceutical companies have extensive experience in product delivery, they can provide local governments and healthcare organisations with support in terms of know-how, resources, models for efficient distribution networks and supply practices, strategies to ensure continuous monitoring of demand levels, and capacity building. Research-based pharmaceutical companies can also leverage their expertise to innovate and create products that are more easily supplied and stored.

When cold storage issues are not addressed, this can fundamentally impede the success of companies' strategies to increase access to diabetes care. For example, evaluations of Eli Lilly-supported programmes (AMPATH's glucose management programme in Kenya and the Tshwane Insulin Project in South Africa) showed that a lack of access to cold storage throughout the day, and a lack of knowledge about the temperature at which insulin needs to be stored, contributed to participants' ongoing issues with controlling blood glucose levels.^{51,52}

Looking for solutions to expand cold chain capacity for insulins

Opportunities regarding new advancements in cold chain capacity can be leveraged. WHO and UNICEF stated in 2015 and reaffirmed in 2020 that it is permissible to use the Expanded Programme on Immunization (EPI) and vaccine cold chain capacity for the storage and transport of other temperature-sensitive pharmaceuticals under certain conditions.⁵³ Following the start of the pandemic and the need for a sustainable cold chain to supply COVID-19 vaccines globally, there has been a great push to build additional capacity in LMICs. This has, for example, been the case in Malawi.⁵⁴ Existing cold chain capacity could be used more frequently and effectively to store and transport insulin. To make this successful, there is a need for collaboration between actors from the immunisation and NCD programmes at global and local levels.

Strengthening diabetes care at all levels

Diabetes is a chronic disease and requires uninterrupted access to healthcare services and all necessary treatments and commodities. Without adequate health facilities and trained healthcare practitioners in reachable locations, the continuum of diabetes care breaks down. This includes preventative efforts (particularly for type 2), as well as screening, diagnosis, referrals, lifelong daily treatment, and monitoring for all people with diabetes at various levels of the healthcare system.

To improve the situation, there is an opportunity for companies to develop and scale up integrated models, based on evidence of local needs and gaps. Manufacturers of insulin can play a role in tackling system challenges, such as those related to information systems, healthcare capacity, education and training. When companies engage in such initiatives, they must implement robust strategies to ensure that any potential conflict of interest is mitigated at all levels. This is not always the case, as some companies currently fail to disclose if or how such strategies are put in place. In line with this, responsible promotional practices must be adopted, including a public disclosure of value transfers to healthcare professionals involved in diabetes capacity building programmes.

One significant challenge is that many people living in LMICs currently have limited access to commodities necessary for diabetes care. Currently, the situation is very fragmented; for instance, a patient may have access to a vial of insulin but no syringe, or may own a glucometer but be unable to obtain compatible test strips due to lack of availability or high prices. A study performed in the LMICs covered by the Life for a Child programme found that in many countries, injection devices were difficult to access, and when available, there were prevailing limitations that led to misuse.⁵⁵ Affordability is a core part of the problem; in Mali and South Africa, for example, the cost of syringes and glucose test strips represents the majority of the cost of diabetes care (also including insulin). For people living with type 1 diabetes in Mali, test strips constitute almost 60% of the yearly cost of care.⁵⁶

As insulin manufacturers make efforts to expand access to their insulin products, partnerships with other stakeholders and companies can be essential to ensure the provision of all necessary tools for ensuring appropriate management of diabetes, whether as donations or at affordable prices.

To tackle the fragmentation of product provision, Novo Nordisk and Sanofi are taking part in the Diabetes CarePak initiative, which is carried out by PATH (the non-profit formerly known as Program for Appropriate Technology in Health). This co-packaging solution aims to increase access to safe administration of insulin and self-care at the primary care level by bundling necessary commodities such as glucometers, test strips, needles and syringes, in line with the needs of people with diabetes. CarePak has been rolled out in Kenya with the support of Novo Nordisk, and in Uganda with the support of Sanofi. The initiative includes partnerships with local ministries of health, people living with diabetes and health care providers.

