Practical guidance on the implementation of the Protocol on Ireland/Northern Ireland for medicinal products for human use approved via MRP/DCP

1. Introduction

Since 1 February 2020, the United Kingdom has withdrawn from the European Union and has become a ‘third country’. The Withdrawal Agreement provides for a transition period ending on 31 December 2020. Until that date, EU law in its entirety applies to and in the United Kingdom. As from the end of the transition period, the Protocol on Ireland/Northern Ireland (‘IE/NI Protocol’) applies.

The information provided in this document complements the Notice to Stakeholders on the Withdrawal of the United Kingdom and EU rules for medicinal products for human use and veterinary medical products and the CMDh Practical guidance for procedures related to Brexit for medicinal products for human use approved via MRP/DCP.

MAHs of nationally approved medicinal products (NAPs) are also referred to the EMA Questions and answers to stakeholders on the implementation of the Protocol on Ireland/Northern Ireland with respect to EMA activities that includes NAPs, e.g. Article 57 database, EudraVigilance, electronic application forms and PSUR repository.

This practical guidance document only reflects the situation as laid down in legal provisions in force on the date of its publication, and without prejudice to any of the ongoing discussions between the Union and the UK concerning the application of the Union acquis concerning medicinal products in respect of Northern Ireland after the transition period, in light of the particular challenges that small markets historically dependent on medicines supply from or through Great Britain are facing. In this regard it has to be borne in mind that the CMDh is not participating in any of the negotiations between the Union and the UK that aim at solving – before the end of 2020 - the particular challenges that small markets face that historically are dependent on medicines supply from or through Great Britain, notably Northern Ireland.
2. Marketing authorisations in UK(NI)

2.1. How should I include UK(NI) in my MRP/DCP application?

According to the Ireland/Northern Ireland protocol, the national MAs for medicinal products issued by the United Kingdom in respect of Northern Ireland, UK(NI), have to comply with Article 17 and 18 of Directive 2001/83/EC, i.e. they have to go through the decentralised procedure (DCP) or the mutual recognition procedure (MRP), if the applicant already holds an MA for the same product in an EU/EEA member state (MRP) or applies for MAs for the same product in any EU/EEA member state(s) (DCP).

Therefore, in the above-mentioned situations, after the end of the transition period MA applicants who wish to obtain a MA for UK(NI) have to include Northern Ireland in the scope of their MA application in the DCP or MRP. An update of the application form and practical guidance on submission to the UK NCA is expected to be published before the end of the transition period.

For MRP/DCP applications that have been submitted with the UK as CMS before the end of the transition period, but for which the procedure will be finalised after the end of the transition period, it is assumed that UK(NI) will remain as CMS until the applicant informs the RMS otherwise. Applicants are advised to inform the RMS as soon as possible after the end of the transition period on their intention with regard to UK(NI).

2.2. How will UK(NI) be managed in existing MRP/DCPs?

After the end of the transition period, UK is no longer a CMS. However, MAs issued by the United Kingdom in respect of Northern Ireland have to comply with Article 17 and 18 of Directive 2001/83/EC. Therefore, for all existing MRP/DCP procedures where UK is CMS and has granted MAs or the procedure is finalised with a positive outcome before the end of the transition period, it is assumed that the MAH intends to keep the MA for UK(NI). At the end of the transition period, UK will therefore automatically be replaced with UK(NI) in existing procedures in the CTS database.

In case the MA in UK(NI) is withdrawn, the MAH should inform both the UK NCA and the RMS. The UK NCA will update CTS accordingly.

2.3. How will products that are only authorised in UK(NI) be managed?

A medicinal product that is only authorised in UK(NI) (i.e. either authorised via the national procedure or in an MRP/DCP with no remaining EU/EEA MS) will be managed by the UK NCA in compliance with the EU pharmaceutical acquis.

These products may be included in EU worksharing variations.

Alternatively, repeat use procedures may be used to (re)introduce UK(NI) authorisation into MRP/DCP procedures in consultation with the EU/EEA RMS.

2.4. How can I obtain marketing authorisations in EU/EEA for a medicinal product that is only authorised in UK(NI)?

As the UK NCA can’t act as RMS it is not possible to initiate an MRP based on the MA in UK(NI). In case the MAH wishes to obtain marketing authorisations in EU/EEA for a product only authorised in the UK(NI), an RMS in the EU/EEA should be chosen and the application submitted via DCP including UK(NI) as CMS. Upon approval, the MAH should discuss with the UK NCA any implications on the national UK(NI) MA. It will not be possible to submit a national MA in one EU/EEA MS while there is a national MA in UK(NI) as this would violate Art. 18 of Directive 2001/83/EC.
2.5. Can I use a reference medicinal product (RefMP) authorised in UK(NI) for my generic, hybrid or biosimilar application?

