Market Access Policy
EU HTA - Looking Back to Better See Ahead

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On 1 February 2018, European Union (EU) member states received a draft regulation from the European Commission setting out the creation of a single, mandatory system for clinical health technology assessments. The intention is for this system to be introduced beginning March 2019 with provisions allowing for a three-year transition period. The draft regulation includes a request for adoption within eight weeks, by 3 April 2018.[1] The primary objective of this draft regulation is to allow expedited patient access to new, essential medicines. While the clinical benefit will be assessed centrally and member states are required to adopt decisions, health economic assessments and pricing and reimbursement decisions will remain within the individual member states. The scope of the draft regulation may be far more reaching than many health technology assessment (HTA) stakeholders anticipated, or indeed, would support.

There should be little surprise considering the activities of the past five to seven years. Before the release of the 1 February regulation, the European Commission announced the 2011 decision on the application of patients' rights in cross-border health care[2]; the 2013 decision on establishing a transparent network of national authorities and bodies in health technology assessment[3]; and several multiannual work programmes on HTA collaboration, such as 2014-2015 and 2016-2020,[4] all of which indicated a move towards a single centralised system.

Historically, member states, and in particular Germany, have justified specific and distinct approaches to value and benefit assessment of new treatments in the form of an HTA as necessary to align with their health system values, health service organisation, and standards of care.[5]

Following the first whispers from the European Commission of the possible introduction of an EU-wide HTA collaboration and assessment in 2011, the topic of health became increasingly relevant to individual EU members states, particularly with respect to general elections.[6-8] As a result, over the last 12 months many EU member states introduced considerable changes to their HTA and pricing and reimbursement systems in response to demands from the electorate in their country.

However, apart from the electorate, national HTA changes need to take into account the greater EU HTA on clinical efficacy benefit to make a concerted effort worthwhile. Policy changes in 2017 and 2018 across all member states should focus on preparing for 1 March 2019 and align national processes to the EU HTA initiative. March 2019 will be here faster than we think, so a key question is how well adjusted are these latest rounds of national HTA changes with the 1 February draft regulation on EU HTA?

To help answer this question, we have looked at selected HTA changes implemented in 2017 in several EU member states and assessed the level of alignment to the broad framework set out in the 1 February draft regulation on EU HTA.

Based on the 1 February draft regulation, the European Commission envisage a single EU system for clinical HTAs, with mandatory cooperation between member states on clinical HTA assessments after 2019. The mandatory

Alignment with 1 February Draft Regulation on EU HTA

● = Good alignment ● = Unclear alignment or further adjustments will likely be needed ● = Poor alignment

France

Key Developments in 2017		Implication on National Price and Reimbursement	Alignment
SMR and ASMR Reassessments	• Some SMR and ASMR ratings were reassessed based on real-world evidence (RWE) data • All the reassessments resulted in a downgrading of the product's rating compared with the product's initial rating • Changes in initial price, as a result of the lower ratings, will follow in 2018	• Trend to proactively manage health care resources based on actual value in real-world (i.e., non-clinical trial) setting	
Updates in HTA Pathways	• Introduction of joint commissioning between TC/ CNEDiMTS/CEESP to evaluate clinical and economic criteria simultaneously	• Pathway becoming more health economics driven • Most important use is expected for joined assessments of economic and clinical value by TC and CEESP	
New Regulations on Interchangeability of Biosimilars	• Interchangeability between biologics and biosimilars at any time in the pathway • ARS have been asked by the Ministry of Health to encourage biosimilars use	• Likely to lead to a shift in the price-focused commercial strategy of current biologics	
New Additional Criteria for CEPS Price Referencing	• External price referencing to be applied regardless of ASMR • Use of net purchase price of competitor products • Use of net treatment cost if concomitant or sequential use with other drugs	• Increase pressure in price negotiations • End of patent and/or first generic entrant can lead to renegotiation of price	
Introduction of Chronic Patient Experience as Part of Drug Evaluation	• Patient participation and experiences will now form part of the clinical evaluation for HAS decision-making • Currently, patient involvement processes are in trial period, but a formalised process is expected	• Influence of patient perspective to increase in the future	

