CLINIGEN

ACCESS TO UNLICENSED MEDICINES

Satellite Symposium Report
Congress of the European Association of Hospital Pharmacists

RIGHT MEDICINE RIGHT PATIENT RIGHT TIME

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On March 23 2017, a satellite symposium sponsored by Clinigen, was held at the 22nd Congress of the European Association of Hospital Pharmacists, to explore the complex and demanding topic of "Access to Unlicensed Medicines; Right Medicine. Right Patient. Right Time."

A panel of experts looked at the changing landscape and growing demand around accessing unlicensed or unavailable medicines. Through a series of presentations and discussions, the experts examined the considerations pharmacists need to take into account when faced with meeting an unmet patient need and how the rise of falsified medicines is increasing the risk to patient safety.

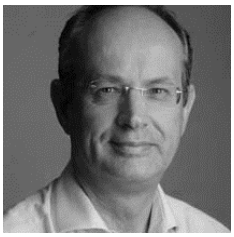
Panel members

Clinigen were joined by guest speakers:

Bernard Naughton (Chair)

Doctoral Researcher
Keele University & University of Oxford

Clinical Pharmacist
Oxford University Hospitals
NHS Foundation Trust



Mike Isles

Executive Director
European Alliance for
Access to Safe Medicines

Summary

"Try and imagine a hospital without medicine"[1]

The need for access to a safe and ethical supply of medicines that are unlicensed or unavailable at the point of care is now, more than ever playing a critical role in ensuring the best possible patient outcomes. Unmet patient need, increasing awareness of and demand for access to unlicensed medicines in the patient community and growing recognition from pharmaceutical companies that patients need access before medicines are commercially available are all driving us towards better early and unlicensed access for patients.

Hospital pharmacists play a crucial role in sourcing and obtaining the timely supply of unlicensed medicines, however the procedures and processes involved are complex and demanding. To compound these challenges the increase in counterfeit or fake medicines is adding an extra and unwanted complexity when securing a safe supply and the public can now access such fake medicines through online pharmacies.

The symposium panel members represented a number of stakeholders involved in accessing the ethical and safe supply of unlicensed medicines to patients. While sharing their expert insights and opinions, the panel outlined the changing landscape on this patient-critical and evolving issue. They discussed the risks and challenges healthcare professionals need to consider when sourcing unlicensed medicines, the scope of risk related to falsified medicines and the opportunity for healthcare professionals to educate patients.

[1] http://www.eahp.eu/ Hospital pharmacists and their role in patient care

A History of Access to Medicines; 30 Years On

"The landscape around access to medicines has changed considerably, with patients increasingly driving demand."

Clinigen

Clinigen opened the symposium by exploring the history of access to medicines, highlighting the thalidomide disaster in the 1960s as one of the most significant events in driving the turning point for global drug legislation. The profound and worldwide effect of this disaster led to tougher testing and drug approval procedures in many countries, shaping the current, rigorous drug legislation we know today.

Prescribing unlicensed medicines – which situations and when?

