

REGULATORY INTELLIGENCE

Highlights - Windsor Framework Pharmacovigilance Updates

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The recent MHRA update on Windsor framework pharmacovigilance rules, which is set to come into force on **01-Jan-2025**, provides a good opportunity to summarise main points of Windsor framework and its impact on pharmacovigilance in EU and UK.

Windsor Framework Overview

The Windsor framework is an agreement between the European union and the UK, which was announced in February 2023. The necessity for such framework arose from the complexities of the original Northern Ireland (NI) Protocol, as the protocol was the source of economic and societal challenges since its Brexit implementation, the new agreement fundamentally amends the text and provisions of the original Protocol. To legally implement the Windsor framework, the EU has adopted Regulation No 2023/1182 in Jun 2023.

The original Protocol applied all EU rules and authorisation requirements for medicines which meant that for **novel medicines, including innovative cancer drugs, it was the European Medicines Agency (EMA), not the UK's Medicines and Healthcare products Regulatory Agency (MHRA), which approved medicines for the NI market**. This failed to recognise or accommodate for the fact that the overwhelming flow of medicines to Northern Ireland is from Great Britain, with medicines provided for the UK market as a whole.

Under the new agreement, it will be for the MHRA to approve all drugs for the whole UK market. **From 01-Jan-2025, MHRA will regulate medicines through UK-wide marketing authorisations (MAs)**. Any authorisation issued on or after this date, will have an MA number with a PL prefix. Medicines authorised before that date will retain their current MA number.

Licensing Changes

Products that fall within the mandatory or optional scope of the **EU's Centralised Procedure** that, following the UK's exit from the EU, were eligible for authorisation by the European Commission (EC) in NI (as a Centrally Authorised Product (CAP)) will no longer be authorised in this manner. Instead, these products will be authorised UK-wide under UK requirements by the MHRA. **From 01-Jan-2025 Union Authorisations issued by the EC will no longer be valid for NI.** Instead, the MHRA will issue UK-wide authorisations for these CAPs.

MAHs will not be able to apply for a GB MA (a PLGB covering only Great Britain) after 31-Dec-2024. The MHRA will retain the right to issue GB MAs after 01-Jan-2025, but this will not be available through application.

By default, existing GB MAs will automatically be converted to UK-wide marketing authorisations on 01-Jan-2025, unless the GB MA is cancelled by the MA Holder or MHRA by 31-Dec-2024. No action is necessary for this conversion for MAHs who only hold a GB MA for a particular product. The MA number including the PLGB prefix will not change after this conversion.

If a MAH currently holds both a NI MA and a GB MA for the same product and wishes to retain authorisation for the whole of the UK, the NI MA will need to be cancelled to enable the automatic conversion of the existing GB MA to a UK-wide marketing authorisation. The MAH cannot hold a UK-wide MA and a NI MA simultaneously for the same product.

For details about conversion options please refer to the guidance on “UK-wide licensing for human medicines”.



The products that were previously within the scope of the EU's Centralised Procedure will be designated in line with definitions in UK law as '**Category 1**'. Category 1 includes the generic, hybrid or biosimilar products of Category 1 reference products.



Medicines outside this scope (which can already be authorised as UK-wide MAs), will be designated as '**Category 2**'. This includes generic, hybrid or biosimilar products of Category 2 reference products.

The Windsor Framework's licensing changes do not impact medicinal products outside of the scope of the EU centralised procedure. Consequently, applicable EU law on medicinal products as amended prior to and by the Windsor Framework will continue to apply to these products after 01-Jan-2025.

Pharmacovigilance Changes

Following the implementation of these arrangements from 01-Jan-2025, pharmacovigilance requirements will remain broadly in line with current requirements. **However, there will be aspects of pharmacovigilance which will be impacted depending on whether the product is Category 1 or 2.**

The tables below are extracted from the MHRA guidance on “UK-wide licensing for human medicines” and “Pharmacovigilance following agreement of the Windsor Framework” and provide insights on requirements for different areas of pharmacovigilance.

