White Paper

Sticking Point: Developing and Retaining Value with Parenteral Products

AARON WRIGHT, Analyst, EMEA Thought Leadership, IQVIA

Table of contents

Introduction

The modern pharmaceutical industry has created countless life-saving medicines that have improved the health and life expectancy of billions of individuals[1]. One of the primary considerations when developing a pharmacotherapeutic is the method of administration, an attribute that can be driven by the nature of the pharmacotherapeutic (as some will never be oral) and that can affect a product's appeal to patients, reimbursement potential, supply chain and manufacturing complexity, and the pharmacokinetics of the medicine itself.

Parenteral delivery (see footnote for full definition) is a vital way of administering medicine, and some of the best-selling products of the past decade are administered parenterally. For parenteral products, both existing and developing therapy areas are highly valuable and see strong value growth, at a time when health systems face unprecedented cost containment pressures. Patient friendly versions of parenterals delivered in subcutaneous pens are currently seeing a huge, consumer-driven expansion powered by the rise of obesity treatments, meaning more patients are self-administering their medications parenterally. However, parenteral delivery also faces competition from other delivery systems, notably orals, and will have to demonstrate the benefits offered to patients, payers and health systems more than ever before.

Parenteral global trends

Parenteral medicines command a first-place proportion of global Rx sales value, with 47% of sales in 2023 at list prices and excluding vaccines (which are themselves largely parenteral), as Figure 1 shows. This share has increased substantially over the past five years, growing at a CAGR of 11%, and up from a 40% market share in 2018. As a result, not only have parenterals been responsible for more than 63% of total Rx pharmaceutical value growth since 2018, but they have also overtaken orals to become the most valuable method of drug administration[2].

Whilst parenteral products make up nearly half of global sales value, the inverse is true for global volume. Only 1.3% of volume measured in Standard Units (SUs)[i] is attributable to them, the lowest share of any method of administration, and a slight decrease from 1.4% of volume share in 2018[3]. This includes insulins which made up around 2 billion SUs in 2023.

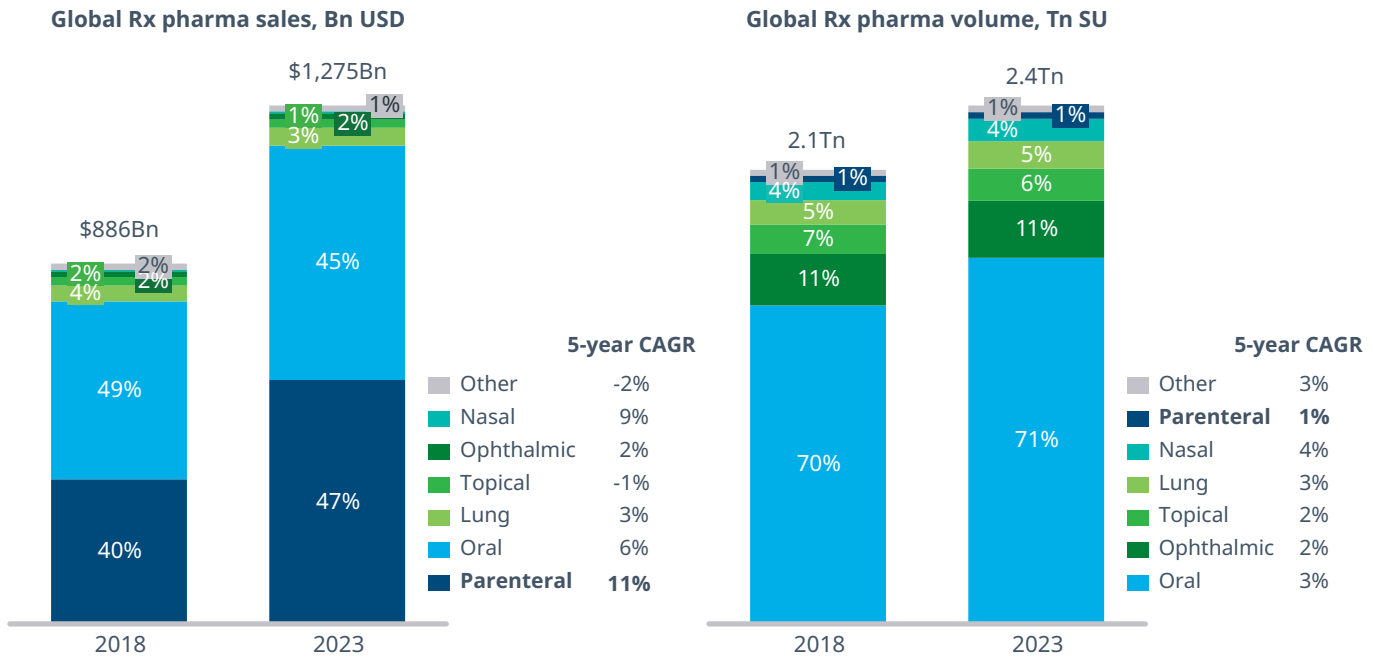
Combining the value and volume shares for parenteral products shows they contain many high-value, low-volume products, and that the average list price of these products has increased significantly during this period, at a faster rate than any other product type.

This is not surprising considering these products tend to be both biologics and specialty medicines, which can generally command higher prices than small molecules or primary care products. In the twelve months to September 2023, 84% of parenteral product sales value came from biologics – of which 7% was from insulin products — and two-thirds were specialty products[4].

84% of parenteral product sales value came from biologics — of which 7% was from insulin products

[i]Standard Units are the number of "standard" doses sold, and is a way of comparing volumes of products in different forms. For instance, for products in tablet form 1 tablet = 1 SU; for products in vials 1 vial = 1 SU, and so on.

Figure 1: Global Rx market split by product type (MAT Q3 2018 – Q3 2023, excl. COVID-19 vaccines)



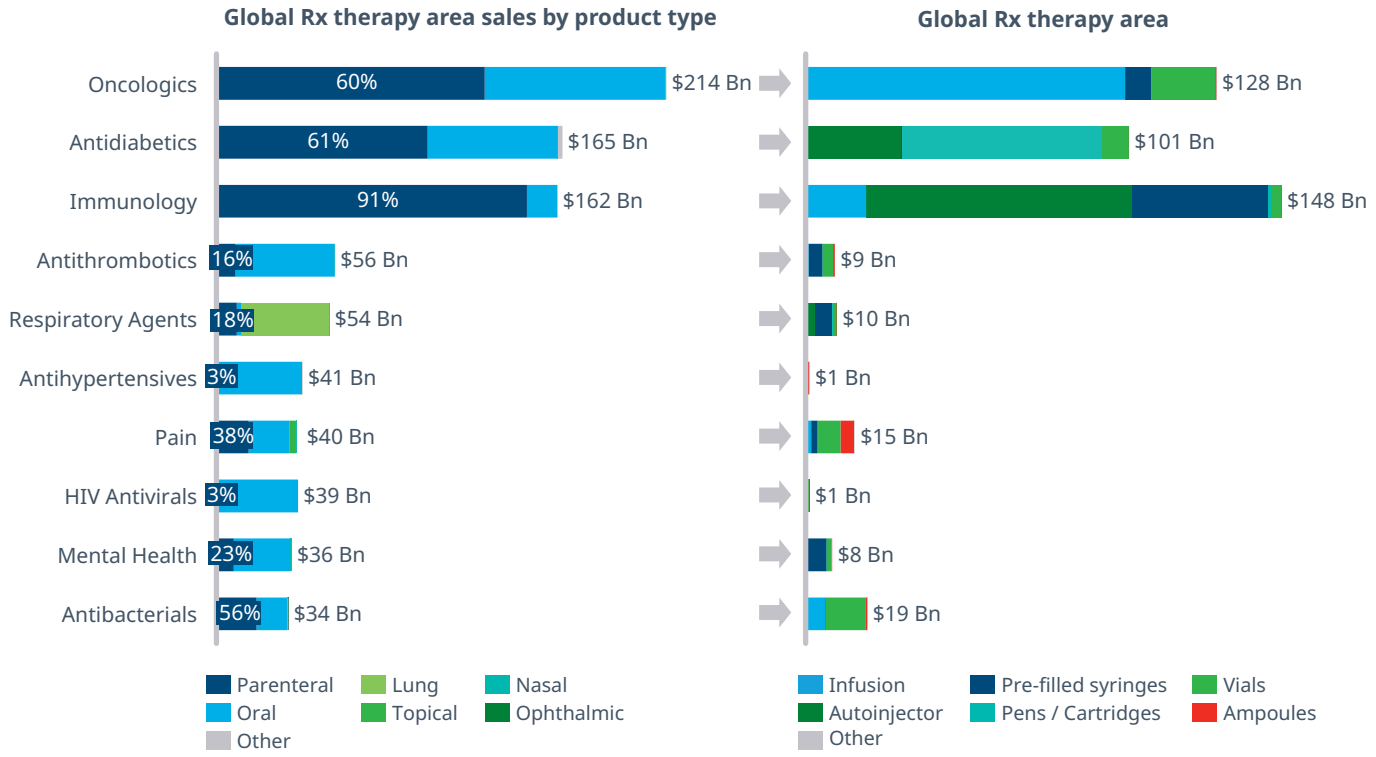
Source: IQVIA EMEA Thought Leadership; IQVIA MIDAS Q3 2023, Ex-MNF prices (excludes discounts and rebates)
Notes: Injectables includes Ophthalmic injectables. Excludes Diagnostics; Hospital Solutions; Imaging; Chinese Medicines; Non-therapeutics; Vaccines; COVID-19 Vaccines; Vitamins & Minerals. NFC2 used for product type segmentation; Sales value shown at constant exchange rate

