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28 May 2021 | **Analysis**

Companies Take Their Products To GB Market Post-Brexit

Approvals Follow In Wake Of EU Marketing Authorizations, With Janssen's COVID-19 Vaccine The Latest

by Pink Sheet Team

Thirteen of the 20 new active substances that were approved in the EU between January and April this year have also now received regulatory clearance in Great Britain, *Pink Sheet* analysis finds. New filing procedures have been in place there since 1 January.

Janssen's COVID-19 vaccine has become the latest new active substance (NAS) that already had EU approval to gain regulatory clearance in Great Britain under new UK filing requirements that came into play after the Brexit transition period ended on 31 December 2020.

Research by the *Pink Sheet* shows how companies are coming to terms with the new requirements.

Twenty NASs, including three COVID-19 vaccines, were approved in the EU under the centralized procedure in the first four months of 2021. The table at the end of this article records the regulatory situation in Great Britain for all 20 NASs.

As of 28 May, 13 of the 20 products had also secured regulatory approval from the UK Medicines and Healthcare products Regulatory Agency for use in England, Scotland and Wales, three of the four nations of the UK. The MHRA became a stand-alone regulator, independent of the EU, on 1 January.

Of the remaining seven products, filings relating to three have been submitted to the UK MHRA. Filings are planned for at least two more, while two companies did not respond to the *Pink Sheet*'s requests for details on their filing plans. *(See bar chart below.)*

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Janssen's COVID-19 vaccine – officially named "COVID-19 Vaccine Janssen – was granted a conditional marketing authorization (CMA) by the MHRA on 28 May. It is one of the 13 NASs that now have approval in both GB and the EU. The vaccine was approved in the EU on 11 March.

The companies involved are likely to have received either a GB MA (Great Britain Marketing Authorization) or a CMA.

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UK Explains New 'Reliance' Routes To Approval Based On EU Dossiers

By Ian Schofield

06 Jan 2021

Companies seeking marketing authorizations in the UK or Great Britain will be able to make use of two new "reliance" procedures offering regulatory assessment times of 67 days or less if their products have already gone through the EU centralized or decentralized approval systems.

Read the full article here

Marketing Approval vs Market Access

Marketing approval is one thing; market access is another. Many of the 20 products will be subject to review by NICE, the UK health technology assessment body, whose job it is to determine whether it considers that the products provide value for money and should or should not be available under the National Health Service.

COVID-19 Vaccines

With the granting of the GB CMA for the Janssen vaccine, the same four COVID-19 vaccines have now been approved for use in both the EU and Great Britain.

Vaxzevria, the Oxford/*AstraZeneca* COVID-19 vaccine, was cleared for use in the UK before it secured EU approval.

In the case of *Moderna*'s COVID-19 vaccine, GB approval came just two days after EU approval. The Moderna vaccine was initially authorized for emergency use in the UK in January 2021 under Regulation 174 of the Human Medicine Regulations 2012 but it later received a CMA.

Comirnaty, the *Pfizer*/*BioNTech* vaccine, was approved in December 2020 in both jurisdictions. Both the Oxford/AstraZeneca and Pfizer/BioNTech vaccines have emergency use authorizations from the MHRA.

Fast Approvals

For several other products, GB approval came less than two weeks after the EU marketing

authorization. They were:

- *BioCryst Pharmaceuticals*' Orladeyo (berotralstat)
- *Incyt*'s Pemazyre (pemigatinib)
- *Seagen*'s Tukysa (tucatinib)

For the following products, the gap was between just over two weeks and a month:

- *Eli Lilly*'s Retsevmo (selpercatinib)
- *Amarin Pharmaceuticals*' Vazkepa (icosapent ethyl)
- *Daiichi Sankyo*/AstraZeneca's Enhertu (trastuzumab deruxtecan)

Most Recent Approvals

Janssen's COVID-19 vaccine is the most recent GB approval. Other products approved in May include *Karyopharm Therapeutics*' Nexpovio (selinexor), *Roche*'s Evrysdi (risdiplam), and BioCryst's Orladeyo. These three products were cleared on 26 May, 25 May and 12 May respectively.

All Change After Brexit

During the Brexit transition period, MAs for products that had gone through the EU centralized procedure applied automatically in the UK. These have now been converted ("grandfathered") into GB marketing authorizations.

As of 1 January this year, companies wishing to market their new products in Great Britain have to apply separately to the MHRA for a GB MA or a CMA.

The situation is different in Northern Ireland, the fourth nation of the UK. As a result of the Northern Ireland Protocol, which is intended to avoid a hard border on the island of Ireland between the UK and the EU, new and existing EU MAs for such products continue to apply there.

The Reliance Procedure

While the UK is no longer part of the EU pharmaceutical regulatory network, it currently relies to a large degree on EU drug approval decisions. It is highly likely that this year's MA filings with the MHRA for products approved through the EU centralized procedure are being submitted

under the UK's European Commission Decision Reliance Procedure (ECDRP).

For products approved centrally at EU level, the reliance procedure offers the possibility of GB approval within 67 days of the application being validated by the MHRA.

In addition, to make sure GB assessment times can be aligned with those of the EU, the procedure includes an incentive for companies to file as soon as possible after the CHMP, the European Medicines Agency's drug evaluation committee, adopts a positive marketing recommendation.

The relevance of the 67-day period is that this is the length of time the European Commission has to issue a formal approval for a product with a positive CHMP opinion.

The ECDRP will operate for two years, finishing at the end of 2022.

Incentive To File Early

As for the incentive to file early with the MHRA, if the company provides the CHMP opinion within five days after it is adopted, the date of the opinion will be designated Day 0 of the ECDRP. The MHRA has said that it will aim to determine the MA GB "as soon as possible after EC approval, and by Day 67 at the latest provided that the EC decision has been received."

If the application is filed more than five days after the opinion, Day 0 will be the date of the UK's validation of the MAA. This, the MHRA has said, could mean determination being delayed. The applicant is responsible for confirming the EC decision to the MHRA, and for confirming the opinion of the EMA's orphan drugs committee (COMP) on orphan designation.

Companies with new products at an earlier stage of development will also be able to use the UK's new Innovative Licensing and Access Pathway (ILAP), which is intended to reduce the time taken to get innovative products to market. (Also see "*UK Vaunts 'New Era' In Drug Approvals*" - Pink Sheet, 4 Jan, 2021.)

Janssen Vaccine CMA

In its announcement of the regulatory clearance of the Janssen COVID-19 vaccine, the MHRA explains how the reliance route works. It notes that the CMA it granted Janssen is valid in Great Britain only, that it was approved via the ECDRP, and that this is when the MA application made by the company references the decision made by the CHMP. "The MHRA reviews this application, together with due consideration of the EC decision, before making an independent decision on the quality, safety, and effectiveness of the vaccine," it said. It further notes: "COVID-19 Vaccine

Janssen is authorized in Northern Ireland under the CMA granted by the EMA on 11 March. This CMA has similar requirements to that granted by the MHRA".

Editor's Note: The final paragraph of this article was added on 4 June 2021. The article was also updated on 7 June 2021 to reflect the fact that the UK MHRA granted Karyopharm Therapeutics' Nepovio (selinexor) on 26 May 2021.

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