TABLE 1. Companies' strategies along the supply chain and the continuum of care

Challenge to address	Examples of companies' strategies to strengthen the supply chain and continuum of care
Forecasting how much insulin will be needed in a particular country, and in which areas and facilities, can be complex.	Industry initiatives include important elements such as forecasting and information systems, which require collaboration with other stakeholders. These have the potential to improve local supply systems and create more sustainable provision of affordable insulin. For example, Novo Nordisk is working to implement a forecasting tool to be used for estimating annual quantities and costs of products for diabetes care, alongside PATH and the Coalition for Access to NCD Medicines & Products.
Procuring insulin can be expensive, especially for countries purchasing insulin in smaller quantities.	Discussions are in place to use existing mechanisms for international non-profit pooled procurement of insulins, specifically for LMICs. Such mechanisms are already in place for other essential medicines, such as vaccines, antiretrovirals and antimalarial treatments, and have the proven benefit of reducing the price of products for many countries.
Insulin needs continuous cold storage, which can be a challenge for distributors and patients in many LMICs.	Some localised efforts are being pursued to improve cold chain management, but expansion is needed. Recent progress in developing insulins that do not need continuous cold home-storage is a positive advancement, especially for patients in rural areas where storage capacity is limited.
Access challenges exist along the supply chain and are difficult to tackle without collaboration.	Companies are engaging in local partnerships with public and private entities to put access strategies in place. Initiatives such as Novo Nordisk's Base of the Pyramid and Sanofi's Ngao Ya Afya have tackled access challenges including continuity of supply, pricing, patients' education and monitoring.
There are challenges in ensuring high-quality diabetes training and education for healthcare providers and patients alike, so that diabetes can be successfully treated.	Initiatives focused on implementing digital information systems for the management of diabetes are becoming more common. Companies including Eli Lilly and Sanofi are leveraging new technologies to improve aspects of care such as clinical training, engagement between providers and users, patient education and self-management.

SPOTLIGHT

Access to insulin for children and young people

Around 1.2 million children and adolescents are currently living with type 1 diabetes worldwide,¹ and each of them requires access to multiple doses of insulin every day to stay alive. However, challenges with screening, diagnosis and access to treatment are prevalent in many LMICs, leading to children with this condition often dying undiagnosed or misdiagnosed with malaria, gastroenteritis or other disorders.⁵⁷ Global mortality due to diabetes (type 1 and 2) in under-25s has been estimated at 16,300 in just one year (2019), with 97.5% of deaths taking place in countries with a low to high-middle socio-demographic index.⁵⁸ Mortality due to diabetes in young people is estimated to be particularly high in sub-Saharan Africa, South-East Asia and some countries in Latin America.^{57,58}

Insulin manufacturers have a range of programmes in place aiming to address specific challenges in access to insulin and diabetes care for children and young people. Some examples are briefly outlined (see below).

Necessary steps to increase access to diabetes care for children and youth

Over the last 15 years, industry initiatives have made great strides and have helped provide thousands of young people with insulin and necessary monitoring tools. There are now signs of longer-term commitment to these programmes; for example, Eli Lilly, through donations and financial support to Life For A Child, aims to extend access to diabetes care to approximately 150,000 people annually by 2030 and reach over 60 countries, including India, Ethiopia and Bolivia. In 2020, it was announced that Novo Nordisk's CDiC was being expanded, with the aim of reaching 100,000 children by 2030.

Children and young people in LMICs continue to experience deep inequalities in access to diabetes care. For low-resource families with children with type 1 diabetes living in countries where the public system does not provide treatment, the costs of diabetes management may take up all of the family's income.⁵⁹ In such cases, industry programmes have brought valuable aid. However, concerns have been raised about how to continue to provide long-term treatment once programmes end or young people 'age out' of these initiatives. Moving forward, industry programmes must continue to work in partnership alongside local governments and stakeholders to ensure young people continue to have long-term access to all necessary commodities for the management of their condition.

