Meeting needs:
making a big difference to small patient populations

CHAPPER healthcare

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Introduction

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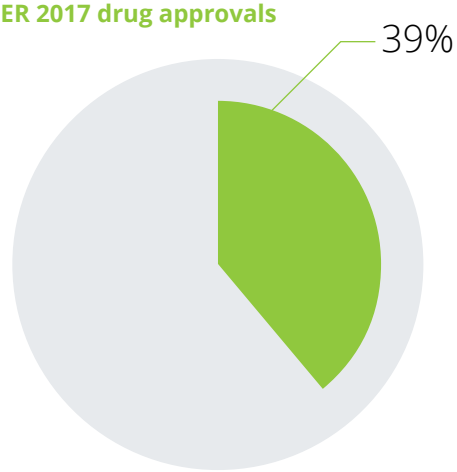
There has been a tectonic shift in the pharmaceutical industry's sales drivers and pipelines, as companies move from the mass market to the niche, driven by the recognition that the sector's traditional blockbuster model had become unsustainable[1].

The consequent rise of specialty treatments for chronic, complex and rare conditions has seen many breakthrough treatments being brought to market and offering new hope to patients.

However, market access for specialty medicines has become increasingly complicated. The smaller size of potential patient populations can lead to price tags for many of the newer drugs that are sky-high. It's a market where tensions in pricing, and therefore access, have yet to fully play out among payers, prompting patients and carers to look for more immediate solutions to the question of how they obtain vital treatments.

2 The rise of specialty medicines

US CDER 2017 drug approvals



18 of the 46 novel drugs approved by the CDER in 2017 were approved to treat rare or "orphan" diseases that affect 200,000 or fewer Americans.[3]

Specialty medicines have enjoyed a decade of continued growth that has put them on course to overtake the value of spending on traditional drugs in many of the world's biggest pharmaceutical markets by 2022, according to IQVIA (formerly QuintilesIMS)[2].

When that comes to pass, it will cap a remarkable period of change for the industry that has seen companies pivot from the mass market blockbuster drug model that proved such a success in the 1990s and early 2000s towards more niche areas.

This refocusing of product pipelines towards conditions that are chronic, complex and rare can already be counted a research success, with many ground-breaking types of treatments being brought to market and offering hope to patients. 2017 was, the US Food and Drug Administration (FDA) noted[3], a year of 'firsts' in many rare diseases, with US approvals including the first new treatment for patients with sickle cell disease in almost 20 years and the first-ever non-blood product to treat with inhibitors patients with haemophilia A. Another addition to the market was Spark Therapeutics' Luxturna™, which last year became the first FDA-approved gene therapy.

However, while each of the last ten years has seen greater spending growth for specialty medicines than their more traditional counterparts[4], market access has become more complex.

Specialised challenges

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One headline example of this came in 2017 when the Dutch biotech UniQure announced it would pull its gene therapy treatment Glybera off the market[5]. Priced at more than €1 million, Glybera was famously the world's most expensive drug, but in the five years since approval it had been used to treat just one patient with the ultra-rare inherited disease lipoprotein lipase deficiency (LPLD). Despite that recipient seeing a dramatic improvement in LPLD symptoms, the therapy's cost proved too much of a roadblock to wider patient access.

The single dose and curative nature of many of these costly treatments has prompted some suggestions that healthcare technology assessment (HTA) methodologies will need to be updated. In the case of the UK's National Institute for Health and Care Excellence (NICE), the HTA body was prompted to run a thorough review of its technology appraisal processes and concluded they could still be applied effectively to regenerative medicines and cell therapies. As if to prove that point, at the turn of this year NICE gave a positive recommendation[6] for GlaxoSmithKline's Strimvelis. The single-dose gene therapy carries a €594,000 price tag, but its effects on Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID or 'bubble baby' syndrome) are thought to be lifelong.

However, many rare diseases don't have a corresponding medicine. Only around 5% have an approved treatment[7] and off-label use of products is often necessary. Problems of either access to, or availability of, treatment are not uncommon in this area, with rare diseases being – collectively at least – not that rare. More than 7,000 rare diseases have so far been identified and between them they affect a large number of patients – some 25-30 million in the US alone[8].