Figure 2 shows how the top three global therapy areas by value all have a majority of their sales coming from parenteral products, though to varying degrees. The composition of parenteral sales for these therapy areas is shown in the second half of Figure 2, illustrating that the split by sub-type varies greatly between therapy areas. Nearly 80% of oncology parenteral sales come from infusion products, which require the presence of a healthcare professional (HCP) compared to only 13% for immunology. Part of the reason for this is safety; many oncology products are cytotoxic and could cause harm if they leak out of a faulty device so simple, secure packaging and HCP supervision are desirable for these products. In immunology, autoinjectors represent the bulk of parenteral sales at just over 50%. For a group of conditions that can be chronic, self-administrable products taken infrequently are more convenient for patients, in terms of both time and effort.

As the only primary care therapy area in the top three, antidiabetics show the highest proportion of parenteral sales from forms that can be self-administered, including subcutaneous delivery of insulin: autoinjectors and pens/cartridges make up over 90% of sales in this therapy area. It is worth noting that the management of diabetes has always been patient-led, as due to the treatment regimens needed, medicines which required HCP administration would be unfeasible.

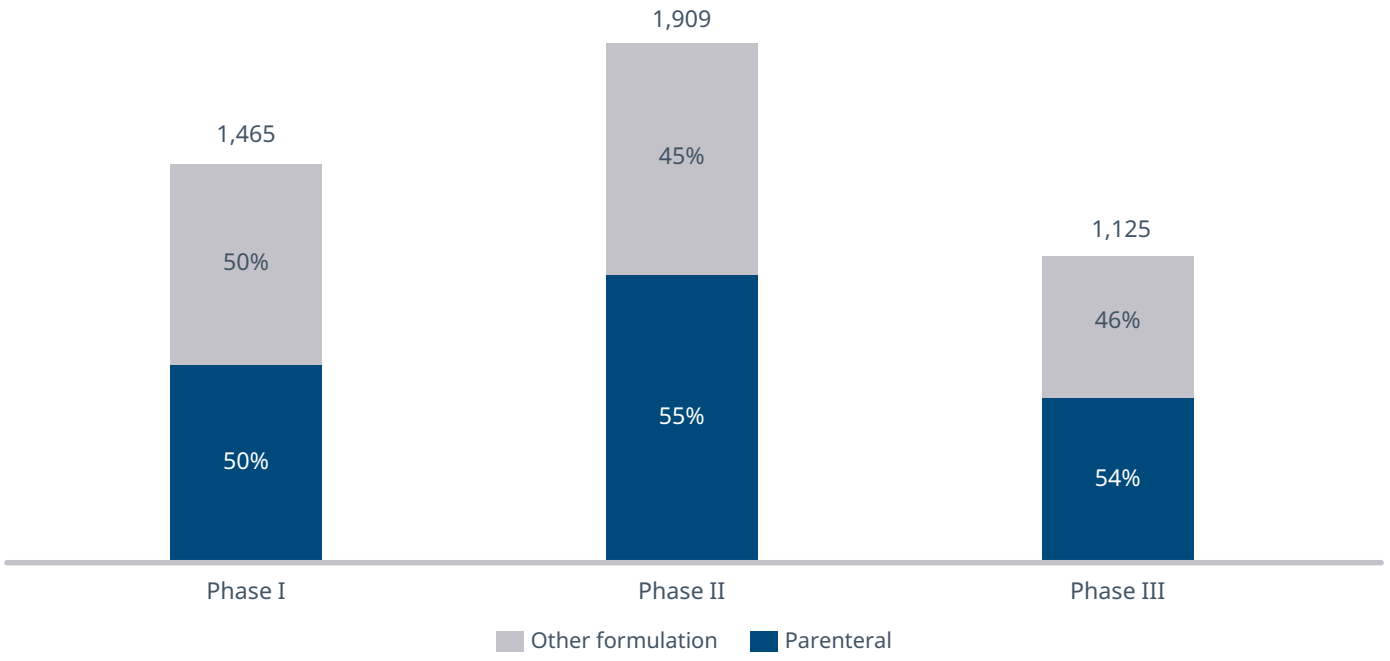
With regards to the clinical trial pipeline, as Figure 3 demonstrates over half of all clinical trials in phases one to three are investigating a parenteral formulation. The high number of biologics and oncologicals in development is a driving factor behind the high number of parenteral products being trialled.

Figure 2: Top ten global therapy areas by product share (MAT Q3 2023, Bn USD, excl. COVID-19 vaccines)



Source: IQVIA EMEA Thought Leadership; IQVIA MIDAS Q3 2023, Ex-MNF prices (excludes discounts and rebates), Rx products only
Notes: Injectables includes ophthalmic injectables. Excludes Diagnostics; Hospital Solutions; Imaging; Chinese Medicines; Non-therapeutics; Vaccines; COVID-19 Vaccines; Vitamins & Minerals. NFC2 used for product type segmentation; Sales value shown at constant exchange rate

Figure 3: Clinical trials pipeline by formulation type (Phase I – III, Global, January 2024, n = 4,499)



Source: IQVIA Pipeline Link January 2024. Phases Preclinical – Phase III (excludes discovery and submitted). Injectable defined as any line entry with at least one of "vial", "Ophthalmic injectables", "Pre-filled syringe" under route of administration.
Note: Clinical trials may be investigating multiple formulations.

Significant value attracts competition

Although parenterals represent a robust sector of the global pharma market, with significant sales and a strong future pipeline, their association with high-value products and indications ensures that current and future competition is fierce.

There have been — and continue to be — many attempts to develop alternatives to parenteral delivery of medicines. Much of the innovation has looked at new ways to administer insulin, such as with inhaled insulins Exhubera and Afrezza, and attempts to create wearable patches with micro needles[5,6,7]. Other development includes creating swallowable pill-like devices with needles to inject in the gut, and even using lasers to push medicine through the skin[8,9]. However, these techniques have not yet significantly challenged parenterals; Exhubera was pulled off the market due to poor sales, Afrezza has not experienced significant commercial success, and the other technologies are still in the development phase. Currently, only one mode of delivery can challenge parenterals' commercial share: orals.

