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European Federation of Pharmaceutical Industries and Associations

IMPROVING ACCESS TO DIGITAL THERAPEUTICS IN EUROPE

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SUMMARY

Digital therapeutics (DTx) deliver evidence-based therapeutic interventions to patients that are driven by software programmes to prevent, manage, alleviate or treat a medical disorder or disease. They are used to optimize patient care and health outcomes. Given the rising importance of DTx for patients, health systems, and the industry, as well as the challenges they face with existing access pathways, the pharmaceutical industry considers it timely to set out how DTx should be defined, their benefits, the barriers to their use, and associated policy areas needing attention.

Currently, the use of DTx in Europe is limited, with progress in integrating DTx into access and care pathways only in a small number of countries. As a result, DTx face unpredictable requirements or standards for much of the development and commercialisation pathway, including authorisation, value assessment, reimbursement, and pricing. Specifically, there are four key challenges:

- Although DTx are governed by EU Medical Device Regulations, there is a lack of harmonization in regulatory requirements due to differences in interpretation
- There are challenges in the harmonisation of evidence requirements and lack of value assessment processes
- There is no standardised or specific reimbursement pathway for DTx in most countries
- There is inadequate funding, and DTx reimbursement pathways do not ensure uptake

While EFPIA welcomes the initiatives already made in promoting access to DTx in some countries, there is a clear opportunity for both policy change within the individual Member States and for harmonisation across the EU. To that end, EFPIA recommends the following actions to be considered at the national and European level to improve access to DTx:

- Harmonized regulatory requirements with clear guidance are required to ensure streamlined access
- Value assessment requirements need to be tailored and fit-for-purpose for DTx and more predictable and consistent, and involve a portfolio of evidence that can include real-world evidence
- Member States and the European Commission should consider supporting collaboration between countries to enable harmonisation of clinical evidence requirements
- European Commission and Member State collaboration will be needed to support data sharing and build infrastructure to realise the potential of data generated by DTx
- Member States should create clear and transparent national pathways for DTx pricing and reimbursement
- Payers should permit flexible approaches allowing provisional access while additional data is generated
- Payers should be willing to implement novel payment models to manage evidence uncertainties
- To ensure that DTx are adequately funded, funding needs to be explicit and budgeted, and should not have a financial burden on patients
- Increasing DTx uptake will require collaborative efforts between policymakers, HCPs, and companies. To develop trust in DTx, stakeholders must be prepared to work together to enhance the education and experience of HCPs and patients.

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INTRODUCTION

Interest in the potential for digital therapeutics (DTx) to transform the treatment of patients has intensified over the last few years, particularly in the wake of the COVID-19 pandemic and as the potential of digital health tools has increased due to advances in artificial intelligence and related technologies. Although overall health digitalisation remains low, many healthcare systems have shown increased interest in the digitalisation of health processes, organisations, and delivery, and have incorporated digital health into pandemic and recovery policy.

Given the rising importance of DTx for patients, health systems, and the industry, as well as the challenges posed by existing access pathways for these products, the pharmaceutical industry considers it timely to set out how DTx should be defined, the benefits they offer, the barriers to their use, and associated policy areas needing attention.