Time presents another factor that is very much of the essence. More than 50% of patients with a rare disease are children[9] and some 35% will die in their first year of life[10]. At the heart of healthcare's mission is responding to unmet patient need, and this is particularly acute in the case of rare diseases where the timelines are compressed, and patients are often already in hospital.

It's cruelly ironic then that in populations with such urgent treatment needs, gaining treatment access is often a slower and more complicated process than for traditional treatments[11].

Managed access

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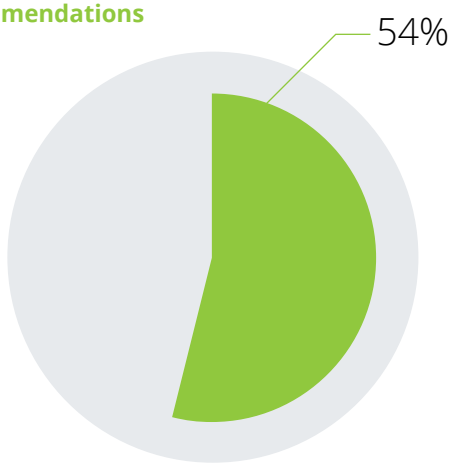
Where access is not available, there is therefore the pressing question of how to provide ethical access to much needed pharmaceutical innovation. One answer that has moved into the mainstream is to run a managed access programme (MAP). Though lacking a single definition, they come in several formats and are known by many different, often interchangeable, names – including managed access, early access, named patient programmes and compassionate use programmes.

It was as 'compassionate use programmes' that they emerged in the US in the late 1980s, driven along by a wave of HIV/AIDS patient activism that demanded access to treatments yet to reach the market. Such non-clinical trial access to unapproved drugs began in 1987 with the first US compassionate use programme, with countries like France and the UK establishing their own versions in the early to mid-1990s.

But, whichever name is used, the intention is the same: to allow the supply of innovative products for which there is no available alternative, either prior to first registration or post-first registration and prior to registration (if at all) in a particular market.

Today, the vast majority of pharmaceutical markets have formal MAPs in place, but developments haven't stopped there. More recently 'right to try' laws have been enacted, or filed for approval, in a majority of US states, though not without their own controversies, and many other countries are working out arrangements for better access to innovative medicines. In the UK's own case that means the Early Access to Medicines Scheme (EAMS) it launched in 2014, with its first positive scientific opinion – for Keytruda® in advanced melanoma – following on a year later. Meanwhile, both the European Medicines Agency's PRIME scheme and the US FDA's breakthrough, fast-track, accelerated approval and priority review designations look to speed the development and evaluation of new innovative medicines.

EMA 2017 drug approval recommendations



19 of the 35 new active substances recommended for EU approval in 2017 were for 'orphan' conditions.[12]

Managed access programme benefits

- ✓ Help patients in need
- ✓ Provide access in countries where commercialisation may not be viable
- ✓ Expose prescribers to new treatment options
- ✓ Gather real-world effectiveness data
- ✓ Maintain supply chain integrity

Well established among big pharma companies, they're now also regularly considered for use by the industry's smaller players, who will often need their chosen service partner to be able to offer a flexible, personalised service. This sort of offering is crucial when at heart a programme could involve sending just one or two packs of a product to a particular nation, with regulations and programmes varying from country to country.

MAPs can provide access to treatments in countries where commercialisation may not be viable or where a formal licence has yet to be issued. In addition, they can also be used for collecting additional, qualitative information on products to bring a 'real world' sense of patient outcomes that would not be available from traditional clinical trials. Third party service providers are very well placed to collect that information and report it back to pharma companies in a regulatory compliant way that both provides useful data and ensures patient anonymity.

Digital disruption as a driver of change

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While the empowered patient is now a well-established reality, within the rare disease area access to digital information and services has seen a significant and important shift in the balance of knowledge around niche conditions. It is critical for pharma companies to understand this new landscape, not only in terms of patient population and medicine supply, but more recently also in identifying drivers of innovation and a new breed of key opinion leaders (KOLs).