ARS=Regional Health Agencies (Agence Regionald e Sante)
ASMR=Improvement of Medical Benefit (Amélioration du Service Médical Rendu)
CEESP=Commission Evaluation Economique et de Santé Publique
CEPS=Economic Committee of Health Products (Comité Economique des Produits de Santé)
CNEDiMTS=Commission Nationale d'Evaluation des Dispositifs Médicaux et des Technologies de Santé
HAS=National Authority for Health (Haute Autorité de Santé)
SMR=Medical Benefit (Service Medical Rendu)
TC=Transparency Committee (Commission de la Transparence)

Germany

Key Developments in 2017		Implication on National Price and Reimbursement	Alignment
Changes Influencing Price Negotiations	• Price moratorium was extended to 2022 for drugs not subject to a fixed price reference group • Flexibility has been introduced to price negotiations when the comparator is a very low-cost treatment • Reference price groups can no longer only include branded drugs	• Price pressure increased through increased scope for manufacturers to negotiate the most appropriate price comparator within the indication • Pharmacy profit margins will be impacted with loss of hospital contracts	🟢
Process Changes	• Manufacturers can start AMNOG re-evaluation after one year (as opposed to 15 months under prior regulation) • Drugs launched before 2011 and still under patent protection can be assessed under AMNOG, if manufacturer applies for new indication	• Opportunity for faster re-evaluation if new evidence is anticipated or becomes available to achieve a more a positive outcome	🔴
Selected Method Changes (per the updated IQWiG methods paper – version 5)[9]	• Subgroup analyses are now only considered if at least 10 events occurred in the subgroup and the significance level has been lowered to α=0.05 • New Methods paper provides guidance on evidence generation, information searches, and expectations to supply RCT data for high risk therapy methods and devices • Evidence transfer between populations and subgroups needed to better accommodate lesser explored patient groups (e.g., children)	• Adjustment to subgroup analyses will be relevant for trials in smaller populations (e.g., orphan drugs) • IQWiG will no longer conduct a benefit assessment for small groups where the manufacturer previously could have reached a positive benefit outcome	🔴

IQWiG=Institute for Quality and Efficiency in Health Care

Italy

Key Developments in 2017		Implication on National Price and Reimbursement	Alignment
Changes to Drug Expenditure Governance Rules Under 2017 Finance Act	• Reduction of industry payback obligations for budget overruns • Innovative drug sales exempt from payback obligations • Dedicated funding of €1 billion a year for drugs designated as innovative; funding split equally between oncology and non-oncology	• These measures represent early moves towards reform of the pharmaceutical governance system, notably the payback burden currently shouldered by industry • Regions have new responsibility to fund drugs when spending exceeds the innovation budget	🟢
AIFA's New Criteria for Innovative Drugs	• Innovative medicines are identified based on unmet need, added benefit and strength of evidence. • Assessments will consider the quality of evidence, therapeutic need, and additional therapeutic value • Final ratings will consider:	• Innovative drug status provides commercial and access advantages, including mandatory listing across regions and reimbursement from dedicated innovation budgets • It is critical to demonstrate innovation along the defined criteria in order to receive these advantages! • Special provisions exist for orphan/ rare treatments where unmet need is high, but evidence is limited • Limited transparency around decision making remains a challenge – to date, no assessments have been made public and decision drivers in individual assessments are not well defined	🔴

Therapeutic Need	Added Therapeutic Value	Quality of Evidence		Outcome Rating	Impact
Major/ Important	Major/ Important	High	=	Innovative	• Automatic listing in regional formularies • Reimbursed through innovation fund • Exemption from payback liabilities • Valid for 3 years
Intermediate situations will be evaluated on a case by case basis considering the relative weight of the individual factors considered			=	Potentially Innovative	• Automatic listing in regional formularies • Valid for 1.5 years
Low/None	Low/None	Low/ Very Low	=	Not Innovative	• Reimbursed at or below price of existing treatments or not reimbursed (class C)

AIFA=L'Agenzia Italiana del Farmaco (The Italian Medicines Agency)
Sources: Legge di Bilancio 2017 (Finance Act 2017), Gazzetta Ufficiale 21/12/2016; Determina AIFA 1535/2017 Criteri per la classificazione dei farmaci innovativi e dei farmaci oncologici innovativi (18/09/2017)