Regulatory compliance:

Compliance area	Category 1	Category 2
Pharmacovigilance	UK Requirements only	UK and EU requirements as applicable
Location of Qualified Person for Pharmacovigilance (QPPV)	UK or EEA	UK or EEA
Territory where applicant for marketing authorisations must be established	UK or EEA	UK or EEA

ICSR reporting:

MHRA reporting	EMA reporting	EMA reporting
All UK ICSRs and third-country serious ICSRs meeting MHRA reporting requirements	Non-serious ICSRs (originating in NI)	Serious ICSRs (originating anywhere in the UK)
Category 1 – UK YES only licence	n/a	n/a
Category 1 – UK YES and EU licence	YES*	YES
Category 2 – UK YES only	YES	YES
Category 2 – UK YES and EU licence	YES	YES

*In line with EMA requirements

PSUR submission:

	Submission to MHRA PSUR portal	Submission to EU PSUR repository
Category 1 – UK only licence	YES	N/A
Category 1 – UK and corresponding EU licence	YES	YES
Category 2 – for UK only and UK and EU licence	Not required*	YES

*Provided the MHRA can access the PSUR from the EU PSUR Repository.

UK QPPV:

	Can reside in EU/EEA or UK	Must reside in EU/EEA	Can reside in UK or EU/EEA
Category 1 – UK only licence	YES	No	No
Category 1 – UK and EU licence	YES	YES	No
Category 2 – UK only	YES	Subject to EU directive*	Subject to EU directive*
Category 2 – UK and EU licence	YES	YES	No

*In line with DIRECTIVE (EU) 2022/642 amending Directives 2001/20/EC and 2001/83/EC as regards derogations from certain obligations concerning certain medicinal products for human use made available in the United Kingdom in respect of Northern Ireland and in Cyprus, Ireland and Malta

UK LCPPV

Following the implementation of the arrangements for human medicines under the Windsor Framework, there are no changes to the requirement to operate an NCP within the UK. Where the company has a UK QPPV residing in the EU, a UK NCP shall need to be nominated and informed to the MHRA.

UK PSMF

Following the implementation of the arrangements for human medicines under the Windsor Framework, a UK PSMF will be required for all UK marketing authorisations regardless of the route of authorisation. There will be no changes to the operational implementation of the UK PSMF; however, the current legislative reference for a product may change if a product is now subject to HMR schedule 12A rather than CIR due to product category. The HMR requirement mirrors that of the CIR and therefore no differences exist in practical terms.

Notification of QPPV and PSMF to XEVMPD

Following the implementation of the arrangements for human medicines under the Windsor Framework, Category 1 products should continue to follow the existing notification requirements. For Category 2 products, in addition to notifying the UK QPPV and UK PSMF details to the MHRA, MAHs must submit information on the UK QPPV and the location of the UK PSMF to the Article 57 database in accordance with Regulation (EC) No 726/2004 Article 57(2).

XEVMPD

After the date on which Regulation (EU) 2023/1182 become applicable, the information recorded in the Article 57 database and any new submission for a medicinal product approved via the centralised procedure and referencing 'EU' as the country of authorisation will automatically no longer include the territory of Northern Ireland. If, after this date a medicinal product authorised by the European Commission via the centralised procedure with a marketing authorisation valid in the EU/EEA is also granted an equivalent marketing authorisation by the UK authorities in accordance with UK authorisation procedures and rules valid in the territory of Northern Ireland, then the MAH may additionally report the product information in the Article 57 database on voluntary basis for that equivalent authorisation. There is no change in the current Article 57 submission rules for medicinal products approved nationally (i.e. via a national procedure, mutual recognition procedure and/or decentralised procedure) by the MHRA and with marketing authorisation valid in the territory of Northern Ireland. I.e.: Marketing authorisation holders continue to report product information on medicinal products authorised nationally with a marketing authorisation valid in Northern Ireland.

Conclusion

The Windsor Framework represents a significant step forward in the regulation of medicines in the UK, as it brings all medicines in the UK under the MHRA oversight. This shift promises to streamline the approval process and improve accessibility to medicines. However, the continuing dual application of EU/UK laws in the territory of Northern Ireland adds an additional layer of complexity to pharmacovigilance.

As a result, MAHs will need to navigate these complexities with precision, ensuring that they carefully assess and implement the necessary regulatory requirements based on the classification of their products into Category 1 or 2.

References

1. Pharmacovigilance following agreement of the Windsor Framework, Aug 2024
2. UK-wide licensing for human medicines, Aug 2024
3. MHRA Windsor Framework collection
4. EMA's Questions and answers to Stakeholders on the implications of Regulation (EU) 2023/1182 for centrally authorised medicinal products for human use, Jun 2024
5. Regulation No 2023/1182, Jun 2023