Cancer Research UK’s (CRUK) ambition is to see 3 in 4 patients surviving cancer for 10 years or more by 2034. Cancer drugs play a crucial role in many patients’ treatment, with the newest drugs offering promising improvements in patient survival and quality of life. CRUK is a major funder in drug development and has played a key role in many discoveries that have improved prospects for patients.

Ensuring patients have swift access to innovative treatments is critical. It’s vital that patient access to new drugs is not jeopardised by changes to the licensing processes (also known as market authorisation) as a result of Brexit.

The first step in bringing a new drug into the health service is for it to be licensed as safe to sell. For this, the UK currently participates in a centralised process managed by the European Medicines Agency (EMA). This is an attractive route for pharmaceutical companies seeking to licence their products, as an EMA marketing authorisation covers 25% of the global drug market. The UK’s main interaction with the EMA is through the Medicines and Health Products Regulatory Agency (MHRA), which provides expertise to medicines approvals conducted by the EMA.

CRUK’s priority as the UK exits the EU is to safeguard the interests of patients and research. Regulatory alignment with the EMA with regard to drugs licensing and clinical trials is critical to achieving this. The reason for this is twofold: ensuring that the UK remains a priority launch market for new drugs through its participation in the centralised process, and ensuring that the centralised process itself is not disrupted, by maintaining the MHRA’s expert involvement.

This paper outlines CRUK’s position on the future of drug licensing. It does not cover drug approval processes after licensing in the UK, or the EMA’s role in regulating clinical trials (which can be seen in a separate policy statement on our website).

Recommendations

The UK and the EU must come to an agreement to ensure the future drug licensing system does not exacerbate delays in access to the most innovative treatments for patients, both in the UK and across the EU.

To achieve this:

- The UK Government should seek an agreement with the EU which would:
  - Allow EMA decisions to apply to the UK
  - Allow the MHRA’s continued participation in decision-making and shaping the regulatory environment, building on their reputation and expertise.
- The UK Government should provide further detail on the specific nature of their desired future relationship with the EMA as soon as possible.
Negotiations should be progressed with haste: the timeline for bringing a drug to market can be long and so there must be clarity soon so that the pharmaceutical industry can plan ahead.

**Background**

Cancer drugs are an important part of treatment for many patients. To improve survival for patients it is vital that they are able to access the best, evidence-based treatments for their condition. The UK plays a strong role in drug development, with one of the largest pipelines globally. Around 25% of the world’s top 100 prescription medicines were discovered and developed in the UK. However, evidence suggests that access to the newest cancer drugs is slower in the UK than in other G5 countries. While this is mostly because of long approval times in the UK, it is important that this problem is not worsened by changes to licensing processes after the UK leaves the EU.

After clinical trials have been completed and before a new drug can be given to patients in a routine setting, it must be licensed (also known as market authorisation). In the EU, this is primarily carried out through a centralised procedure, led by the European Medicines Agency (EMA).

Under the centralised procedure, pharmaceutical companies submit a single marketing authorisation application to the EMA. The Committee for Medicinal Products for Human Use (CHMP) carry out a scientific assessment and recommend whether it is safe to authorise the drug. The European Commission then grants the marketing authorisation and it becomes valid to sell in all EU member states as well as in the European Economic Area (EEA) countries: Iceland, Lichtenstein and Norway.

In the UK, national bodies like the National Institute for Health and Care Excellence (NICE) then decide whether the drug should be routinely prescribed to patients, based on the drug’s clinical and cost-effectiveness.

Between 1996 and 2015, 98 new medicines for use in oncology were licensed in Europe. 95 of these were approved by the EMA and the number approved annually by the EMA has increased over time. Over the last ten years there has been a significant shift towards targeted therapies and immunotherapies, with targeted therapies making up 90% of the late phase pipeline in 2016. For these newer and more targeted drugs, it can be more challenging to gather evidence on efficacy quickly since the patient populations are smaller.

In response to this, the EMA has increased their support for early access, for example through issuing conditional marketing authorisations – which grant market authorisation before complete data is available so as to speed up access. It has also launched several initiatives to encourage innovation and early access to medicines, for example through piloting the Medicines Adaptive Pathways for Patients (MAPPs) and through the PRIME programme. These programmes seek to accelerate access to priority medicines by engaging with manufacturers to shape their clinical trial designs, optimising the data collection and accelerating the drug’s later assessment.

As well as evaluating market authorisation applications, the EMA continuously monitors and supervises the safety of medicines that have been authorised for use in the EU. This function is carried out by scientific committees, comprised of experts from member state countries. The EMA
also develops guidelines, coordinates pharmacovigilance obligations and engages with patients, health professionals and the public.

**The UK’s relationship with the EMA**

The UK has a long history of contributing to the centralised regulatory procedure and the UK’s Medicines and Healthcare Products Regulatory Agency (MHRA) is recognised as one of the leading national authorities in the field\(^8\). The MHRA authorises UK clinical trials and regulates medicines and medical devices, as well as sharing knowledge and expertise with the EMA. Between 2008 and 2016\(^9\), the MHRA acted as Scientific Advice Coordinator in at least 20% of centralised EMA medicine approval procedures and provided data in about 50% of all decentralised medicine approval procedures. In 2015 the MHRA’s contribution to more approvals than any other nation: over 27 in comparison to 15 by Germany and 14 by Spain and the Netherlands combined. Loss of this expertise could mean that the EMA’s decision-making processes slow down, at least in the short term, which does not benefit patients in the UK or across Europe.