No, according to the IE/NI protocol, a medicinal product authorised in UK(NI) after the end of the transition period shall not be considered as a RefMP in the EU/EEA. For products authorised in the UK before the end of the transition period, see Q&A 34 in the CMDh Practical guidance for procedures related to Brexit for medicinal products for human use approved via MRP/DCP.

2.6. Can the MAH be located in Northern Ireland?

The marketing authorisation holder (MAH) for medicinal products authorised under EU law has to be established in the EU/EEA, i.e. the MAH cannot be established in Northern Ireland. Only for MAs in UK(NI) the MAH may be established in Northern Ireland (cf. 2nd indent of section 20 of Annex 2 to the IE/NI protocol), but not in Great Britain. However, the CMDh acknowledges that the MAs for UK(NI) are within the responsibility of the UK NCA.

3. GMP and manufacturing

3.1. Can batch release control, batch release and batch certification be conducted by a manufacturer located in Northern Ireland?

In accordance with Article 51(1) of Directive 2001/83/EC, the qualified person of the manufacturing and importation authorisation holder is responsible to certify that each batch of medicinal product intended to be placed on the EU market was manufactured in accordance with EU GMP requirements and the marketing authorisation.

Each batch imported into the EU/EEA has to undergo upon importation a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of medicinal products in accordance with the requirements of the marketing authorisation.

Based on the provisions of Protocol on Ireland/Northern Ireland, the batch release by an importer/manufacturer established in Northern Ireland will be recognised in the EU/EEA also after 31 December 2020. Similarly, quality control testing for the purpose of release to the market conducted by testing sites established in Northern Ireland will be recognised in the EU/EEA.

Conversely, medicinal products shipped from Great Britain to Northern Ireland after 31 December 2020 will be considered imports and will be subject to the above requirements concerning importation, quality control testing and batch release. However, it should also be noted that products that have already been placed on the UK market before 1 January 2021 will not be considered imports in such situation, as explained in part B of Notice to Stakeholders on the Withdrawal of the United Kingdom and EU rules for medicinal products for human use and veterinary medical products.

Where packs of medicines are shipped from one part of the internal market (e.g. France) to another part of the internal market (i.e. Ireland) via the ‘land bridge’, i.e. by using the transit procedure of the Common Transit Convention, these products are not placed on the UK market and hence do not require to be imported, to undergo quality control testing and QP release upon arrival in Ireland. The same applies to medicines shipped from the EU/EEA to Northern Ireland.

3.2. Can Official Control Authority batch release (OCABR) be conducted in Northern Ireland?

For medicinal products placed on the market as of the end of the transition period, OCABR in accordance with Article 114 of Directive 2001/83/EC cannot be carried out by an Official Medicines
Control Laboratory (OMCL) located in Northern Ireland. OCABR has to be carried out by an OMCL located within the EU.

3.3. How will the manufacturing and import authorisations, GMP certificates and GMP non-compliance statements for sites in Northern Ireland be issued and made available?

Manufacturing and Import Authorisations (MIA) as well as certificate of good manufacturing practice (“GMP certificate”) and GMP non-compliance reports issued by UK Authorities after the end of the transition period for manufacturers located in Northern Ireland will continue to be made available in the EudraGMDP database by the UK competent authorities and will be recognised in the EU/EEA. The European Commission decision of 16/10/2020 (C(2020) 7126 final) foresees that from 1 January 2021 the UK authorities will have partial access to EudraGMDP database (write access via Gateway submissions for information in relation to sites located in Northern Ireland).

3.4. How will the wholesale distribution authorisations, GDP certificates and GDP Non-Compliance statements for sites in Northern Ireland be issued and made available?

Wholesale Distribution Authorisations (WDA) as well as certificate of good distribution practice (“GDP certificate”) and GDP non-compliance reports issued by UK Authorities after the end of the transition period for wholesalers located in Northern Ireland will continue to be made available in the EudraGMDP database by the UK competent authorities and will be recognised in the EU/EEA. The European Commission decision of 16/10/2020 (C(2020) 7126 final) foresees that from 1 January 2021 the UK authorities will have partial access to EudraGMDP database (write access via Gateway submissions for information in relation to sites located in Northern Ireland).

3.5. What requirements will apply to sourcing of active substances from Northern Ireland?

According to Article 46b(2) of Directive 2001/83/EC, active substances for medicinal products for human use are to only be imported in the EU if, inter alia, the active substances are accompanied by a written confirmation from the competent authority of the exporting third country which, as regards the plant manufacturing that exported active substance, confirms that the standards of good manufacturing practice and control of the plant are equivalent to those in the EU.

After 31 December 2020 shipments of active substances manufactured in Northern Ireland will not need to be accompanied by a written confirmation issued by the UK authorities. However, active substances manufactured in the rest of the UK (i.e. Great Britain) and shipped after 31 December 2020 to Northern Ireland or the EU/EEA will have to be accompanied by a written confirmation issued by the UK authorities.