Challenges faced by children and young people with diabetes

- ▶ Lack of access to screening and diagnosis.
- ▶ Lack of access to appropriate treatment.
- ▶ Stigma, insufficient community awareness, and barriers to accessing schooling.
- ▶ Difficulties with the types of delivery and monitoring devices available, such as higher perceived pain from injections via a syringe or from finger-prick tests for glucometers. Such difficulties can reduce adherence to treatment.
- ▶ Lack of regular access to healthcare workers with specific clinical expertise in diabetes management and insulin dosing – which is especially key for children as they grow and their insulin needs change.

Eli Lilly - Life for a Child:

This programme provides insulin free of charge for people under the age of 26 with type 1 diabetes in 44 countries (including 41 in scope). The programme includes the provision of monitoring tools, as well as education for health professionals through the support of other partners.

For more, see page 13.

Novo Nordisk - Changing Diabetes in Children:

Novo Nordisk's programme includes training of healthcare professionals, establishing clinics, support for patient education, and donations of human insulin for people up to 25 years old in 24 countries (including 22 in scope). The programme also provides commodities such as glucometers and test strips through a partnership with Roche.

For more, see page 16.

Sanofi - the KiDS project

This educational programme, co-created by Sanofi, works with schoolteachers, nurses and policymakers and to foster safe environments for children between 6 and 13 years old. The programme aims to promote education about diabetes, raise awareness and reduce related stigma. KiDS programmes have been implemented in 10 countries (including 5 in scope).

For more, see page 19.

Partnerships and sustainable access

Even though some industry programmes have been in place for many years, many local health systems in LMICs have not yet succeeded in being able to take on the mantle of diabetes care on a sustainable, long-term basis. Companies are attempting to find solutions to build sustainability and scale up access, so that more children have access to treatment, and so that people with diabetes are able to continue treatment after ageing out of paediatric programmes.

Pursuing partnerships is one key approach. For example, Novo Nordisk works with global partners such as the International Society for Paediatric and Adolescent Diabetes and the World Diabetes Foundation, industry partners such as Roche Diabetes Care and local partners including ministries of health and national diabetes associations. The activities developed in each context are based on priorities identified by partner countries across workstreams such as data systems, research and innovation. CDiC entered a partnership with Harvard University T.H. Chan School of Public Health to strengthen data systems and registries to identify cost-effective interventions in LMICs. CDiC continues to seek local partners and governments to look for ways to strengthen national health systems and create a financially sustainable model.

Sanofi seeks sustainable change through its KiDS project by pursuing local policy changes regarding the management of type 1 diabetes and prevention strategies for type 2 diabetes in children. For this approach to be successful, local partnerships with a variety of stakeholders are necessary. KiDS was co-created with the International Diabetes Federation, in collaboration with the International Society for Paediatric and Adolescent Diabetes – but with a key role for local partners such as the Public Health Foundation of India, the Brazilian Diabetes Society and the Associação de Diabetes Juvenil (ADJ) of Brazil.

Eli Lilly has also explored collaborative approaches, and in 2022 the company entered a partnership with UNICEF to support care for children and adolescents with non-communicable diseases in five LMICs. In the coming years, evaluation of outcomes will be essential to assess the reach and impact of this initiative.

Indeed, evaluating outcomes can be a useful step in working towards sustainability. Novo Nordisk's CDiC programme measures and reports outcomes via independent evaluations (e.g. by University College London), which helps to build greater understanding of the impact of the strategy. The company publicly discloses the number of children reached and outcomes such as the number of educational sessions and professional trainings.

The global manufacturers of insulin have taken big steps in the 21st century to set up paediatric programmes and reach more children in LMICs with diabetes. While most of these programmes are focused on insulin donations and local capacity building, companies are seeking ways to build long-term sustainability of access and have begun to explore different strategies to achieve this aim. However, chronic challenges remain and solutions must be found so that children with type 1 diabetes can access the treatment they need to live long, healthy lives.