Orals versus parenteral products

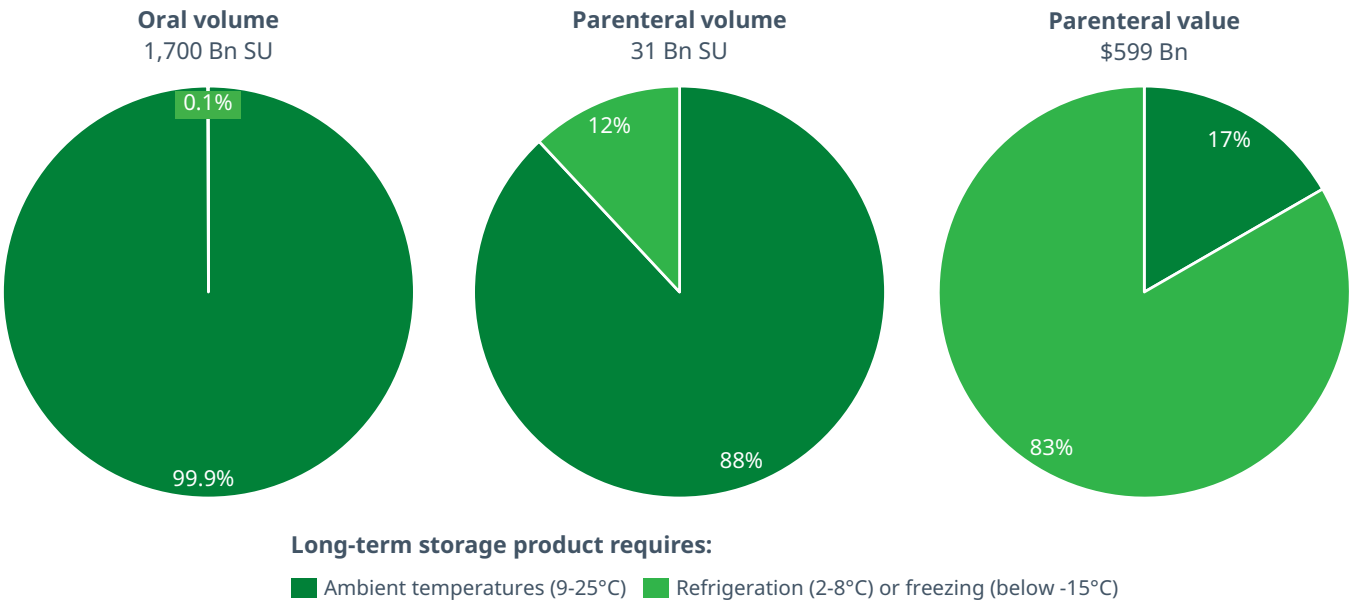
Together orals and parenterals make up essentially the entire pharmaceutical value, as seen above in Figure 1. Orals also show a 5-year CAGR of 6%, second behind parenterals but have by far the largest share of pharmaceutical volume, at 71% in 2023. Oral products can offer an alternative to patients who are uncomfortable with injections and are much quicker to administer with little or no preparation required; it takes seconds to ingest an oral product compared to minutes or even hours depending on the type of parenteral product used[10,11]. However, despite their easier administration, it is not guaranteed that patients will prefer to take orals over parenteral products. Other factors such as frequency of administration — as with long-acting parenterals for anti-psychotics — and advances in parenteral administration through thinner needles and easier to handle devices, can play a role in patient preference[12].

Currently, one major advantage parenterals have over oral products is that they are much more suited to the delivery of biologics, as well as complex and large molecules. As previously mentioned, 84% of parenteral sales value came from biologics in the twelve months to September 2023. In the same period biologics accounted for just 2% of oral value. This lead is not likely to diminish anytime soon as most biologics, and notably the high-value monoclonal antibodies (mAbs), are ill-suited to oral formulations due to poor penetration across the gut and their susceptibility to degradation[13]. Though there is ongoing research into methods for oral administration of biologics, barring a major breakthrough in mAb absorption parenteral delivery will remain the most suitable way to administer most types of biologics in the near future[14].

In terms of long-term storage, oral medications are less sensitive to temperature changes than parenteral products. As Figure 4 highlights, 99.9% of orals by volume do not require any special long-term refrigeration requirements, compared to only 88% of parenterals (excluding vaccines)[15]. However, the 12% of parenterals that do require long-term cooling represent 82% of total parenteral sales value in 2023.

Most of the parenteral products that can be stored at ambient temperatures long-term are high-volume generics contained in either ampoules, vials or in lyophilised form. In addition, the storage temperature can differ when a product is about to be used compared to when it is stored long-term. With lyophilised products, once they have been mixed they often must be chilled and then used within 24 or 48 hours. Similarly, self-use insulin pens will be kept in fridges, but can be carried around at ambient temperatures for a time before the insulin spoils. These cooling requirements have the knock-on effect of limiting the distribution of valuable parenterals to countries and regions that have the infrastructure and logistical capabilities to handle them. Currently all major markets have these capabilities, but this is not the case for many low and middle-income countries where investment in cold chain infrastructure may be lacking. This contributes to lack of access to

Figure 4: Temperature requirements for storage of parenterals and orals(MAT Q3 2023, Global, excl. COVID-19 vaccines, incl. powder products before mixing)



Source: IQVIA EMEA Thought Leadership, MIDAS Q3 2023
Notes: Excludes Diagnostics; Hospital Solutions; Imaging; Chinese Medicines; Non-therapeutics; Vaccines; COVID-19 Vaccines; Vitamins & Minerals. NFC2 used for product type segmentation; cooling requirements are applied based on the molecule level

parenterally delivered therapeutics, something which contributes to, for example, under-vaccination and the persistence of "zero dose" children, those who have never received any vaccination, a situation greatly exacerbated by the COVID-19 pandemic[16]. While improvements in cold chain infrastructure and technologies are required, ambient temperature formulations are also potentially important.

The distribution of COVID-19 vaccines gives a glimpse of how solutions can evolve; early in the vaccine rollout, the innovative mRNA vaccines initially required ultra-cold storage of -80°C. Subsequent testing showed that these products could in fact be stored at normal refrigeration temperatures, albeit for a shorter time than if they are frozen[17,18]. There is ongoing research into making parenterals, and particularly vaccines, that do not require refrigeration. Methods differ depending on the active ingredient and there are still obstacles to overcome, but many scientists are hopeful these ambient products will be available within a decade[19]. Orals, though, do not have to overcome these challenges.

Competition between parenteral sub-types

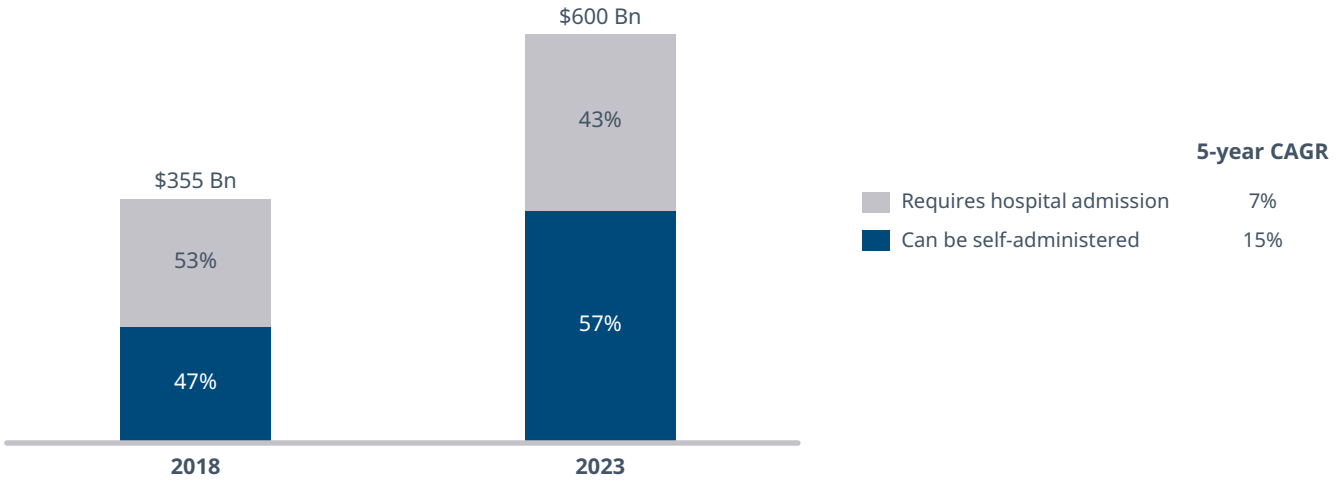
Alongside the external competition parenteral products face from oral formulations, there exists substantial internal competition between different parenteral sub-types. This can be due to efforts to differentiate products in the same indication, alongside other more traditional factors such as efficacy and tolerability. A good example of this can be seen in the PD-(L)1 checkpoint inhibitors market in oncology. With the global market expected to be $58Bn in 2025, manufacturers are looking for ways to differentiate to boost their share of value[20].

As part of this there is a race to develop subcutaneous versions of products, when initially all those launched were IV-based. Roche's Tecentriq (atezolizumab) is currently winning the race, after the UK's MHRA approved the use of a subcutaneous formulation in August 2023[21]. The EMA and FDA are also considering approvals for the subcutaneous formulation, and other checkpoint inhibitors are in late-stage trials, such as top-selling Keytruda (pembrolizumab)[22,23]. These therapies, while subcutaneous, are not currently self-administrable though and require HCP administration due to the possibility of adverse side-effects.