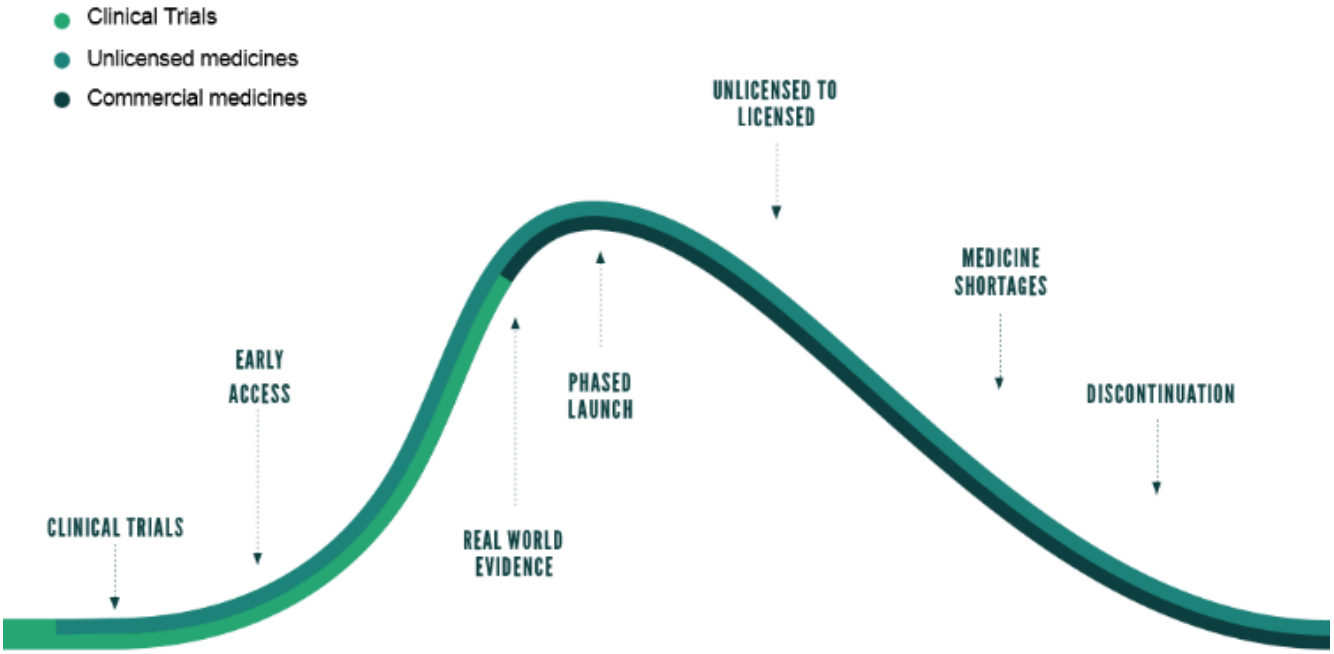
Current legislation allows for the use of medicines outside of their marketing authorisation, with unlicensed or off-label medicines often prescribed in order to achieve the best patient outcomes. A common example of this is in paediatric care. A survey of unlicensed and off-label drug use in paediatric wards in European countries[2] reported that almost half (46%) of all drug prescriptions in the study were either unlicensed or off-label, being as high as 80% in the neonatal intensive care unit. The European Medicines Agency introduced the requirement of having a Paediatric Investigational Plan (PIP) prior to the start of the phase 2 clinical trials.

Unlicensed medicines may be prescribed for use in a number of other situations; for example, there is no licensed medicine available to treat a specific disease, there is a shortage of commercially available medicines; an unusual formulation is required; or an unlicensed medicine is considered to be the best and most appropriate treatment for the patient.

Clinigen provided clarity around the various terminology and points of access to unlicensed medicines throughout the product lifecycle. Pre-launch medicines that are not yet commercially available may be accessed for serious and life threatening situations when there is no alternative available. This type of access can be known as pre-market access, early access, named patient access, compassionate use and, in France, ATU (Temporary Authorisations for Use). Once medicines are made commercially available in a specific country, they can no longer be prescribed on an unlicensed basis. However, the same medicine may not be approved in other countries for a number of reasons; for example a staggered commercial launch, delays in approval or awaiting agreement on reimbursement. In these cases, the medicine can be prescribed on an unlicensed basis and approved for importation.

As the product lifecycle continues, commercially available medicines may experience supply disruptions or be discontinued, so the use of an alternative unlicensed medicine that allows patient treatment to continue uninterrupted can be considered.

Access to Unlicensed Medicines through the Product Lifecycle



Increasing demand for unlicensed medicines – what are the drivers?

Discussing the increasing demand for unlicensed medicines, patients, patient advocacy groups and their physicians were highlighted as the driving force in demanding access to medicines that aren't commercially available. Access to information via the internet, coupled with the determination of a desperate patient or family member, leads to patients across the globe being better informed and demanding access to the right treatment. High unmet need, often in the areas of oncology, paediatric use and infectious disease was raised as another key driver of demand.

Increasing antibiotic resistance was shared as an example and is a growing, global threat[3] . Loss of effectiveness of existing antibiotics, for example tetracycline, erythromycin and vancomycin, drives the need for new compounds or the use of existing antibiotics for new indications to be tested. The use of unlicensed medicines is, therefore, often the only option when there's an urgent medical need.

Trusted, compliant and ethical supply

For good clinical reasons, the use of unlicensed medicines in hospitals is essential and often required in urgent and potentially lifesaving situations. There are, however, associated risks and challenges healthcare professionals have to consider ensuring they can quickly, safely and compliantly access the medicine the patient needs. Speed and reliability of supply, supply chain security, patient safety, and regulatory hurdles all need to be taken into account.

Whilst there is overarching European legislation in place regarding unlicensed medicines, how this is applied differs for each member state; healthcare systems, reimbursement agreements, regulations and hospital structures being just some of the variances. This reinforces the need for healthcare professionals to have a trusted partner they can rely on, when their stakeholders are depending on them. Clinigen's mission is to deliver the right medicine to the right patient at the time, connecting pharmacists and their patients in over 100 countries with the medicines they need and providing the necessary experience and expertise to overcome the highlighted challenges.