Newer monitoring and delivery methods bring benefits for children – when accessible and affordable

Insulin pens were introduced over 35 years ago. In comparison to syringes, they are easier for children and their carers to use, more convenient to administer during school and outdoor activities, and less likely to attract stigma.⁶⁰ Pens can also be used with short, thin needles that minimise pain and discomfort during injection. Some pens are adapted to provide more specific dosing, which can benefit children who need their insulin dosage tailored as they grow.

Currently, insulin pens are only sometimes included within paediatric programmes. However, Novo Nordisk announced that, from 2022, its CDiC programme would upgrade from syringe and vial to pen devices “in a country-by-country phased approach as appropriate”.⁶¹ Similarly, Eli Lilly recently announced it is aiming to increase donations of reusable pens, as well as to cover costs associated with packaging and shipping.

In high-income countries, more recent innovations in delivery methods have already revolutionised diabetes care. These include smart pens, which can connect with a smartphone and track insulin dosing, and increasingly sophisticated insulin pumps, which are attached to the body and deliver continuous and customised doses of insulin. Using insulin pumps can significantly improve the management of diabetes in children, decreasing adverse events and improving their quality of life and psychosocial functioning.^{62,63} However, these delivery devices are far less likely to be available in LMICs. As technology and science advances, a bigger gap in access is being observed between what is available for young people in high-income contexts and those living in lower-resource settings.

In LMICs, many children and young people do not have access to glucometers and necessary test strips at home. Without their own glucometer, a child will need to travel to a health facility for regular measurements, or may have no choice but to skip testing altogether. Paediatric programmes such as Life for a Child and CDiC do provide these tools to young people by engaging with manufacturing partners. However, many young people in LMICs not covered by these programmes still have no access to these essential diabetes products due to their prohibitive cost.

NEXT STEPS

How to meet the challenge of expanding access to insulin

As the analysis in this paper has shown, there has been progress over the last decade, with insulin manufacturers starting to implement more strategies and initiatives focused on making insulin more accessible in contexts where access is limited. However, to counteract the rising burden of diabetes, increase competition, and make sure all people living with diabetes have a choice of insulins, efforts must be increased.

This section sets out the key actions that insulin manufacturers, including manufacturers of biosimilar insulins, can take to expand access to their products in LMICs. Critical priorities have been identified, in order to strengthen efforts to expand access to insulin in LMICs and guide action towards achieving the targets and some of the key asks laid out in the WHO Global Diabetes Compact.

Expand registration of human and analogue insulins in LMICs to increase patients' access and choice

Continue to expand the registration of insulins, prioritising low-income countries and lower-middle-income countries with a high burden of disease.	When seeking to expand access to their insulin products, companies can prioritise filing for registration in the regions and countries where the need is most urgent. This includes regions with a high burden of diabetes, such as the West Pacific, and regions with limited access to insulins, such as sub-Saharan Africa (see map, page 24). Companies should prioritise registering the insulins – both analogue and human – that have been classed as 'essential medicines' by the World Health Organisation (WHO).
Submit products for WHO prequalification and collaborative procedures, as well as filing for registration with Stringent Regulatory Authorities.	These procedures can facilitate product registration in LMICs and expand the reach of new and existing products, including quality-assured biosimilar insulins.
Register biosimilar insulin products in a greater number of LMICs.	Manufacturers of biosimilar insulins can file their products for registration, both in countries where the original insulin (the 'reference product') has been launched, and in countries it has not. Expanding their footprint in LMICs could increase access to affordable insulin in these countries.