A DEFINITION OF DIGITAL THERAPEUTICS

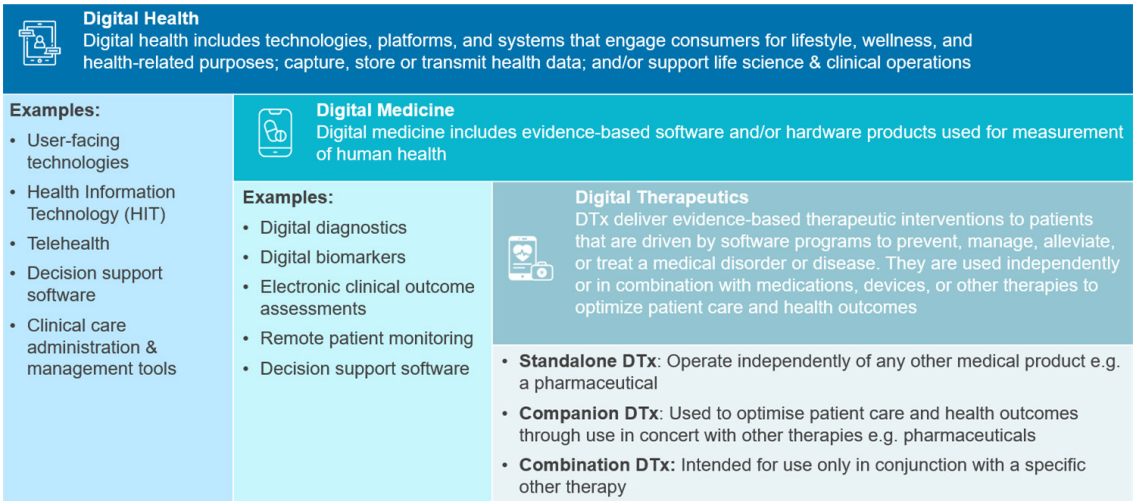
DTx are a subset of the broad area of digital health. Digital health includes health apps, telehealth and telemedicine, and a wide range of health information technologies used by healthcare systems and providers. Digital medicines are a subset of digital health, and DTx are in turn a subset of digital medicine.* DTx deliver evidence-based therapeutic interventions to patients that are driven by software programmes to prevent, manage, alleviate, or treat a medical disorder or disease. They can be used independently or in combination with medications, devices, or other therapies to optimise patient care and health outcomes, and their aim to is achieve positive clinical outcomes and / or deliver patient-relevant improvements in the process and structure of healthcare systems. Under this definition, DTx are classified as medical devices according to the Medical Device Regulation 2017/745. The definition of DTx includes interventions which have an associated hardware component, as long as the software is the driving component of the therapeutic effect.[1] The distinction between DTx and digital health is illustrated in Figure 1.

There are three main types of DTx: standalone DTx, which operate independently of any other medical product such as a pharmaceutical; companion DTx (disease-specific), which are used in concert with medications, devices, or other therapies to optimise patient care and health outcomes, with a single DTx having potential applications as a companion to different therapies; and combination DTx (product-specific), which comprise software and one or more other components (drug-software, device-software, drug-device-software) intended for use only in conjunction with each other.[2†] DTx encompass a wide range of therapeutic areas and are based on several digital health tools, including apps, web-based interventions, videogames, and virtual reality, including where these digital tools interact with hardware components such as wearable measurement devices.[3]

* Digital health includes technologies, platforms, and systems that engage consumers for lifestyle, wellness, and health-related purposes; capture, store or transmit health data; and/or support life science & clinical operations. Digital medicine includes evidence-based software and/or hardware products used for monitoring/measurement of human health

† This is in line with EU MDR in delineating drug-device combinations "placed on the market in such a way that they form a single integral product which is intended exclusively for use in the given combination"

FIGURE 1: Definition and types of digital therapeutics



Source: CRA drawing on Deloitte report on Digital Therapeutics (2021)

BENEFICIARIES OF DTx INCLUDE PATIENTS, CLINICIANS, AND HEALTHCARE SYSTEMS

DTx deliver benefits to patients, clinicians, healthcare systems, payers, regulators, and other bodies that govern patient access to innovative therapies.