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England

Key Developments in 2017		Implications on National Price and Reimbursement	Alignment
Fast Track NICE Technology Appraisal Process for Promising Technologies Falling Below £10,000 per QALY	**Conditions for Fast Track Assessment (FTA)** • Company's base-case ICER is less than £10,000 per QALY gained • Most plausible ICER likely to be less than £20,000 per QALY gained; highly unlikely to be greater than £30,000 per QALY gained • NICE is satisfied the proposed place in therapy is appropriate • Sufficient information exists to make recommendations through an FTA • Uncertainties in the evidence and consequences of decision error are manageable	• For new drugs that are highly likely to be cost-effective, a fast track appraisal will result in a NICE recommendation within 32 weeks of submission, compared with the standard 43 weeks • This is intended to drive rapid reimbursement and uptake of highly cost-effective innovative technologies	🔴
Budget Impact Threshold of £20 Million Per Annum Will Result in Commercial Agreement With NHS England	• NHS is committed to providing the 'most effective, fair, and sustainable use of finite resources' • Increased focus on the management of the introduction of cost-effective therapies that have a significant impact on the NHS budget • NICE and NHS England have introduced a 'budget impact test' to assess the level of the affordability challenge that new drugs present • NHS England will review the policy in 2020 to determine impact on access and uptake for new drugs and any potential policy adjustments	• For drugs with a predicted net budget impact of ≥£20m per year, in any of the first three years of use, a commercial discussion will be triggered with NHS England (with a risk of delayed access without an agreement) • Discussion will include ways to introduce the product that is acceptable to both the company and NHS England; may involve pricing or model options for how to pay for the product • If agreement is not reached, NHS England can apply to NICE to allow phased introduction of the product over period longer than the standard 90 days	🔴
NHS England Will Automatically Fund Highly Specialized Technologies (HST) Up to £100,000 per QALY	• HSTs with ICER above £100,000 per QALY can also be considered for funding • Funding from routine NHS commissioning will be made available to medicines for very rare ultra-orphan diseases (assessed by the NICE HST programme) with an ICER up to £100,000/QALY	• For HSTs, large QALY gains are common. This suggests the proposed weights may be a regular consideration for appraisals • Estimating the lifetime QALY gain requires extrapolation from sparse data. This is more likely to rely on mortality rather than morbidity, **implying that patients must be young enough to accrue sufficient QALYs**	🔴
Establishment of 4 Regional Medicines Optimisation Committees (RMOCs) in England	• The 4 RMOCs (London, South, North, Midlands/East of England) will operate as a single, strategic medicines optimization system for England • Participants will include decision makers, clinicians, patients and public representatives • RMOC recommendations are advisory and do not affect statutory legal responsibilities and duties of the NHS	• RMOCs will coordinate evaluations and make recommendations to guide the adoption of new medicines that are not scheduled for review by NICE	🔴

ICER=Incremental Cost-Effectiveness Ratio
NHS=National Health Service
NICE=National Institute for Health and Care Excellence
QALY=Quality-Adjusted Life Year
RMCO=Regional Medicines Optimisation Committees

Sources:
https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/process-guide-addendum-fast-track.pdf
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joint assessment will be limited to examining the clinical evidence and the comparative efficacy with the final recommendations binding on all member states. There would be no option to re-evaluate these assessments at the national level. Pricing and reimbursement (P&R) decisions, based on these joint assessments, would remain the responsibility of national-level governments as would the assessment of health economic evidence. At the same time, member states have been introducing changes and innovations to their HTA and P&R systems, some of which appear to go against this EU strategy.

This raises the question of the level of policy preparedness and alignment that exists for both the EU members and the EU Commission. Therefore, to allow the transformation of this draft regulation to become a policy decision providing the greatest benefit to the patient, fundamental questions still need to be addressed, including:

- Will an EU HTA assessment of clinical benefit reduce payer uncertainty in member states with respect to P&R decision making when measured by national standards of evidence needs for P&R?
- How will real-world evidence feature in EU HTA assessments or at the national member states level or the local level? This is particularly important as many high technology treatments may not be able to develop all the data required for comparative efficacy assessments.
- How many adjustments will be required for the national health economic assessments?
- How are patients intended to contribute to the EU HTA clinical benefit assessments?
- How will differences in standard-of-care and patient pathways across member states be considered in comparative efficacy assessments?
- How do price building processes within the member states need to be adjusted if comparative efficacy may not allow for value ratings and clinical benefit re-assessments are not allowed at individual member state level?

Hence, policy discussions must take place across all member states and the European Commission as soon as possible to address these key questions to ensure that the intended patient benefit is appropriately introduced. ■

For more information, please contact info@evidera.com.

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