Address affordability and accessibility challenges to promote sustainable access to insulin in the long term

Work towards the development of systematic approaches to access for LMICs.	Manufacturers should expand efforts to increase access to affordable insulin for more people in more LMICs by moving away from fragmented social responsibility models and towards a systematic access approach that addresses every payer's ability to pay (i.e. national authorities, public and private insurers and people paying out-of-pocket). Such approaches should tackle barriers to access for vulnerable groups such as children, young people, and all patients at the base of the economic pyramid.
Ensure that access strategies address context-specific gaps and contribute to long-term sustainability and integration into health systems.	Manufacturers should work with local and national health authorities, diabetes patient groups and other local stakeholders to gain a better understanding of the local needs of different patient populations and align initiatives to regional and local government priorities. Strategies that prioritise meeting local needs and working towards integration within the local health system can help achieve lifelong sustainable access to chronic care for people with diabetes.
Increase efforts to monitor, measure and publicly disclose the impact of access strategies and initiatives.	Evaluating and publicly sharing the impact of strategies can reveal success factors and remaining gaps and can also show what conditions are necessary to make a strategy sustainable in the long term – potentially facilitating peer-to-peer learning between companies so that they can pursue successful access strategies. Companies can strengthen their approaches to monitoring and evaluation either by implementing robust evaluation plans in-house, or by partnering with third-party organisations and academic institutions.
Pursue partnership approaches to address challenges that patients face in accessing both insulin and other essential products for diabetes care.	Collaborations between insulin manufacturers, manufacturers of monitoring and diagnostic tools and other sector partners can help increase access to essential commodities needed by many people living with diabetes, such as glucometers and syringes.

Invest in optimising insulin supply and distribution

Support global efforts to develop digital tools to increase product traceability and forecasting of insulin demand.	Such tools, developed by stakeholders including non-profit organisations, governments, and pharmaceutical companies, have the potential to improve the efficacy of the supply chain by ensuring greater visibility of where products are. Digital tools can be used to help benchmark procurement prices and adequately meet product demand across different locations.
Participate in pooled procurement mechanisms to support the supply of insulin in regions where access is limited.	Manufacturers should enter international and/or regional mechanisms, such as those facilitated by UNICEF and IDA Foundation, to support the expansion of access to insulin for countries with limited access and purchasing capacity.
Collaborate with local distributors and logistics providers to identify bottlenecks in the supply chain and strengthen last-mile delivery of essential products.	When local stakeholders in LMICs request assistance from companies and seek to work in partnership, manufacturers can work together with these local stakeholders to facilitate last-mile delivery of insulin and necessary diabetes supplies for people living in hard-to-reach areas. Key steps can include decentralising insulin supply and building healthcare providers' capacity at the primary care level.

Continue to invest in, and accelerate access to, adapted and novel diabetes treatments or delivery methods

Prioritise and invest in the development of adapted and/or novel insulin products to meet the needs of people living in LMICs, and plan ahead to ensure that products reach patients in these countries.	People living in resource-poor settings, and patients facing particular challenges such as children and young people (see page 32), benefit from products that have been designed or adapted to meet their needs. This includes insulin products that reduce the need for continuous cold chain storage of insulin, as well as insulin products that provide more flexibility around frequency of administration. When developing or adapting products, companies should establish detailed plans during product development and ahead of launch to ensure that, after they are approved, these products reach the people who need them the most.
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Catalysers for expanding access to insulin

Aside from companies, other stakeholders with essential roles to play in facilitating the expansion of access to diabetes care include national and local health authorities, national regulatory authorities, global health organisations, manufacturers of essential commodities, and local partners.

Here, in the context of the broader healthcare ecosystem, the Foundation highlights how challenges can be tackled by other stakeholders in order to 'catalyse' the expansion of access to insulin and speed up companies' progress.

Catalysers include:

- ▶ **Continued progress toward strengthening local regulatory capacity in LMICs.** Current efforts to support more effective regulatory systems, such as by the WHO's Regulatory System Strengthening programme, will be essential to facilitate the registration and availability of quality-assured products in LMICs, including of biologic products.
- ▶ **Global and regional harmonisation of regulation for medical products.** If countries' or regions' regulatory requirements and registration procedures are streamlined and/or aligned with other countries', this can expedite registration and also encourage more companies to file their products for registration. This can include streamlining technical requirements for marketing authorisation of products, such as legislation, technical guidelines, and regulatory documentation.
- ▶ **Improved knowledge and awareness of biosimilars.** Initiatives such as evidence-based training for healthcare providers and patient education programmes, guided by health authorities and patient and clinicians' associations, can help inform the use and role of biosimilar insulins. These initiatives can also encourage the adoption of guidelines regarding interchangeability and increase the use of biosimilar insulins whenever they are the most affordable option.