The most direct beneficiaries of DTx are patients themselves. DTx can empower patients by improving their experience and outcomes, the coordination of their care, and their engagement with healthcare providers.[5] Furthermore, DTx can mitigate treatment side effects. The potential applications of DTx have already become very broad. Many focus on delivering behavioural changes through cognitive behavioural therapy (CBT). For example, there are DTx used to treat patients with depression and depressive moods by delivering CBT,[6] and apps aimed at treating insomnia that are effective for patients as an alternative to sleeping pills.[7] Other examples demonstrate the varied uses of DTx such as in the self-management of diabetes;[8] digital interventions for cancer patients found to increase overall survival;[9] and those supporting remote rehabilitative care following hip and knee and weight-loss surgery.[10] Many DTx allow patients to be treated at home and to be more directly in control of their care, which can increase patient engagement and participation. For example, an interactive app enabling self-management for cancer patients was found to promote patient participation in their care.[11] There is also potential for more holistic patient management with tailored approaches based on the individual patient's needs.

The potential benefits of DTx extend beyond patients to include stakeholders throughout the healthcare system. For clinicians, DTx offer alternative or improved therapeutic options, improving overall monitoring of treatment and information on care and patient response. DTx often enable data sharing between patients and healthcare professionals (HCPs). For example, there are tools for managing epilepsy which collect data that can be shared directly with clinicians.[12] In particular, DTx can provide continuous exchange of information with clinicians, compared to the fragmentary level of information gathered during personal interactions between patients and HCPs.

For healthcare systems, DTx could be used to target unmet needs or underserved areas in healthcare by leveraging the unique characteristics and benefits they can deliver to patients. For example, DTx may be launched in indications with limited or inadequate treatment options, thereby addressing the unmet need and alleviating healthcare system pressures. One digital therapeutic used in lung cancer patients decreased the use of imagining procedures by 49% per patient per year compared to the standard of care,[13] and was found to be cost-effective in reducing follow-up costs compared to conventional monitoring.[14] DTx have significant potential to reduce the overall burden on healthcare systems, such as by preventing hospital visits by improving self-management or providing therapy remotely. For example, a DTx that delivers neurobehavioral therapy for opioid use disorder

was found to be associated with fewer inpatient, emergency department, and other clinical encounters, increased case management/rehabilitative services, and lower net costs over six months.[15] Healthcare systems would similarly benefit from DTx valuable for prevention, potentially addressing public health needs. For example, there are diabetes-focused DTx that help patients modify behaviours and eating habits through CBT.[16] There may also be a potential to integrate the data generated into healthcare systems more broadly, improving patient care and allocation of resources at the macro-level. DTx enable data to be collected, processed, and analysed, and then tailored to an individual's medical needs. There is also a new opportunity for regulators and payers to integrate data into decision-making, such as the collection of real-world evidence (RWE), to support the implementation of value-based healthcare.

THE USE OF DTx TODAY

Despite the extent of their potential benefits, the use of DTx in Europe is still limited. In only a handful of Member States there has been progress in integrating DTx into market access and care pathways. These existing approaches are summarised in Table 1. Germany was the forerunner in terms of improving market access pathways for DTx in its implementation of the Digital Healthcare Act (Digitale Versorgung Gesetz, DVG) in 2019.[17] The Act established a "Fast-Track" process for qualifying apps ("DiGA") that leads to inclusion in a central directory of digital health applications, for which reimbursement becomes available, although this is currently limited to standalone DTx with low to medium (MDR Class I and IIa) risk.[18] As of January 2023, 161 applications were submitted to the DiGA for review – 125 for provisional listing and 36 for final listing. Of these applications, the BfArM has made 40 positive decisions for either provisional or final listing.[19]

TABLE 1: Existing approaches to DTx market access in selected markets*

Country	National value assessment framework	National reimbursement pathway	Available funding mechanisms
 Belgium	✓ DTx clinical and/or socioeconomic value evaluated through Validation Pyramid	✓ Apps in Level M3 of Validation Pyramid reimbursed by payers	✓ Centralised funding for mHealth apps
 Germany	✓ DiGA process: Standalone DTx evaluated by BfArM	✓ DiGA process: All listed DiGA are reimbursed	✓ GKV-SV centralised funding for DiGA
 France†	×	✓ Apps in Level M3 of Validation Pyramid reimbursed by payers	✓ Centralised funding for mHealth apps
 Italy	×	×	×
 Netherlands	×	×	✓ Covered by individual health insurers

*In order to develop this white paper a landscape assessment of policies around digital therapeutics was conducted for these 8 European markets

†In addition to the existing medical device pathway, France is introducing a pathway for fast access for reimbursement of telemonitoring activities and digital medical devices with therapeutic aim. As of January 2023, implementation decrees are still to be published.