Clinigen Global demand 2016

[3] http://cddep.org/publications/state_worlds_antibiotics_2015

Fulfilling Patient Needs; A View From the Sharp End

"45% of pharmacists experience medicine shortages on a weekly basis, so knowing where to go for access to medicines can help them overcome the associated challenges."

B Naughton

Based on first-hand experiences as a clinical pharmacist, Bernard Naughton provided insights during his symposium introduction and presentation into the challenges pharmacists face when the medicine a patient needs is not available, driven by a supply disruption, treatment of a rare disease or other options being unsuitable or simply not working. Bernard emphasised the need for access to medicines that are either unlicensed or unavailable at the point of care in these cases, to ensure the best possible patient outcomes are achieved.

Complexities and challenges in accessing unlicensed medicines

Whether an unlicensed medicine is newly prescribed or for an ongoing treatment regime, the intricacies and additional processes associated with getting access to these medicines is complex and time consuming for increasingly busy pharmacists. While the prescriber is initially responsible for following the appropriate guidance[4], it is the pharmacist who is relied upon to source the medicine. A number of the common challenges experienced were discussed. These included knowing where to go to in order to source the medicine, ensuring patient safety and product quality, understanding the related internal processes within the hospital as well as the regulatory requirements, along with cost considerations and continuity of supply. Time was seen as the biggest issue, both in terms of the pharmacist's time involved in sourcing and procuring the medicine and the often short timeframes within which the patient needs to be treated.

Case studies

A number of case studies were shared to demonstrate the impact of these complexities and challenges. For example, the importation of BabyBIG from Europe for the treatment of infant botulism in the UK, the need to apply a usage restriction on a dexamethasone due to the impact of price increases on budgetary approvals and delays experienced in dispensing and administering clindamycin for patient treatment in an urgent situation, due to the documentation required being in a foreign language.

Medicine shortages

Medicine shortages were discussed at a global level, with a recent EAHP survey[5] highlighting 45% of responding pharmacists experienced shortages every week and 55% reported that 5 hours a week were spent on managing the situation and finding a solution.

Medicine Shortages Survey Results

86%

Of hospital pharmacists reported medicines shortages as a current problem

75%

Agreed that medicine shortages have a negative impact on patient care

55%

Reported 5 hours a week of staff time spent dealing with medicine shortages

45%

Experience shortages every week

Solutions for overcoming challenges

A recent survey carried out by Clinigen showed that over half (58%) of healthcare professionals consider the time spent sourcing unlicensed medicines and managing the complexities around accessing unlicensed medicines (57%) to be two of the biggest challenges they face. The expectation is on pharmacists to provide a solution for all stakeholders involved, often in a time sensitive situation and suggestions around proactively overcoming the challenges to better manage access to medicines at the point of care were discussed. Having a thorough understanding of what's involved including internal processes for procuring unlicensed medicines before the need arises; ensuring you know where to go to obtain reliable information, documentation and support, both internally and externally; prioritising effectively and, where possible, planning ahead were all highlighted as being key.

[4] http://www.gmc-uk.org/guidance/ethical_guidance/14327.asp

[5] EAHP's 2014 survey of the medicines shortage problem http://www.eahp.eu/practice-and-policy/medicines-shortages

Falsified Medicines; the Role of the Pharmacist in Raising Patient Awareness

Mike Isles opened his presentation with a powerful video from Fondation Chirac[6], which highlighted the health consequences and risks of buying medicines online due to the high number of illegally operating websites selling falsified medicines.

The extent of the problem

Mike's passion around the topic of falsified medicines and the associated risks to patient safety was clearly visible. There are over 30,000 websites that are operating illegally by selling falsified medicines that target the European population. Mike emphasised the need for greater collaborative initiatives to tackle both the supply side (those manufacturing fake medicines) and the demand side (the mostly unwitting public using the internet to buy medicines) was paramount in defeating this rising threat to public health.

The results of Operation Pangea IX[7] were shared, showing the broad range of falsified and potentially life-threatening medicines seized in 2016's operation, well beyond the lifestyle medicines you may expect. A related MHRA press release from a previous Pangea operation[8] highlighted 60 types of medicines were seized, including treatments for serious and chronic diseases such as cancer, HIV and diabetes.

"The exact size of the counterfeit medicines problem is unknown. Due to the criminal nature of their activities, counterfeiters seek to avoid detection, concealing the extent of the crimes committed, which makes data collection and reporting extremely difficult. One measure we have – the number of seizures reported by enforcement authorities around the world – is likely to represent only the tip of the iceberg."

