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The Implications Of The New EU HTA Regulation For Companies

Joint Clinical Assessments Will Become A Key Part Of The New Environment

by Alexander Natz

Legal and industry expert Alexander Natz sets out key questions and answers to help companies prepare for new EU regulations on health technology assessments, one of the biggest developments to affect the pharmaceutical industry in over a decade.

Regulation (EU) 2021/2282 on health technology assessment (HTA) is now in force and will bring important and wide-reaching changes that pharmaceutical companies need to understand.

Arguably the most important implication of the regulation is the introduction of EU-level joint clinical assessments (JCAs) that will start to become applicable in a few years' time. These joint assessments are essentially relative effectiveness assessments that will be conducted by designated national HTA experts at the EU level. The new procedure will impact all centrally authorized medicines and some medical devices and serve as the basis for national value assessments and price negotiations. Hence, it is of utmost importance for industry, payers and patients.

About the Author

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According to the European Commission, EU cooperation on HTA aims to help make innovative health technologies available to patients in Europe, make better use of available resources and improve business predictability. It said the new rules seek to ensure that when HTA is performed, the methodologies and procedures applied are more predictable across the EU and that JCAs are not repeated at national level, thereby avoiding duplication and discrepancies.

In the Q&A below, lawyer and industry expert Alexander Natz highlights the potential impact for health technologies subject to JCAs, from the choice of comparator to the importance of scientific advice.

Q: From what date will Regulation (EU) 2021/2282 be applicable to medicinal products?

A: Regulation 2021/2282, which amended Directive 2011/24/EU on cross-border health care, was published in the *Official Journal of the European Union* in December 2021. It came into force in January 2022 and its provision relating to JCAs will become applicable from 12 January 2025 for medicinal products with new active substances for oncological indications and advanced therapy medicinal products (ATMPs). From 13 January 2028 onwards, manufacturers of orphan drugs will have to submit a dossier for the joint clinical assessments. All other medicines approved under the EU centralized procedure will be subject to JCAs from 13 January 2030. Any marketing authorization application filed with the European Medicines Agency for these products on or after those dates will trigger the need for a JCA dossier.

Q: Which products are affected by the regulation?

A: All EU centrally approved medicines as well as new indications of EU HTA-assessed medicines are covered by Regulation 2021/2282. Some Class IIb and III medical devices and some Class D diagnostics will also be affected. The commission will specify which diagnostics and medical devices will be affected.

Q: What is the duration of the JCA procedure for pharmaceuticals?

A: The company has to submit its dossier of evidence for the JCA 45 days before the EMA's Committee for Medicinal Products for Human Use (CHMP) issues its opinion on whether the medicine should be granted a marketing authorization. The JCA report will be published at the latest 30 days after the commission formally approves the medicine. This means that the national procedures that will build on this report will start rather quickly after EU approval. It also means that the JCA report will be among the first assessments globally. It will therefore have significant global effect.

Q: Who will oversee EU level JCA reports?

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A: The Member State Coordination Group, established under Regulation 2021/2282, is composed of representatives from national HTA bodies and will be responsible for overseeing the JCAs and other joint work carried out by designated national experts organized in sub-groups dedicated to specific types of joint work.

Q: What exactly will be included in the joint clinical assessment report?

A: Recital 14 of the regulation specifies: "…, the joint clinical assessments …. constitute a scientific analysis of the relative effects of the health technology as assessed on the health outcomes against the chosen parameters which are based on the assessment scope. The scientific analysis will further include consideration of the degree of certainty of the relative effects, taking into account the strengths and limitations of the available evidence."

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Q: Will the assessments make decisions on cost-effectiveness or value?

A: No. The JCA will include only a clinical assessment. Any cost-effectiveness assessment will remain in the domain of member states, as will value assessments and the price negotiations or decisions. The JCA should not contain any recommendation on a product's value or whether to reimburse it. However, the decisions about the choice of the comparator and the endpoints will be made at the EU level in the future, which is very important also for the price negotiations.

Q: What effect will JCAs have on national health technology assessments?

A: The JCA report is meant to replace national assessments with respect to the clinical part of health technology assessments and should serve as a basis of national decisions in all EU countries. However, national HTA bodies have significant discretion to diverge from the JCA report, ask for new data and evidence and even for new comparators. The JCA report is not legally binding. However, because the new regulation applies to all EU countries, it can be expected that the acceptance of JCAs at national level will be high as the national HTA bodies will be involved in the EU decision-making.

Q: Can companies seek scientific advice?

A: Yes, the new regulation gives affected companies the opportunity to request a joint scientific

consultation from the Member State Coordination Group as long as the clinical studies are still in the planning phase. The following aspects could be subject of the consultation: the clinical trial design, choice of comparator, endpoints, interventions, health outcomes and patient populations. Unfortunately, the Coordination Group can only provide a certain number of joint scientific consultations each year due to limited resources. This means that not all companies with affected products will be able to seek scientific advice. This will be challenging for companies.

Q: What is the level of evidence to be provided for the joint clinical assessments?

A: The evidence provided by the company should follow the international standards of evidence-based medicine, and randomized, blinded, controlled, direct comparative studies are recommended where appropriate. This leaves some room to accommodate different trial designs but also establishes randomized controlled trials (RCTs) as gold standard. It is likely that the methodology chosen for the EU HTA will build significantly on the already developed EUnetHTA methodology.

Q: Can individual EU member states request additional evidence?

A: Yes. Recital 15 specifies: "… Member States should be able to perform complementary clinical analyses relating, inter alia, to patient groups, comparators or health outcomes other than those included in the joint clinical assessment report, or using a different methodology if that methodology would be required in the overall national HTA process of the Member State concerned." This means that there is wide discretion to conduct additional national assessments. However, the JCA report has to be taken into consideration when making the national decision.

Q: Who will choose the comparator?

A: The subgroups of the Coordination Group will make the important decision of choosing the comparator. Further methodology and guidelines will be developed in that respect. This means that a decisive decision is already made at the beginning of the EU procedure that will have a considerable impact on the pricing of medicines, as this also indirectly sets a framework for price negotiations.