In shaping this transformation over the last two decades, the role of the internet cannot be overstated, with a new wave of online-driven pressure from the physician and patient communities emerging as a key theme within the healthcare environment.

The roots of patient activism can be traced to survivors of the 1950s and 1960s polio epidemics and thalidomide disaster, but the patient voice truly came of age in response to the public health emergency presented by HIV/AIDS in the 1980s, and it has been rising in volume ever since. Patients are now in a position to be more informed and empowered than ever before. This is driven by the 'Dr Google' phenomenon, whereby patients go to see their doctor armed with a wealth of information from healthcare websites.

Healthcare information has always been life-saving, but in rare diseases it is particularly important given the difficulty of obtaining a diagnosis. Indeed, research by DRG Digital (formerly known as Manhattan Research) found that 60% of US rare disease patients go online to try and figure out what their condition is before they visit a doctor[13]. In such instances the empowered patient quickly becomes the expert patient (or expert carer), bringing a laser-guided focus to researching and understanding one condition on a level that is just not possible for a general physician.

60% of US rare disease patients go online to try and figure out what their condition is before they visit a doctor[13]

"**43%** of online adults in the UK, Italy, Spain, France and Germany attempt to self-diagnose their symptoms or condition by using online sources before they consult a doctor"[14]

It's a similar picture with wider patient populations in Europe. The Cybercitizen Health 2017 study by DRG Digital found that 43% of online adults in the UK, Italy, Spain, France and Germany attempt to self-diagnose their symptoms or condition by using online sources before they consult a doctor[14]. In many countries this patient-led research is actively encouraged by governments to help increase the effectiveness of cost-constrained healthcare budgets, as in the case of the UK's National Health Service and its NHS Choices website, which registers over 10 million visits a week.

Hand-in-hand with this rise in information seekers, has been a concomitant increase in more direct action by rare disease patients and carers. Emblematic of this is Rare Disease Day. The annual, global day of action and awareness-raising was first launched after a patient-led campaign in 2008 by the European rare diseases alliance EURORDIS and its Council of National Alliances. Its profile has grown in tandem with that of rare diseases themselves and this year one of the many initiatives to mark Rare Disease Day came from the FDA. The US regulator used it to take the opportunity to promote patient participation in policy and research through the launch of a joint pilot project with The National Organization for Rare Disorders (NORD) to help medical reviewers better understand the experience of patients with their rare diseases.

In addition to its integral place within the modern patient experience, the internet has assumed a central position in the way today's doctors practice medicine, providing them with access to information and perspectives they might not otherwise see. Professional use of Google searches or Wikipedia is now commonplace[15], with US physicians carrying out on average six professional internet searches each day, with two-thirds prompted to use a search engine because patients were asking for more information during the consultation. Such searches come in addition to any paid-for online resources a physician may have access to. This pattern appears more pronounced among younger doctors, who tend to be more reliant on digital sources of information than their older counterparts[16]. It's a trend that is only going to become more pronounced as millennials rise through the ranks.

For both doctors and patients this has been turbocharged by the arrival of social media. It has connected patients and carers around the world in a way like never before through Facebook groups and hashtag-curated Twitter conversations. Such informal patient networks even see them compare treatment protocols and regimes. Meanwhile, doctors now have a greater ability to share information among themselves, extending the annual meeting with their peers at a congress into a year-round space for discussions as they keep in touch virtually.

The awareness of treatments – and levels of access – has led patients to speak up and request them from their doctors. Within a particular part of a region, Eastern Europe for example, patients can be found crossing the border from one country to another in order to obtain the treatment they need. Clearly, when there are no alternative treatments available, patients will take matters into their own hands to get appropriate access to unobtainable treatments for serious, life-threatening or debilitating diseases.

Beyond awareness and calls for action, rare disease patients and their families are also taking research matters into their own hands, and acting individually or together to fund the discovery and development of potential treatments. They can even be seen to be performing roles that are analogous to business development or principal investigator positions[17]. One such example is Duchenne UK, set up by two mothers whose sons were diagnosed with the condition and who utilised innovative funding models to accelerate development within the disease area. This enabled them to raise millions which has been used to directly fund new research and clinical trials while also raising awareness internationally.