- ▶ **Strategies to address unnecessary mark-ups to the price of insulin.** Reviewing, optimising and enforcing national regulations related to taxes, import tariffs and wholesale and retail mark-ups can help reduce the magnitude of mark-ups along the insulin supply chain and ensure the lowest possible local insulin price for patients.
- ▶ **Optimisation of local supply chains for insulins.** Investment in local distribution and forecasting technologies can lead to more effective management of the supply chain in LMICs, reducing the risk of disruptions and ensuring better continuity of supply. Similarly, action to strengthen and expand cold chain capacity, for instance by promoting the integration of insulin within the cold chain system for vaccines, can help ensure access in resource-limited settings.
- ▶ **Prioritisation of diabetes in LMIC governments' policy and funding.** Adopting national diabetes targets, in line with international agreements (e.g., World Health Assembly resolutions), and taking steps to meet these targets, for example by improving access to screening at the primary care level, are essential to strengthen diabetes care. Such efforts must be supported by increased investment in diabetes care.

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APPENDIX

I. METHODOLOGY

This paper was developed through direct data collection from the insulin manufacturers in scope, as well as a review of public sources and interviews with stakeholders, as detailed below.

Data collection

- Data submitted to the 2022 Access to Medicine Index
- Supplementary data requests to companies
- Publicly available information (including annual reports, peer-reviewed literature, and other publications)



Data collected on a diversity of topics, including registration of insulin products, company governance, access strategies and supply and manufacturing related to diabetes in LMICs.

The following companies were invited to provide information: Biocon, Eli Lilly, Novo Nordisk, Sanofi.

Stakeholder consultations

- Targeted consultation process including 16 experts from 14 different affiliations. This included 6 experts from 6 LMICs in scope.
- Included in-country clinicians, academic researchers and implementing partners, as well as representatives from local ministries of health, global health organisations and patient groups.



Insights used to define current challenges, practices and priorities in expanding access to insulin, as well as broader diabetes care, in LMICs.



Expert session

'Closing the gaps in access to diabetes care in low- and middle-income countries', 7 July 2022.



Expert representatives from industry, public sector partners and global health organisations met to discuss practices and solutions for closing the gaps in access to diabetes care in LMICs.

II. PRODUCT SCOPE

TABLE 1. Products in scope of this study

● Yes

○ No

Product name (International Nonproprietary Name)	ATC code*	Manufacturer	On-patent? **	Registration data available? ***
Human insulins				
Insulin human (rdna)	A10AB01	Biocon	○	●
Insulin human (rdna)	A10AB01	Eli Lilly	○	○
Insulin human (rdna)	A10AB01	Novo Nordisk	○	●
Insulin human (rdna)	A10AB01	Sanofi	○	●
Isophane human insulin	A10AC01	Biocon	○	●
Isophane human insulin	A10AC01	Eli Lilly	○	○
Isophane human insulin	A10AC01	Novo Nordisk	○	●
Isophane human insulin; human insulin	A10AD01	Biocon	○	●
Isophane human insulin; human insulin	A10AD01	Eli Lilly	○	○
Isophane human insulin; human insulin	A10AD01	Novo Nordisk	○	○
Analogue insulins				
Insulin aspart	A10AB05	Biocon	○	●
Insulin aspart (l-arginine)	A10AB05	Novo Nordisk	○	○
Insulin aspart (niacinamide)	A10AB05	Novo Nordisk	●	●
Biphasic insulin aspart	A10AD05	Novo Nordisk	●	○
Insulin aspart	A10AD05	Sanofi	○	○
Insulin degludec	A10AE06	Novo Nordisk	●	●
Insulin degludec/ insulin aspart	A10AD06	Novo Nordisk	●	●
Insulin degludec/ liraglutide	A10AE56	Novo Nordisk	●	●
Insulin detemir	A10AE05	Novo Nordisk	●	●
Insulin glargine	A10AE04	Biocon	○	●
Insulin glargine	A10AE04	Eli Lilly	○	○
Insulin glargine	A10AE04	Sanofi	○	●
Insulin glargine/ lixisenatide	A10AE54	Sanofi	●	○
Insulin glulisin	A10AB06	Sanofi	○	○
Insulin lispro	A10AB04	Eli Lilly	○	○
Insulin lispro	A10AB04	Sanofi	○	●
Insulin lispro; insulin lispro protamine	A10AD30	Eli Lilly	●	○