Thomas T. Kubic, President & CEO, Pharmaceutical Security Institute[4]

There is no doubt that this is a growing and global issue and Mike emphasised the dire need for the public to be aware of the risks. Consumers are becoming increasingly reliant on and trusting of the internet for purchases. Patients may be naïve to the risks involved in buying medicines online, the ease and benefits of buying online becoming increasingly attractive for a number of reasons; for example convenience, time-saving, remote access to products, price and discreet purchasing. It is estimated that, at any one time, there are over 30,000 fake pharmacy websites[9] accessible by the European population and, with 18% of Europeans surveyed reporting they had bought medicines online[10], the risks are high at an estimated 130 million people when extrapolated across the population in Europe. Mike shared a case study of a fake website that ran in Germany, with over 360,000 hits and estimated sales of €35m in just 9 weeks.[11]

"With 18% of Europeans saying they have bought medicines online, we need to take every opportunity to educate patients around the potential threat of falsified medicines"

M Isles

[6] https://www.youtube.com/watch?v=khR5EGCG0Q8
[7] https://www.interpol.int/Crime-areas/Pharmaceutical-crime/Operations/Operation-Pangea
[8] http://www.psi-inc.org/index.cfm
. Accessed November 25, 2016
[9] Confident compliance https://www.legitscript.com Accessed November 25, 2016
[10] HappyCurious for Sanofi. Europeans and counterfeit medicines. http://www.happycurious.fr/wp-content/uploads/2016/07/36553_2014-05-15_Counterfeit_medicines_EN.pdf. Accessed November 25, 2016.
[11] European Commission on Public Health. Medicinal products for human use – falsified medicines. http://ec.europa.eu/health/human-use/falsified_medicines/index_en.htm
. Accessed November 25, 2016.12

Raising public awareness

A number of organisations are working to raise public awareness such as: Fight the Fakes, Fondation Chirac, CSIP, ASOP Global, EAASM, Fakeshare and IRACM . Various related supply chain security initiatives were also discussed; the introduction of the Falsified Medicines Directive, which the EAASM were influential in bringing about and is focused on the patient safety issue. All pharmaceutical manufacturers will be required to fully implement the directive by February 2019. In addition, a Google ad word campaign[12] is providing the opportunity for visitors to learn more about how to avoid falsified medicines as well as active involvement from regulatory agencies, such as the MHRA's public facing campaigns.[13]

Hospital pharmacists – alerting patients to the risks of online medicines

Hospital pharmacists were positioned as having a crucial role to play in informing the patient, at the point of care, about the risks of buying medicines online. Suggested approaches were discussed, conscious of the need for the balance of appropriate communication, and involved; understanding what medication patients are on and where they get them from when reviewing their medicine history; highlighting the risks of buying fake medicines online; alerting patients to the fact that 96% of websites selling medicines in to the EU are operating illegally[14]; highlighting the typical signs of an illegitimate website, such as:

- "Too good to be true" prices or deals that are unavailable in local pharmacies
- Websites hiding a physical address
- Websites that don't require a prescription for an Rx medicine
- The requirement for legal online sellers of medicines in the EU to display the Common Logo which clicks through to Member State's regulatory website[15]

Mike believes that pharmacists have a key role to play in the fight against fake medicines and will continue to work with all stakeholders to drive awareness and action.

Conclusion

The demand for access to unlicensed imported or unavailable medicines at the point of care is growing. Hospital pharmacists play a vital role in sourcing a supply of unlicensed medicines to ensure patients can benefit from the best possible treatment and outcomes. However, the associated processes are complex and demanding, with the need to protect patients from the increasing rise of counterfeit or fake medicines an additional consideration. It is, therefore, critical for healthcare professionals to work with a trusted partner who can provide ethical, compliant and timely access to unlicensed imported or unavailable medicines.

Following the symposium, an article 'What's in a word? Falsified/counterfeit /fake medicines – the definitions debate' was published by Mike Isles, focused on the evolution of the definitions in this space and recommendations that a consensus be formed to describe such medicines that reach the public. Further articles relating to the topic of falsified medicines can also be found in the same journal; https://uk.sagepub.com/en-gb/eur/medicine-access-point-of-care/journal203456