6 The challenge of specialty medicines logistics

Distributing specialty medicines requires a flexible, specialist approach. The one paramount requirement is that a product arrives in pristine condition with the highest degree of efficacy at the patient level. To ensure this, temperatures must be controlled during shipping and local conditions managed effectively. Regulators have been placing increasing importance on temperature control of shipments and, more generally, storage, driven by Good Distribution Practice (GDP) regulations. Whether a shipment requires cool chain or controlled ambient distribution, there's now a more stringent focus on ensuring the correct temperature range. But this is not without its challenges.

From the extremes of shipping to Saudi Arabia in the height of summer or the Nordic countries in the depths of winter, temperatures can vary by as much as 70 degrees, and technological solutions must confirm that the product has been maintained in the correct temperature range throughout the transit.

Moreover, the product has to reach its destination within the correct temperature range in a cost-effective manner. To guarantee a product's arrival can come with a prohibitive cost, depending on the value of the product versus the freight costs, and an effective sourcing and distribution partner should always be able to provide advice on such a potential mismatch and how to possibly overcome it.

Security amid uncertainty

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The fundamental and constant challenge of operating within Europe is the region's complexity when it comes to language, regulation, politics, healthcare systems, country sizes, rates of modernisation, and local customs and business practices. Dealing effectively with Europe's regulatory differences is vital in an area like the supply of non-registered medicines, where there is no common regulatory framework. The concept exists under EU legislation, but it's effectively up to each individual country to put it into practice in its own way. So, for example, for a US speciality pharmaceutical manufacturer looking for a route into Europe but used to dealing with a single language and no internal borders, having a specialist European partner can be a real strategic advantage.

Another issue for the pharmaceutical sector in Europe is the once-in-a-generation change as the UK prepares to leave the European Union. Brexit will certainly cause custom, distribution and logistics arrangements between the EU and the UK to evolve, but it's a change for which forward-thinking companies will be well prepared. Ensuring that they have access to a dedicated European hub located within the future European Union (EU27) is an obvious move to make.

8 Patient-centricity in action

As the oft-stated principle about medication adherence notes, a medicine can only work if a patient takes it. By extension, a patient can only take the medicine they require if they have access to it.

The rise of speciality care medicines, as pharmaceutical companies are forced to evolve beyond the traditional blockbuster model, has produced many new treatments for chronic, complex and rare conditions. In tandem with this paradigm shift, patients and carers have proved they will exercise their voices in pursuit of better access to new and innovative treatments.

Working with patients, carers and healthcare professionals to help facilitate this is not without its challenges, with geographic, regulatory and logistical issues present though manageable. But there is a clear opportunity for forward-thinking companies to meet this demand and put patient-centric theory into action.

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10 About CHAPPER healthcare

For over 40 years, CHAPPER healthcare has been improving patients' access to medicines by successfully supplying pharmaceuticals, including orphan drugs, non-registered medicines, and emergency medicines to clients across the world.

We also work with manufacturers on a managed access basis, supplying products globally, either prior to first-registration or before registration in the relevant country, to satisfy patient need.

Our experienced, multilingual team pride themselves on delivering exceptional customer service and supplying products safely, securely and on time. We take pride in our role in improving the health and wellbeing of individuals around the globe.

Author Bios

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Jonathan Chapper

Chief Executive Officer

Jonathan Chapper is CEO of CHAPPER healthcare. He joined CHAPPER healthcare in 2013 from a successful career in law where he worked at leading city law firms, as well as in an investment bank. Jonathan brought with him a wealth of commercial and legal experience, which he now applies to the pharmaceutical industry. CHAPPER healthcare is a leading specialist wholesaler and distributor and supplies pharmaceuticals to over 60 countries world-wide.

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Erica Fearnley is Marketing Manager at CHAPPER Healthcare. Prior to joining CHAPPER healthcare Erica spent 10 years at IQVIA (formerly QuintilesIMS) working with a range of pharmaceutical companies on a regional and global basis. Erica has also worked in the healthcare team at the business consultancy Frost & Sullivan. Erica holds a degree in biochemistry from the University of Birmingham.

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