* The Anatomical Therapeutic Chemical (ATC) classification system is the gold standard for international drug utilisation monitoring and research. ATC codes can be consulted at the WHO Collaborating Centre for Drug Statistics Methodology website (https://www.whocc.no/atc_ddd_index/).

** The patent status reported is not intended to be a presentation of patent rights worldwide nor does it capture all patents that might apply to a product. It should only be used as a proxy description, which was based on information from regulatory authority websites (i.e., South-African CIPC Intellectual Property database, the US FDA

Orange Book, Health Canada) and/or patent databases (MedsPaL4 and Pat-INFORMED5). Where possible, patent status was verified with companies. It cannot be used as an indication of patent status outside of South Africa and/ or the US and Canada.

*** 'Registration data' represents data provided by companies regarding whether the product has been registered– or filed for registration – in any of the countries in scope. Registration data available for analysis in this paper included 15 insulin products (6 human insulins and 9 insulin analogues).

III. GEOGRAPHIC SCOPE

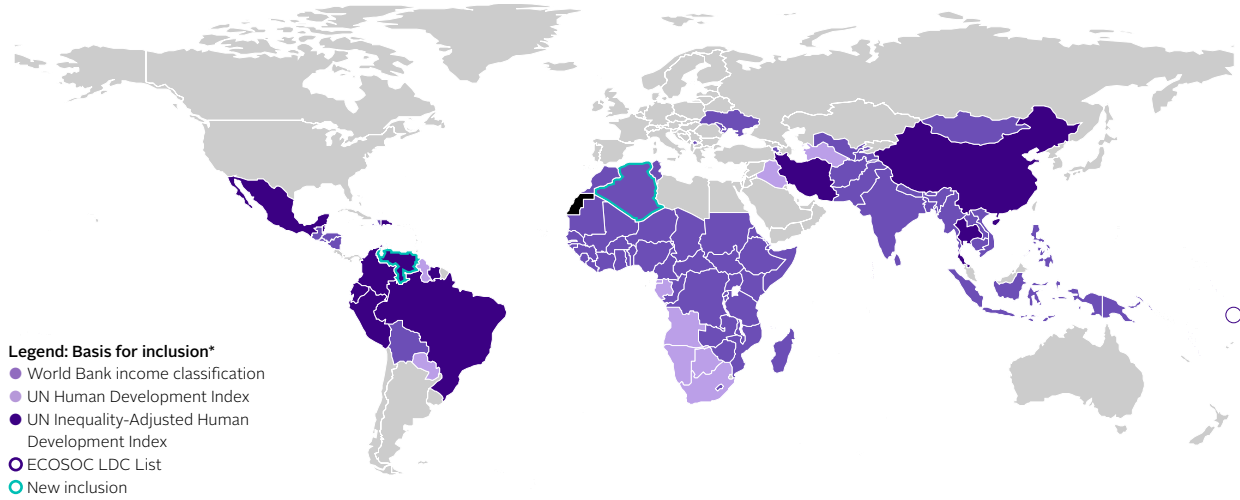
TABLE 2. The 108 low- and middle-income countries in scope of this paper