Generally, subcutaneous, intramuscular (IM), and intradermal (ID) injections are more likely to be self-administrable than IV formulations, as indicated by the self-administered IM product Plegridy (peginterferon beta 1a) for multiple sclerosis, and the subcutaneous Humira (adalimumab) for multiple indications. Products that have the potential to be self-administered have seen significant growth in recent years, growing twice as fast as products that would require hospital admission, highlighted in Figure 5. Compounding factors have further boosted the demand from payers for these types of products, especially due to knock-on effects from the COVID-19 pandemic. Existing problems such as underfunding in healthcare systems and chronic understaffing have been exacerbated: the global cost of COVID-19 vaccines alone is expected to add $213Bn to medicine spend between 2021-2028, which may draw funds away from other important areas, and the rate of new HCPs entering the job market is not sufficient to replace those who have retired or quit[24,25]. Additionally, in the medium-long term demographic changes, namely increasing numbers of elderly people who tend to require more care, mean these funding and infrastructure issues will not be temporary.

Self-administrable formulations have grown twice as fast as products that would require hospital admission

Figure 5: Growth of self-administrable parenterals (MAT Q3 2018 – 2023, Bn USD, Global, excl. COVID-19 vaccines)



Source: IQVIA EMEA Thought Leadership, MIDAS Q3 2023

Notes: Excludes Diagnostics; Hospital Solutions; Imaging; Chinese Medicines; Non-therapeutics; Vaccines; COVID-19 Vaccines; Vitamins & Minerals. NFC2 used for product type segmentation; NFC2 used for product type segmentation; Sales value shown at constant exchange rate

As a result, payers are looking to ways to control medicine spend and free up capacity by relieving the burden on infusion centres and hospitals. Self-injectable formulations can help in accomplishing this. Compared to formulations such as IV, these medicines have a much shorter administration time meaning HCPs can engage with a greater number of patients in a given time, resulting in greater cost-effectiveness. The breast cancer product Phesgo (trastuzumab / pertuzumab) provides a good indicator of the time saved: it combines two products that required IV infusion into a single injection administered by an HCP, leading to time savings of two-and-a-half hours in cases[26]. If the self-administrable products do not require any HCP involvement and can be performed by the patient at home — drug safety and side effects permitting — these savings become even greater.

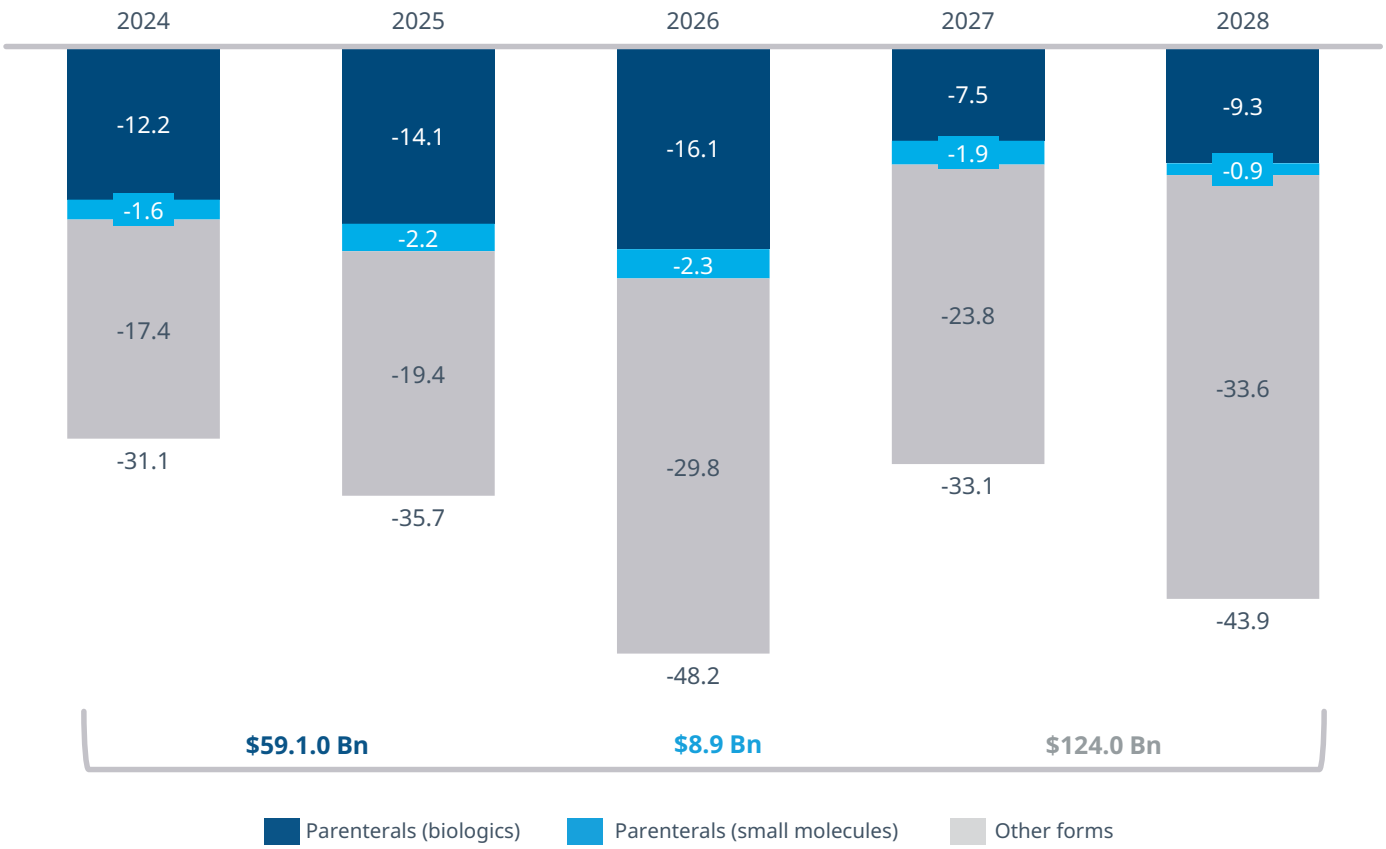
Biosimilar and generic erosion

When their active agent loses exclusivity parenteral products can see low-cost competition in the form of small molecule generics and biosimilars. As Figure 6 shows, $68Bn worth of parenterals are at risk from loss of exclusivity over the next five years in the top 10 developed markets. This is a significant saving for payers, and policymakers are likely to continue enforcing cost-reducing policies such as switching patients from the reference product to a biosimilar or generic. It is worth noting though that despite these policies, competition is not equal for all products. For biologics especially, various factors can impact the appeal of developing biosimilars, leading to products where there are little to no biosimilars in development[27].

Due to the cost constraints on payers and the savings these policies can affect, manufacturers should not expect this environment to change any time soon, nor to be able to prevent erosion in the long term. Despite this, there are innovation approaches that can be taken to make this erosion more manageable by spreading it out over a longer period, while at the same time offering greater convenience to patients and cost savings to health systems.

