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UK Confirms It Will Accept EU Marketing Authorizations For Two Years

Accelerated and Rolling Review Processes Kick In Next Year

by Ian Schofield

New guidance from the UK covers the recognition of EU approvals, accelerated assessment, rolling reviews, and much else besides.

The UK says it will recognize EU centralized marketing authorization (MA) decisions for two years in Great Britain after the Brexit transition period ends on 31 December this year, subject to "a risk-based review" that takes account of any GB-specific conditions.

The medicines regulator, the MHRA, has also confirmed that its new accelerated assessment procedure will produce a decision on approval in just 150 days, and will apply to products containing either existing or new active substances, including orphan drugs.

New *guidance* on the post-Brexit licensing systems issued on 27 October also says that a new GB rolling review will be available for novel substances, including biologicals/biosimilars, and that mechanisms will be put in place for conditional and exceptional circumstances approvals.

The new procedures are being established to allow the newly freestanding MHRA to handle all types of applications, including those that fall within the mandatory scope of the EU marketing authorization system, from 1 January, when the UK leaves the EU single market and customs union. They were discussed at a 27 October webinar held by the MHRA.

The Reliance Route

As a result of the Northern Ireland Protocol, EU marketing authorizations will continue to apply to Northern Ireland from next year, but they will not be valid in Great Britain, which will issue its own approvals via national licensing procedures.

However, the MHRA says that "for two years from 1 January 2021, Great Britain will adopt decisions taken by the European Commission on the approval of new marketing authorisations in the community marketing authorization procedure."

Under the so-called "reliance route," which was first flagged in September, companies will still have to file an approval application with the MHRA. (Also see "*How To Get A 'Great Britain' Drug Approval In 2021*" - Pink Sheet, 2 Sep, 2020.) The application should include all the information that was provided to the European Medicines Agency and its human medicines committee, the CHMP, during the centralized procedure.

It should be "accompanied by all iterations of the CHMP assessment report including the final CHMP opinion," together with a declaration of conformity of the Great Britain application with the dossier approved by the commission, the guidance says.

Keith McDonald, deputy director of the MHRA's licensing division, said the agency would recognize EU decisions "subject to a risk-based review in the context of UK clinical practice and any GB-specific considerations." If the application is submitted as soon as the CHMP opinion is available, "the GB MA approval will be made at the time of the EC decision," he told the webinar.

Non-Centralized Approvals

The UK will also have the power to take account of MA decisions by EU member states under the mutual recognition and decentralized procedures when considering applications for approval in the UK.

In addition, as a result of the Northern Ireland Protocol, Northern Ireland will be able to be included as a "concerned member state" in non-centralized EU procedures, although this will result in an MA that is valid only in Northern Ireland. McDonald said that two additional MA number (product license) prefixes – PLGB and PLNI – would be introduced for products that were not authorized for the whole of the UK and these would need to appear on product packs.

Products approved in Northern Ireland can be filed for a GB MA using the "unfettered access" route, but on two conditions: the applicant must be an "NI qualifying business," and once they are manufactured the goods must reach GB via Northern Ireland, McDonald noted. Unfettered access applies to goods moving from NI to other parts of the UK internal market, under the Northern Ireland Protocol.

Being Established In GB

For UK and GB approvals, the MA holder (MAH) must be established in the European Economic Area, and must also be established in the UK before 1 January 2023. If not, contact details of a named individual residing in the UK must be provided and they may be contacted by the licensing authority for information on the MA.

"We also want to be clear that the 24-month period after 1 January contains provisions for continuity for industry" in that most of the current EU guidance will be copied over to Great Britain, including variation classifications rules and classification of advanced therapy medicines, McDonald noted.

Accelerated Assessment

The new GB 150-day accelerated review mechanism will be open to new MA applications (MAAs) for both new and existing active substances that are submitted directly to the UK. Eligible products include orphan drugs, medicines submitted for conditional and full MAs, and those for approval under exceptional circumstances.

"Conditional marketing authorization applications and applications submitted under exceptional circumstances will be evaluated in accordance with UK legislation and MHRA will initially adopt the relevant technical guidance published by EMA," the guidance notes.

Applicants who want to seek accelerated assessment (AA) should contact the MHRA before the intended date of submission, and the letter requesting AA should state any intention to seek orphan status or an exceptional circumstances MA. The agency will operate a "fixed submission date" system with a program of dates to facilitate planning for and agreeing the submission date and coordinating with appropriate meeting dates of the MHRA's Commission on Human Medicines.

A valid AA application should include common technical document modules 2-5, a UK specific CTD module 1, and an appropriate risk management plan. "Appropriate justification and compliance with GB paediatric requirements and investigation plans should be included," according to the guidance.

The assessment process will consist of two phases totaling 150 days, with an intervening clock-stop period between phase 1 and phase 2. The first phase, including CHM consultation, will be completed 80 days after clock start, and any questions arising from the initial assessment will be raised with the applicant and should be addressed in the clock-stop period of up to 90 days. Phase 2 assessment will begin when the applicant's responses are received.

Assessment in phase 1 will also address eligibility for the grant of orphan status or a conditional MA. "Based on the assessment, the MHRA will provide an opinion on approvability of the product by day 150, and if positive, will grant the MA."

Rolling Review

The rolling review is a new "phased, modular, iterative" licensing route intended to enhance the development of novel medicines by offering ongoing regulatory interaction and advice, allowing applicants to "get it right first time," the MHRA says. Eligible products are any new active

substances including biological/biosimilar medicines, based on the submission of a full GB MA application.

The quality, non-clinical and clinical modules can be submitted separately or in combination, depending on the individual circumstances as data become available. “It is expected that each module will be near completion to avoid multiple iterations of assessment of the same module,” the guidance notes.

Each assessment phase will progress independently, and any questions raised will offer the applicant the chance for a comprehensive update of the modules before final submission. “The final phase will involve submission of a complete application including updated versions of the modules evaluated previously.” The final assessment is expected to be a single phase with the decision on marketing authorization and will include the risk management plan.

The guidance also mentions the new innovative licensing pathway that was first announced in September and offers an “innovative medicine designation” and a “target development profile.” (Also see "*UK Presents New Licensing Pathway For Innovative Drugs*" - Pink Sheet, 18 Sep, 2020.) The pathway was discussed in depth at the webinar and this will be covered in a forthcoming *Pink Sheet* article.