Key for this list:

LIC	Low-income country, based on World Bank income classifications
LMIC	Lower-middle income country, based on World Bank income classifications
LDC	Least Developed Country, based on ECOSOC LDC List
LHDC	Low Human Development Country, based on UN Human Development Index
MHDC	Medium Human Development Country, based on UN Human Development Index
HiHDI	High Human Development Country with high inequality, based on UN Inequality-Adjusted Human Development Index

East Asia & Pacific		Honduras	LMIC	Dem. Rep. Congo	LIC
Cambodia	LMIC	Mexico	HiHDI	Rep. Congo	LMIC
China	HiHDI	Nicaragua	LMIC	Côte d'Ivoire	LMIC
Indonesia	LMIC	Paraguay	MHDC	Equatorial Guinea	MHDC
Kiribati	LMIC	Peru	HiHDI	Eritrea	LIC
Dem. People's Rep. Korea	LIC	Suriname	HiHDI	Ethiopia	LIC
Lao PDR	LMIC	Venezuela	HiHDI	Gabon	MHDC
Micronesia, Fed. Sts.	LMIC			The Gambia	LIC
Mongolia	LMIC	Middle East & North Africa		Ghana	LMIC
Myanmar	LMIC	Algeria	LMIC	Guinea	LIC
Papua New Guinea	LMIC	Djibouti L	MIC	Guinea-Bissau	LIC
Philippines	LMIC	Arab Rep. Egypt	LMIC	Kenya	LMIC
Samoa	LMIC	Iran	HiHDI	Lesotho	LMIC
Solomon Islands	LMIC	Iraq	MHDC	Liberia	LIC
Thailand	HiHDI	Morocco	LMIC	Madagascar	LIC
Timor-Leste	LMIC	Palestine, State of /		Malawi	LIC
Tonga	LMIC	West Bank Gaza	LMIC	Mali	LIC
Tuvalu	LDC	Syrian Arab Republic	LMIC	Mauritania	LMIC
Vanuatu	LMIC	Tunisia	LMIC	Mozambique	LIC
Vietnam	LMIC	Rep. Yemen	LMIC	Namibia	MHDC
				Niger	LIC
Europe & Central Asia		South Asia		Nigeria	LMIC
Armenia	LMIC	Afghanistan	LIC	Rwanda	LIC
Kosovo	LMIC	Bangladesh	LMIC	São Tomé and Príncipe	LMIC
Kyrgyz Republic	LMIC	Bhutan	LMIC	Senegal	LIC
Moldova	LMIC	India	LMIC	Sierra Leone	LIC
Tajikistan	LMIC	Maldives	HiHDI	Somalia	LIC
Turkmenistan	MHDC	Nepal	LIC	South Africa	MHDC
Ukraine	LMIC	Pakistan	LMIC	South Sudan	LIC
Uzbekistan	LMIC	Sri Lanka	LMIC	Sudan	LMIC
				Swaziland/Eswatini	LMIC
Latin America & Caribbean		Sub-Saharan Africa		Tanzania	LIC
Belize	HiHDI	Angola	LHDC	Togo	LIC
Bolivia	LMIC	Benin	LIC	Uganda	LIC
Brazil	HiHDI	Botswana	MHDC	Zambia	LMIC
Colombia	HiHDI	Burkina Faso	LIC	Zimbabwe	LIC
Dominican Republic	HiHDI	Burundi	LIC		
Ecuador	HiHDI	Cabo Verde	LMIC		
El Salvador	LMIC	Cameroon	LMIC		
Guatemala	LMIC	Central African Republic	LIC		
Guyana	MHDC	Chad	LIC		
Haiti	LIC	Comoros	LIC		

FIGURE 1. Countries in scope of this paper – 108 Countries



* The latest country income and development classifications are available through the World Bank and UNDP data.

Due to scaling, countries may not be visible on the map (e.g., Tuvalu)

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