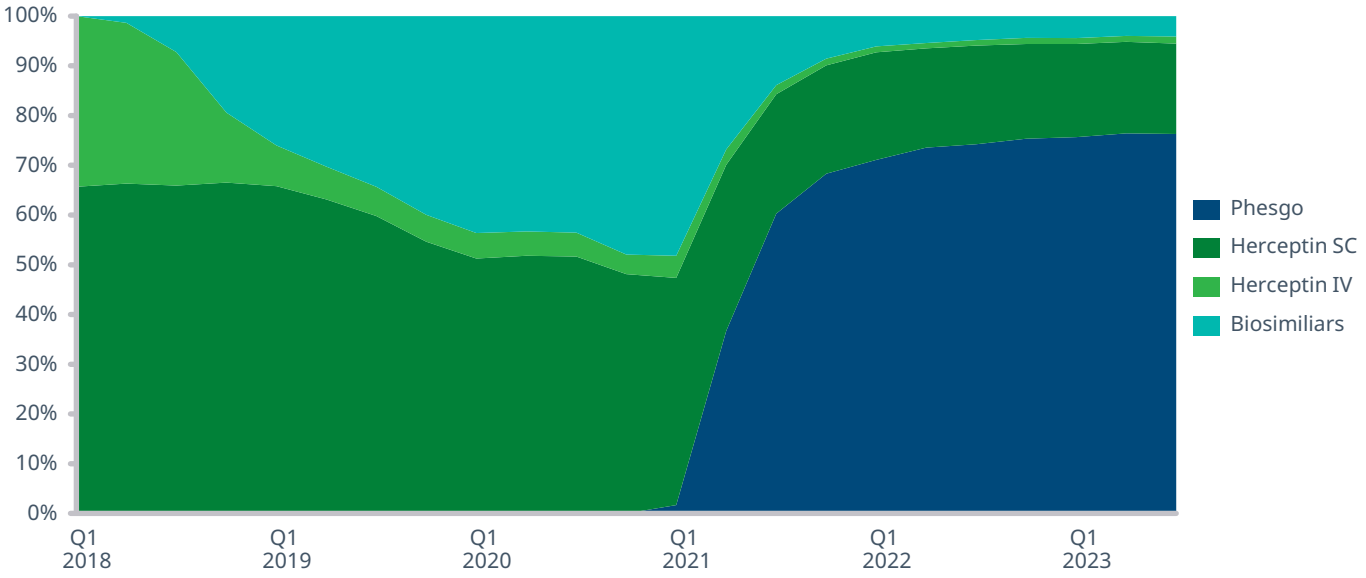
Again, Phesgo can be used as an example: Figure 7 highlights the market dynamics of trastuzumab products in the UK following the entry of the first biosimilars. These biosimilars, which could only be in IV infusion form, quickly ate away at the reference products sales share, primarily in the IV form followed by some erosion of the subcutaneous. This eventually led to a market where nearly half of the value was taken up by biosimilar sales. Then, in 2021 the release of the innovative and subcutaneous product Phesgo quickly came to dominate the market, comprising 70% of value in Q3 2023. Of course, Phesgo also offered a genuine advance in the HER2 breast cancer space, and came at a time when the demand to reduce patient attendance in care centres was sky high, both of which combined to help its launch.

Figure 6: 10 developed countries impact of brand losses of exclusivity 2024 – 2028 (Bn USD, Forecast)



Source: IQVIA EMEA Thought Leadership, IQVIA Institute Nov 2023, IQVIA Market Prognosis September 2023

Figure 7: Trastuzumab market dynamics following biosimilar entry in the UK (Q1 2018 – Q3 2023, Mn USD)



Source: IQVIA EMEA Thought Leadership, IQVIA MIDAS Q3 2023, Sales shown at Ex-MNF prices. Discounts, rebates and VPAS pricing scheme not included. Sales calculated at Constant Exchange Rate

Supply chain and climate impacts

The requirement to store and transport the majority of high value parenterals at one of a range of refrigerated temperatures has been mentioned previously. However, the cold-chain aspects of these products are only the tip of the iceberg when it comes to the manufacturing, transportation and disposal of parenterals.

Manufacturing and transport

Ensuring sterility for medicines during their manufacture and transportation is essential, and for parenterals the requirement for a drug delivery device to allow administration of the medicine introduces a source of potential contaminants. This is in addition to sources of potential contamination that result from the production of the medicine itself, and which are present for products of all formulations. Interaction between the device materials and medicinal product can cause chemicals to leach into the medicine, affecting its purity and possibly modifying the drug's efficacy and safety. There are multiple instances of product recalls and warnings related specifically to the device used in a product , including the FDA raising concerns around potential failure of syringes manufactured in China[28].

Although all medicinal products will interface with their packaging — oral tablets may be enclosed in plastic and foil — the close involvement of drug delivery devices for parenterals in administering the product means they are some of the highest-risk products, as Table 1 highlights[29]. This risk results from a greater likelihood of interaction between the device and medicinal product combined with the risk surrounding injection: an injected medicine bypasses filtration in the gastrointestinal tract, and IV products particularly will also not be filtered by the kidneys, so the threat from contaminants is higher.

There are multiple instances of product recalls and warnings related specifically to the device used in a product

Table 1: Packaging concerns for common classes of drug products

		Likelihood of packaging-medicinal product interaction		
		High	**Medium**	**LOW**
Degree of concern associated with the route of administration	**Highest**	• **Injections and injectable suspensions** • Inhalation aerosols and solutions	• **Sterile powders and powders for injection** • Inhalation powders	
	High	• Ophthalmic solutions and suspensions • Transdermal ointments and patches • Nasal aerosols and sprays		
	Low	• Topical solutions and suspensions • Topical and lingual aerosols • Oral solutions and suspensions	• Topical powders • Oral powders	• Oral tablets • Oral capsules

Source: Guidance for Industry; Container Closure Systems for Packaging Human Drug and Biologics, US Department of Health and Human Services, FDA, May 1999

When it comes to transporting parenteral products, a variety of factors must be considered to ensure secure delivery from factory to end-user, including:

- **Shelf-life and storage:** Improper storage conditions for cold-chain products and disruptions to normal supply chain operation can result in products expiring before use. COVID-19 demonstrated the fragility of the medical supply chain, and in 2021 the Ever Given container ship blocked the Suez Canal for 6 days, showing how one-off events can have outsized impacts[30].
- **Damage to packaging and product:** All types of parenteral products are at risk of damage during transit. IV bags can split, glass vials can break, cold-chain products can spoil, and syringe stoppers can displace or stick due to pressure changes during air transport. Maintaining sterility of parenteral products, particularly needles, is also imperative because of the contaminant risk.
- **Counterfeiting:** While not strictly related to transport of genuine products, high value parenterals are susceptible to counterfeiting, potentially leading to reputational damage due to the fake's inefficacy or safety profiles. The recent huge surge in demand for weight-loss products has led to an explosion of counterfeit and unlicensed products globally[31,32].

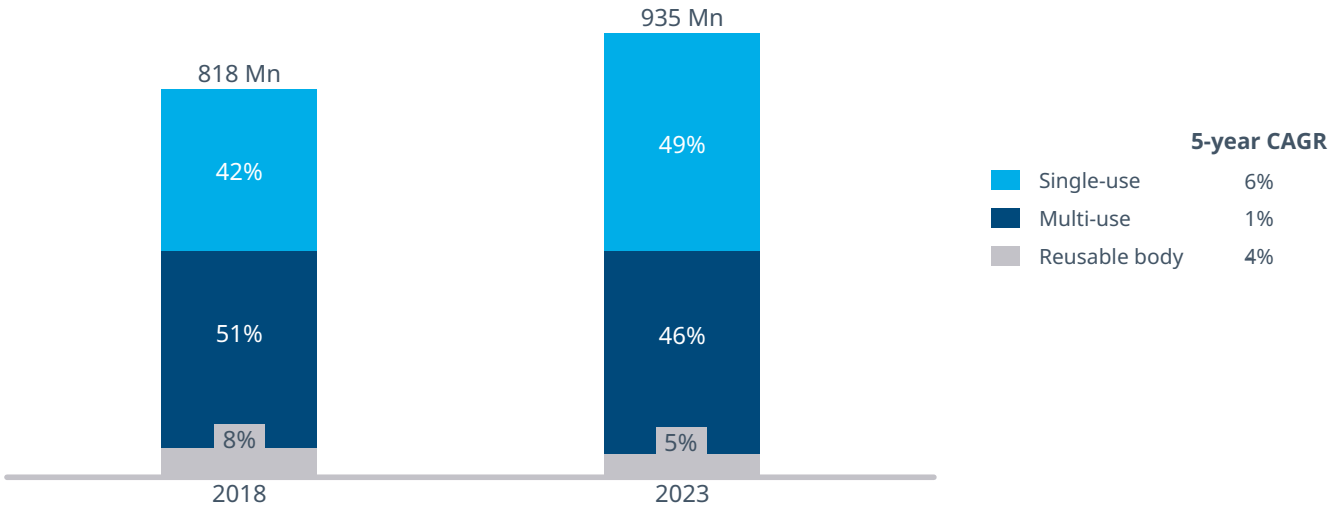
Wastage and disposal

Medicine wastage can occur with parenterals where dosage is based on the patient's weight or body size and that come in single dose packages such as vials or ampoules. Because these products must be used almost immediately after opening, and because dose volumes will vary depending on the patient, the full volume in the package is rarely used completely, with valuable medicine being disposed of. Despite this, the cost will often be based on the volume in the package increasing the cost relative to the average dose[33].

Due to already strained healthcare systems financing, payers are keen to find ways of reducing this wastage. Whilst there are ways to mitigate it already such as vial-sharing, manufacturers will face pressure to change packaging to reduce waste from their end[34].