The MHRA has also been instrumental in designing and delivering the regulatory environment across the EU for clinical trials, ultimately driving faster access to new medicines for patients across Europe\(^10\). This was referenced in a joint letter by UK and EU industry leaders\(^11\) and the MHRA have made their desire to stay involved in the EMA’s process clear, in a statement immediately following the Brexit vote\(^12\).

**CRUK’s preferred option**

Since there is no precedent for a member state leaving the EU, there is no precedent set for continued involvement with the EMA. However, Norway and Iceland are both involved through their membership of the EEA and Lichtenstein has passed a law making EMA decisions automatically valid without delay.

Several non-EEA countries have a mutual recognition agreement (MRA) with the EMA, such as Switzerland, Canada and Japan. The European Commission is responsible for negotiating MRAs with partner countries on behalf of the EU. Although all are different in scope, having an MRA can support market access and encourage greater international harmonisation, while maintaining a focus on patient safety\(^13\). Specifically, these agreements allow:

- Reliance on each other's Good Manufacturing Practice (GMP) inspection system
- The sharing of information on inspections and quality defects
- Waiving batch testing of products on import into their territories

For example, the mutual recognition agreement between the EU and Switzerland covers the regulation and trade of pharmaceuticals, as well as commercial licenses and authorisations for a range of other medical products such as vaccines\(^14\). This agreement is part of a broader arrangement covering the regulatory conformity not only of medical devices but also a range of non-medical sectors. However, it should be noted that Switzerland also accepts free movement of EU nationals.

CRUK agrees with others, such as EFPIA\(^15\), that a break in regulatory continuity would represent “an unacceptable risk to patient health”\(^16\). Our preferred option would therefore be for the UK Government to seek an agreement with the EU which would allow the MHRA’s continued participation in EMA decision-making and in shaping the regulatory environment. This would help
ensure that the UK remains an attractive launch market for pharmaceutical companies bringing
drugs to market, and therefore that UK patients are able to access innovative medicines quickly.
Crucially it would also benefit the EMA as a whole by providing valuable continuity in expertise.

We recognise and support the UK Government’s commitment to maintaining swift patient access to
medicines in the recent position paper on Science and Innovation17, including the suggestion that
other countries’ MRAs provide precedents that the UK and EU could seek to build on18. However, we
would welcome further detail on the specific nature of the desired future relationship with the EMA
and a clear commitment to an agreement that maintains the MHRA’s key role.

Why not go it alone?

One alternative mechanism would be for the UK to develop its own separate regulatory procedure,
led by the MHRA. This option is not favoured by CRUK, the UK Government or by industry. However,
it may become necessary if a deal is not reached that enables a continued working relationship.

A report by the UK EU Life Sciences Steering Group estimated that such a divergence in regulation
would lead to the UK becoming a second priority market in relation to the EMA area, resulting in
delayed access to new medicines for UK patients19. This can be explained by looking at global
pharmaceutical sales covered by each regulator: the EMA covers an area responsible for 25% of
global sales, whereas the UK accounts for just 3%20. The same report also predicts a compromise in
patient safety across the EU if the UK were to leave the EMA, since the UK could no longer be
involved in pharmacovigilance databases and processes.

If the UK did develop its own regulatory process, this could be mitigated by the MHRA automatically
recognising authorisations given by the EU. However, this could still result in delays in patient access
– across the UK as well as in the EU – since the MHRA and EMA would not be able to share expertise
and capacity as they did previously. This would not be favourable: the MHRA is a world-leading
authority and it is vital that their expertise can still contribute. This is vital to patients across the EU
as well as in the UK: disruption to the centralised processes caused by the UK’s exit could lead
pharmaceutical companies to prioritise launching medicines outside of Europe.

Why not align with the FDA?

Another option would be to leave the EU’s regulatory frameworks completely and seek to align with
the US Food and Drug Administration (FDA). This may seem initially attractive given that drug
manufacturers often prioritise the US for launching new drugs, and that the FDA is relatively quick to
approve new drugs. However, there would be significant uncertainty in this approach. The US
President has suggested deregulating the FDA, which has caused some concern among
pharmaceutical companies, since this could pose a risk to patients.

Furthermore, the healthcare system is very different in the US, as is the way that drugs are paid for –
with insurance companies playing a significant role rather than a national budget for drugs. Similarly,
aligning with the FDA would necessitate a much wider assessment of the UK’s approval processes
and its wider regulatory framework, such as those governing clinical trials or medical devices, which
is far more consistent with that of the EU than the US, due to years of collaboration between the
MHRA and EMA. Any significant step away from current practice would necessitate significant
resource and would be incredibly risky, especially given the relatively short timelines involved. This
would lead to further uncertainty and could jeopardise recent progress made to streamline UK drug approvals.

References

2 ibid.
9 ibid.
15 Membership body for the European pharmaceutical industry
18 ibid.
20 BMI Research, Pharmaceutical sales, USDbn, 2015