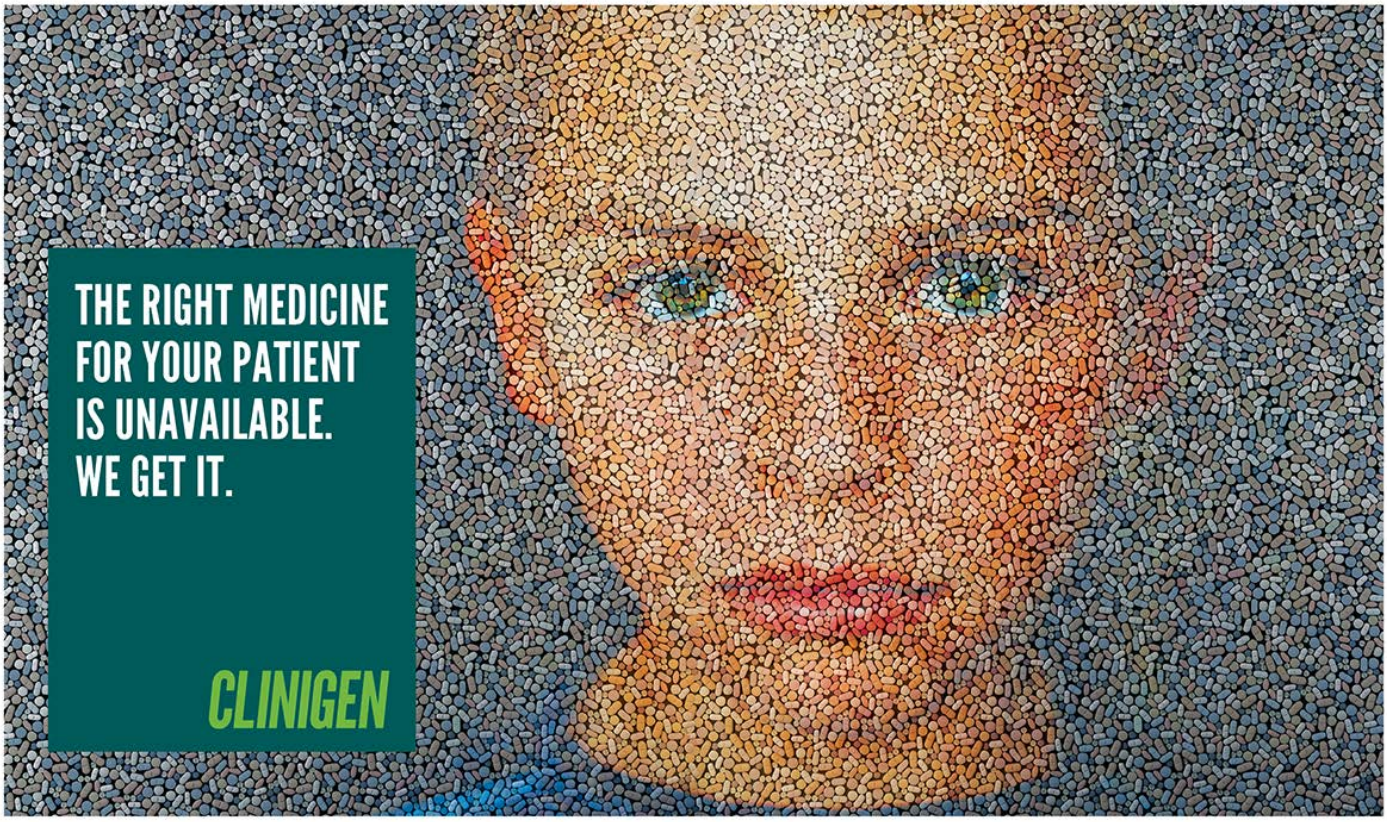
[12] European Alliance for Access to Safe Medicines. The Alliance for Safe Online Pharmacy in the EU. Fighting fakes by raising public awareness.http://asop.eu/cache/downloads/8h23cbi9xo8w4o0k8o0gwo04w

[13] Fighting Fakes by Raising Public Awareness - ASOP EU and EAASM report May 19 2016.pdf. Accessed November 25, 2016.

[14] Medicines and Healthcare products Regulatory Agency. Dodgy diet pills: dying to lose weight? https://www.gov.uk/government/news/dodgy-diet-pills-dying-to-lose-weight. Accessed February 14, 2017.http://www.safemedsonline.org/wp-content/uploads/2016/01/The-Internet-Pharmacy-Market-in-2016.pdf

[15]European Commission on Public Health. Falsified Medicines Directive.https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2011_62/dir_2011_62_en.pdf. Accessed February 14, 2017.

About Clinigen



TRUSTED BY HOSPITAL PHARMACISTS FOR THE PROVISION OF ACCESS TO UNLICENSED MEDICINES

When the right medicine for your patient is not licensed in your country, experiencing a shortage or has been discontinued, access to unlicensed medicines plays an essential role in ensuring the best possible patient outcome.

Clinigen is the global leader in delivering ethical, compliant and timely access to unlicensed medicines, providing pharmacists with solutions to meet the patient's needs.

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