This also ties into the drive to widen adoption of reusable devices. Figure 8 demonstrates that the proportion of devices that can administer multiple doses before disposal, or that have a reusable body has decreased in the past 5 years[35]. This is not as a result of a significant switch from more reusable devices to single-use ones; rather, it is due to large numbers of single-use products being added that are associated with high value medicines, such as autoinjectors and pre-filled syringes for immunology products.

Figure 8: Parenteral devices by level of reusability (Top 7 markets, MAT Q2 2018 – 2023, branded products only, number of devices sold*)



Source: IQVIA EMEA Thought Leadership; IQVIA MIDAS Q2 2023, Devices based on number of standard units
Notes: *Represents a subset of total injectables sales rather than the entire market. Top 7 markets are US, Japan, UK, Germany, France, Italy, Spain

This high number of single-use devices creates significant waste, and these devices are sharp medical products they cannot be disposed of with normal recycled waste. Although some efforts have been made to improve on this such as with insulin pen collection schemes, these efforts have been faltering and often fail to gain wide adoption. However, a more directed and multi-stakeholder approach, such as Novo Nordisk's UK PenCycle scheme involving patients, health systems and manufacturers could result in less waste and even repurposing of used pens[36]. Typically, more complex devices like autoinjectors are harder to dispose of and have a higher carbon footprint. To combat this there are ongoing efforts to develop more sustainable autoinjectors that have a lower carbon footprint and that can be disposed of more easily[37,38].

Emissions

Of the top 100 pharmaceutical companies 41 have reported time-bound commitments to reduce emissions, and at least 75 countries have committed to developing climate-resilient and low-carbon health systems[39,40]. As a result, countries may start introducing legislation to encourage the purchasing of low-carbon medicines.

Parenteral products have emissions from production and packaging like all medicines, though the requirement for a drug delivery device adds an additional source of emissions compared to others such as orals. Sourcing low-carbon materials and changing production processes to reduce emissions may increase costs for manufacturers. Though this cost may not impact on the margin of high-value innovative products, those that operate at lower margins like generics and biosimilars may feel the squeeze. For manufacturers of these products, engaging with payers to develop tenders with additional requirements apart from cost, such as product emissions, could be a way to mitigate this risk and add another way to differentiate products.

Opportunities and the future

The value growth rate of the parenteral market is forecast to be a CAGR of 9.4% over the next five years, significantly higher than the overall Rx growth of 6%. Primary factors include the growth of obesity products and biosimilar erosion[41].

Competition will remain strong, although new opportunities to stand out are available by aligning products with patient preference. Furthermore, new technologies and markets will provide opportunities to diversify products and provide new revenue streams.

Patient-focused products

Aligning parenteral device design with patient preferences will become increasingly important as competition increases. This is especially true for formulations that can be self-administered as patients are more likely to be engaging directly with the devices.

There are numerous patient characteristics than can be used to inform design, and multiple components of the drug-device combination that can be changed to accommodate them, as highlighted in Figure 9. Primary patient characteristics can be physical (e.g., dexterity, grip strength, vision) and mental (e.g., needle-aversion, memory), yet it is also vital for manufacturers to consider the broader elements of the patient experience.

This requires a more holistic approach to device design to ensure minimal impact on the patient's daily life. For example, direct delivery of an autoinjector each week to a patient's home simplifies logistics for them, as opposed to having to collect it from a pharmacy. Alternatively, there may not be large benefits for home delivery for those who are on other therapies that may require attending a specialist centre regardless (as may be the case for oncology patients receiving radiation therapy). Certain patients like the young and elderly may have a caregiver, and the impact a drug-device combination has on them must be considered.

Creating patient support programmes centred on the patient experience and paired with a suitable device can be an important way to improve the appeal of an offering, particularly when overall patient numbers may be small such as with rare diseases. Digital or "smart" design elements can also have an impact, and these aspects are discussed in more detail in the deep dive below.

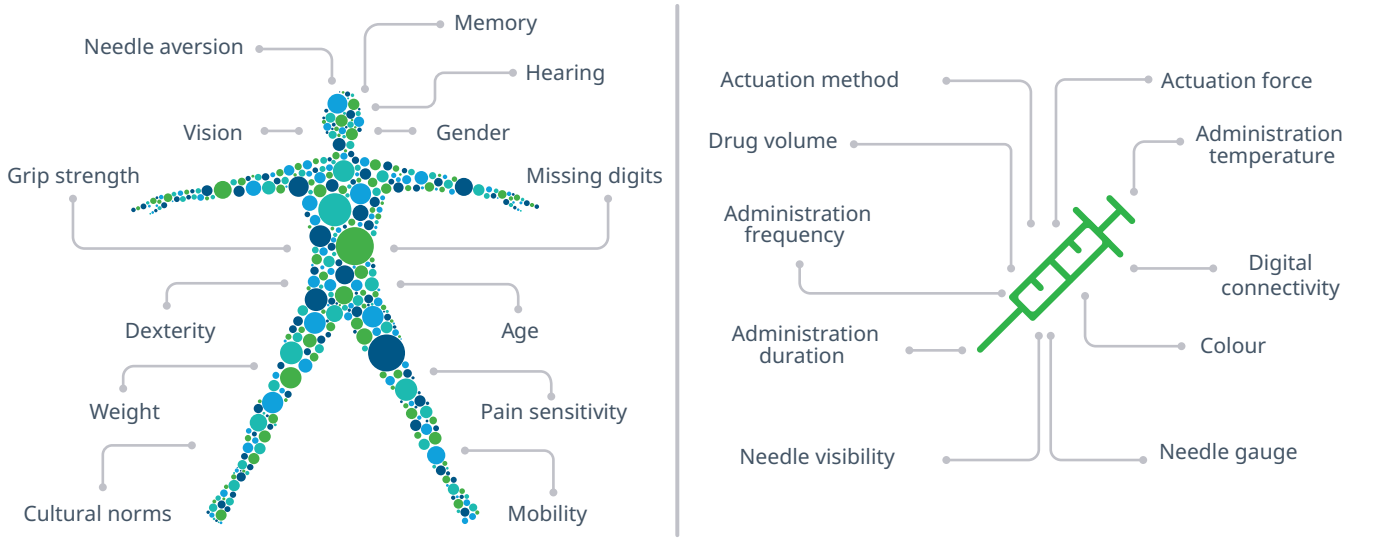
Human factors testing of devices can be performed to better understand how changes to device elements impact user preference and acceptance. Manufacturers should be aware that every decision matters: in Europe the colour red is associated with passion, anger and danger; in China it is associated with happiness and good fortune. To achieve the best outcomes manufacturers will need to develop or expand user design and experience teams, and involve patients as early as possible in the design process.

Aligning with patient preferences can also have benefits for health systems and payers, increasing their desire for patient-aligned products:

- Self-administrable formulations move patients out of the hospital and can free up HCP capacity.
- If patients are satisfied with their device they are more likely to take the product, improving adherence and reducing wastage from non-adherence. Even a small increase in adherence is desirable for payers, as it can lead to significant savings which can be spent elsewhere[42].

The value growth rate of the parenteral market is forecast to be a CAGR of 9.4% over the next five years

Figure 9: Patient characteristics and device design elements (Not exhaustive)



Source: IQVIA EMEA Thought Leadership
Notes: *Represents a subset of total injectables sales rather than the entire market. Top 7 markets are US, Japan, UK, Germany, France, Italy, Spain

Deep dive: Smart devices

An increasingly important aspect of device design is digital connectivity, another trend that has been amplified post-COVID-19. There are various levels of smart capabilities for devices: from apps that only offer reminders to take a medicine or information on the product, but do not have any link to the device itself; third-party apps and sensors that can be attached to a typical pre-filled syringe to record data on usage; and devices with in-built sensors and connectivity designed by the primary manufacturer.

Although accelerated by COVID-19, the desire for smarter devices was present before 2020 due to the benefits they can offer to stakeholders:

- Smart devices can collect data on product usage to better understand the effects of the product in real-world conditions. Examples of these kind of these devices already exist in diabetes, such as with Lilly's Tempo platform and Novo Nordisk's NovoPen 6, which can help with better disease management by HCPs by providing data to inform dose frequency or strength[43,44]. There is also the opportunity for this kind of patient-mediated real-world data to be used by manufacturers in real-world evidence studies to present to regulators and payers.
- Smart devices can grant patients a greater sense of control over their care. Information on how to use a product and the effects of the medicine can be more readily displayed on a connected smartphone than on paper. This also can increase the number of markets a product can be included in without having to tailor leaflets, and ties in with the proposal for greater use of electronic product information in the EU's proposed pharmaceutical legislation revisions.

However, these benefits are not without some challenges. The first is that smart devices are inherently more expensive and complicated to manufacture than devices without digital connectivity. Including digital connectivity for a device can also introduce extra required steps for the administration of the medicine, increasing the chance that the process is performed incorrectly. This risk is further elevated in patients with less technical familiarity and as such, digital elements should ideally be designed to augment functionality whilst remaining decoupled from the critical steps needed to administer the medicine. These digital components can also push up the carbon emissions required to produce these devices and make them more difficult to dispose of after use. With sustainability issues becoming more pressing for healthcare systems, manufacturers should ensure sustainability criteria are included during the device design phase.

The collection of highly sensitive patient data from a smart device opens avenues to security concerns around improper use, dissemination and storage, meaning cybersecurity, and adherence to regulations on patient data protection and privacy, must be a primary focus in designing these devices. There are also concerns around how a wider use of smart devices can be integrated into HCPs existing workflows, as physicians may be exposed to multiple data sources from multiple patients, adding to an already busy schedule. Further questions arise around the technical integration of this data into electronic health records, and with whom liability would sit if a bad decision were made that relied upon data from a smart device. As a result, it is important manufacturers of connected devices seek HCP buy-in and advice when designing products. Finally, device classification could also change depending on a device's digital capabilities, and devices using Artificial Intelligence (AI) would likely be classed as high-risk under the EU's AI Act, requiring a greater level of scrutiny[45].

Ultimately, digital connectivity for devices is another element of device design that must involve research and decision making to ensure that targeted to the patient population alongside all other stakeholders involved in the patient's care.

New markets and therapy areas

The emergence of new therapy areas provides opportunities for parenterals by opening up new markets. One of the most notable is the obesity market, which could reach between $39Bn to $131Bn globally by 2028, depending on treatment guidelines, commercial uptake and outcomes for different countries[46]. There are currently 61 parenteral products in clinical trials between pre-clinical — phase III for obesity, representing 51% of the pipeline[47]. However, these would face considerable competition from orals, and there are intense efforts to develop oral formulations of GLP-1 products for obesity indications. Looking at current clinical trials for GLP-1 products 40% of 25 active trials are investigating oral formulations including some in Phase III trials, although success is not guaranteed as Pfizer's oral lotiglipron has shown[48,49].

New types of advanced therapies also provide new markets for parenterals. Technology platforms such as mRNA, which are currently only administrable in parenteral format have shown their viability and mass-market potential. With a robust pipeline, including multiple ongoing trials in combination with checkpoint inhibitors for cancer indications, these new therapies could provide another boost to sales in the near future.

Large volume autoinjectors

New innovations continue to ensure parenterals remain competitive and provide new features to customers. One area for research is large volume autoinjectors, which are those capable of administering doses above 2mL, and have the potential to replace larger volume pre-filled syringes with a more patient-focused device. A conservative estimate — looking at pre-filled syringe products with a volume greater than 2mL — puts the annual global market for these large volume autoinjectors at $4Bn. Whilst there are a handful of products using autoinjectors with a maximum volume of 2.25mL, the total current market in that size is small[50].

Primary concerns around large volume autoinjectors include a longer required administration time – traditionally the gold standard for an autoinjector is around 10 seconds — as well as pain levels experienced by the patient, and the pharmacokinetic effects of changing a formulation to fit into an autoinjector[51]. These autoinjectors may also experience competition from on-body injectors, although patient preference between these products varies depending on the comparative administration time, frequency, and quality of life of the patient[52].

Despite these obstacles, multiple companies are developing autoinjectors with administrable volumes up to 10mL as the potential market for these products offers a significant return.

Conclusion

Parenteral products are a significant contributor to global pharma value and will continue to be so for the foreseeable future, as they are the method of choice for most high-value and innovative products. There are several key trends to watch out for:

1. A significant growth in the number of self-administered parenteral products, driven by the rise of obesity medications and the desire of healthcare systems to reduce burden on strained resources.
2. As a result, the prevalence of more patient-focused self-administrable devices will increase. Many of these products will have smart capabilities that will be able to provide better support to patients and carers through data collection and analysis.
3. New technologies for injection, such as large volume autoinjectors, will move out of development and into the commercial phase becoming a segment for growth.
4. Similarly, efforts to make biologics more stable at room temperature will extend the reach of high-value biologic parenterals. This is particularly important as biologics continue to show high growth and a strong pipeline, and parenterals are currently the only suitable method of delivery.
5. There will be a concomitant rise in competition from oral products, especially in the obesity space. Currently though, no oral obesity medications have come to market.
6. Concerns around sustainability will lead to a greater emphasis on design considerations to improve the sustainability of complex, single-use smart devices. This will also offer opportunities for differentiation of products.

All in all the outlook for parenteral products is strong, and opportunities for manufacturers to increase market share are available to those willing to more closely engage with the needs of patients, payers and healthcare systems.

Footnotes

In this white paper, the definition for parenteral products includes several formulations as defined by their NFC2 (New Form Codes) class: ampoules, vials, infusions, pens and cartridges, autoinjectors, and on-body injectors. The scope of this paper only considers the prescription market and does not include vaccines (including COVID-19 vaccines and therapeutics) due to limited data coverage.

References

1. Frank Lichtenberg, "How Many Life-Years Have New Drugs Saved? A 3-Way Fixed-Effects Analysis of 66 Diseases in 27 Countries, 2000-2013. National Bureau of Economic Research, January 2019. DOI: 10.3386/w25483
2. IQVIA MIDAS MAT Q3 2013 – 2023. Value shown at ex-manufacturer prices.
3. IQVIA MIDAS MAT Q3 2013 – 2023.
4. IQVIA MIDAS MAT Q3 2023.
5. Changwei Yang et al. ,Glucose-responsive microneedle patch for closed-loop dual-hormone delivery in mice and pigs.Sci. Adv.8,eadd3197(2022).DOI:10.1126/sciadv.add3197
6. Afrezza, https://afrezza.com/ Date accessed 09/02/2024
7. Exhubera, https://www.ema.europa.eu/en/medicines/human/EPAR/exubera Date accessed 09/02/2024
8. World Economic Forum, https://www.weforum.org/agenda/2021/10/new-technology-could-allow-you-to-have-a-needle-free-injection/#:~:text=Researchers%20in%20the%20Netherlands%20are,contamination%20associated%20with%20traditional%20injections Date accessed 09/02/2024
9. Rani Therapeutics, https://www.ranitherapeutics.com/technology/, Date Accessed 09/02/2024
10. NICE, https://bnf.nice.org.uk/medicines-guidance/guidance-on-intravenous-infusions/ Date accessed 23/01/2024
11. Genentech, https://www.ocrevus-hcp.com/dosing/administration.html Date accessed 23/01/2024
12. Lintzeris N, Dunlop AJ, Haber PS, et al. "Patient-Reported Outcomes of Treatment of Opioid Dependence With Weekly and Monthly Subcutaneous Depot vs Daily Sublingual Buprenorphine: A Randomized Clinical Trial." JAMA Netw Open. 2021;4(5):e219041. doi:10.1001/jamanetworkopen.2021.9041
13. Ovacik M, Lin K. Tutorial on Monoclonal Antibody Pharmacokinetics and Its Considerations in Early Development. Clin Transl Sci. 2018 Nov;11(6):540-552. doi: 10.1111/cts.12567. Epub 2018 Aug 7.
14. Oral mRNA delivery using capsule-mediated gastrointestinal tissue injections, Abramson, Kirtane et. Al., https://www.sciencedirect.com/science/article/pii/S2590238521006809, Date Accessed 29/01/2024
15. IQVIA MIDAS MAT Q3 2023.
16. Gavi, https://www.gavi.org/our-alliance/strategy/phase-5-2021-2025/equity-goal/zero-dose-children-missed-communities, Date accessed 12/02/2024
17. FDA, https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/downloads/storage-handling-label.pdf Date accessed 23/01/2024

18. FDA, https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/downloads/storage-handling-label.pdf Date accessed 23/01/2024

19. Science, https://www.science.org/content/article/here-s-how-scientists-are-designing-vaccines-can-ditch-fridge, Date accessed 09/02/2024

20. IQVIA, https://www.iqvia.com/-/media/iqvia/pdfs/library/white-papers/iqvia_in-the-eye-of-the-storm_pd-1-inhibitors-weathering-turbulence_05-22-forweb.pdf Date accessed 24/01/2024

21. NHS, https://www.england.nhs.uk/2023/08/nhs-world-first-rollout-of-cancer-jab-that-cuts-treatment-time-by-up-to-75/ Date accessed 24/01/2024

22. Fierce Pharma, https://www.fiercepharma.com/pharma/roches-subcutaneous-tecentriq-hits-fda-delay-amid-manufacturing-process-changes Date accessed 24/01/2024

23. ClinicalTrials.gov, https://clinicaltrials.gov/study/NCT04956692 Date accessed 24/01/2024

24. The Global Use of Medicines 2024: Outlook to 2028, IQVIA, https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/the-global-use-of-medicines-2024-outlook-to-2028 Date accessed 24/01/2024

25. Health and care workforce in Europe: time to act, WHO, Published September 2022. ISBN: 9789289058339

26. BBC News, https://www.bbc.co.uk/news/uk-england-merseyside-56648455, Date Accessed 24/01/2024

27. Assessing the Biosimilar Void, IQVIA, https://iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/assessing-the-biosimilar-void Date accessed 09/02/2024

28. FDA, https://www.fda.gov/medical-devices/safety-communications/evaluating-plastic-syringes-made-china-potential-device-failures-fda-safety-communication Date accessed 24/01/2024

29. Guidance for Industry; Container Closure Systems for Packaging Human Drug and Biologics, US Department of Health and Human Services, FDA, May 1999

30. Miller FA, Young SB, Dobrow M, et al, Vulnerability of the medical product supply chain: the wake-up call of COVID-19BMJ Quality & Safety 2021;30:331-335.

31. Forbes, https://www.forbes.com/sites/ariannajohnson/2023/11/09/counterfeit-ozempic-wegovy-mounjaro-pens-reported-to-fda-how-to-spot-a-fake/?sh=d00241814395. Date accessed 24/01/2024

32. European Medicines Agency, https://www.ema.europa.eu/en/news/ema-alerts-eu-patients-and-healthcare-professionals-reports-falsified-ozempic-pens. Date accessed 24/01/2024

33. Bach P B, Conti R M, Muller R J, Schnorr G C, Saltz L B. Overspending driven by oversized single dose vials of cancer drugs BMJ 2016; 352 :i788 doi:10.1136/bmj.i788

34. Cozzio M, Melis A, et. Al. Vial Sharing of High-Cost Drugs to Decrease Leftovers and Costs: A Retrospective Observational Study on Patisiran Administration in Bologna, Italy. Healthcare (Basel). 2023 Apr 2;11(7):1013. doi: 10.3390/healthcare11071013.

35. Analysis based on IQVIA MIDAS MAT Q2 2018 – 2023. Number of injectables devices estimated from standard units. This analysis does not represent the total number of injectables devices sold in these markets.

36. Novo Nordisk, https://www.pen-cycle.co.uk/, Date accessed: 25/01/2024

37. Palmer-Felgate J, "An Eco-Friendly and Economical Approach to Autoinjectors". ONdrugDelivery, Issue 156 (Jan 2024), pp 64–67.

38. YpsoMed, https://yds.ypsomed.com/en/products/autoinjectors/ypsomate-zero.html, Date accessed 09/02/2024

39. Based on IQVIA MIDAS sales data

40. World Health Organisation https://www.who.int/initiatives/alliance-for-transformative-action-on-climate-and-health/country-commitments Date accessed 31/01/2024

41. IQVIA Forecast Link, January 2024. Injectable defined as "vial", "ophthalmic injectables", "pre-filled syringe" under route of administration.

42. International Longevity Centre UK, https://ilcuk.org.uk/doctors-orders/, Date accessed 25/01/2024

43. Novo Nordisk, https://www.novonordisk.com/our-products/smart-pens/novopen-6.html Date accessed 06/02/2024

44. Eli Lilly, https://investor.lilly.com/news-releases/news-release-details/lilly-begin-rollout-tempor-personalized-diabetes-management Date accessed 06/02/2024

45. European Commission, https://health.ec.europa.eu/system/files/2021-10/mdcg_2021-24_en_0.pdf, Date accessed 12/02/2024

46. Why the anti-obesity drug market could grow to $100 billion by 2030, Goldman Sachs, https://www.goldmansachs.com/intelligence/pages/anti-obesity-drug-market.html, Date accessed 23/01/2024

47. IQVIA Thought Leadership research, IQVIA Analytics Link, Refinitiv Workspace, TD Cowen, Clinicaltrials.gov

48. Pfizer, https://www.pfizer.com/news/press-release/press-release-detail/pfizer-provides-update-glp-1-ra-clinical-development Date accessed 05/02/2024

49. IQVIA Pipeline Link, January 2024

50. IQVIA MIDAS Q3 2023. Estimates based on value of pre-filled syringes with volumes greater than 2ml

51. Andreas Schneider, Reto Jost, Christoph Jordi & Jakob Lange (2023) Autoinjectors for large-volume subcutaneous drug delivery: a review of current research and future directions, Expert Opinion on Drug Delivery, 20:6, 815-830, DOI: 10.1080/17425247.2023.2219891

52. Andreas Schneider, Harald Kolrep, Hanns-Peter Horn, Christoph Jordi, Sina Gierig & Jakob Lange (2023) Understanding patient preferences for handheld autoinjectors versus wearable large-volume injectors, Expert Opinion on Drug Delivery, 20:2, 273-283, DOI: 10.1080/17425247.2022.2162037

About the author

AARON WRIGHT
Analyst, Thought Leadership at IQVIA

Aaron is a Thought Leadership analyst, responsible for helping to develop positions on a wide array of topics, and producing content in the form of blogs, articles and white papers. He has been part of the team since 2021 and can offer insights across the pharma spectrum. His recent work has been focused on drug delivery devices, and how healthcare can be delivered nearer to the patient. He holds a Master of Engineering from Imperial College London.

Acknowledgements

The author would like to thank the following people for their contributions and insights: Aurelio Arias, Sarah Rickwood, Dheeman Vaidya, Pumi Ludidi and Paul Villa.

You may also be interested in

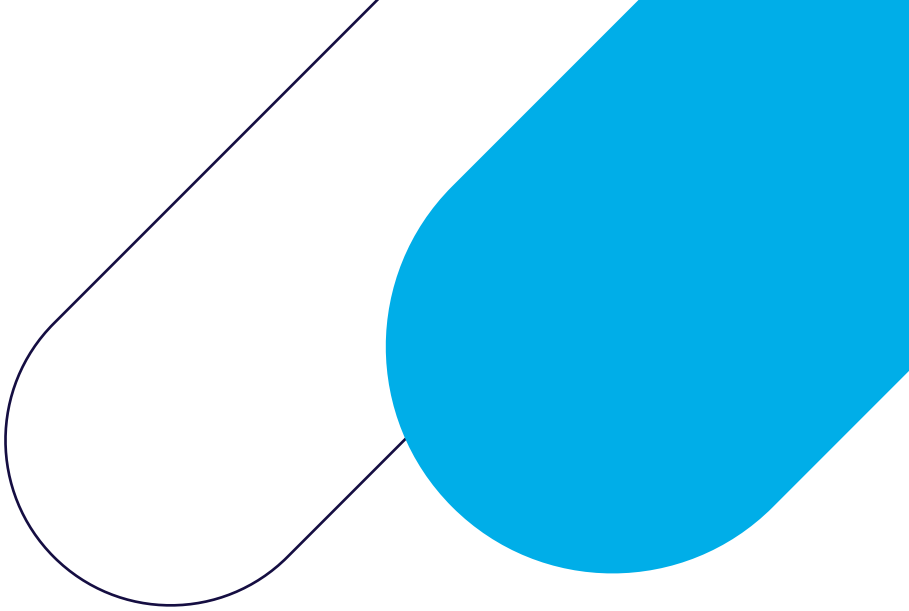
White Paper - Pharma's Frozen Assets: Cold chain medicines

White Paper - In the Eye of the Storm: PD-(L)1 Inhibitors Weathering Turbulence

Solution - EMEA Thought Leadership

Solution - IQVIA MIDAS: Harmonize Your Market Views Worldwide

Solution - IQVIA Analytics Link Ecosystem: Enhance Business Decisions with Connected Insights



CONTACT US

iqvia.com