 Spain	×	×	✓ Evidence of limited regional reimbursement
 Sweden	×	×	×
 UK	✓ NICE has developed evidence standards framework for digital health technologies	×	✓ Can be funded locally by Integrated Care Systems

Belgium provides a second notable case where a distinct access pathway for DTx has been implemented. The mHealthBelgium platform collects all apps that have received a CE mark as medical devices and assesses them through the "validation pyramid" into three levels.[20] Only mHealth apps that show "social-economic evidence" and reach Level 3 of the pyramid can be reimbursed. However, progress in utilising the pyramid to improve access for patients has been very gradual: although the pyramid was created in 2018 and Level 3 rolled out in 2021, only one app has reached Level 3, which is currently only categorised as Level 3 light, providing temporary reimbursement (as of January 2023).[21]

The other notable example is the United Kingdom. In England, there has been progress in establishing a value assessment framework for DTx, although wider access pathways are less developed than in Germany or Belgium. Specifically, DTx are classified by the National Institute for Health and Care Excellence (NICE) based on their functions and then stratified into evidence tiers based on the potential risk to the user.[22] The shortcoming of the UK's current progress is that there is no funding mandate for digital health technologies that are recommended by NICE, in contrast to pharmaceuticals,[23] although NICE are making conditional recommendations for digital cognitive behaviour therapies as part of an Early Value Assessment pilot.

For the other countries assessed in the development of this paper (Table 1), there is a lack of specific national pathways or frameworks for DTx. However, in some countries access has been possible under existing frameworks, especially through the medical devices route. In France, for example, the common pathways for medical devices also enable DTx evaluation and pricing, with specific guidelines and requirements that have been published,[24] and in the Netherlands, there has been reimbursement of health apps by individual health insurance companies.[25] In 2022 France introduced additional pathways on top of the already existing medical devices route, specifically, a standard pathway for telemonitoring activities (non-DTx) and a fast access for temporary reimbursement of telemonitoring activities and digital medical devices with a therapeutic aim, which includes DTx.[26]

BARRIERS TO DTx ACROSS THE MARKET ACCESS PATHWAY

Several barriers are hindering the adoption of DTx, and there are no specific market access pathways for these technologies in most markets. As a result, DTx face the challenge of unpredictable requirements or standards for much of the development and commercialisation pathway, including authorisation, value assessment, reimbursement, and pricing.[28] Specifically, there are four major challenges impeding access to digital therapeutics:

- **LACK OF HARMONIZATION IN REGULATORY REQUIREMENTS ACROSS EU MEMBER STATES DUE TO DIFFERENCES IN INTERPRETATION.** DTx are subject to the European Regulation on Medical Devices 2017/745 (MDR) and are regulated by National Competent Authorities. Although the CE mark by a notified body is recognised across Europe, interpretation of the dossier requirements can vary between Member States as DTx products are novel and innovative, and expertise is still building.
- **CHALLENGES IN EVIDENCE REQUIREMENTS AND LACK OF PROCESSES FOR DTx VALUE ASSESSMENT.** Due to lack of specific frameworks, it is unclear what evidence DTx requires for positive value assessments. There is a concern that payers will expect all DTx to be supported with evidence from randomised controlled trials (RCTs), which are not always the best approach for DTx evidence generation. This also exacerbates the problem that evidence requirements are not harmonised between countries, leading to difficulties for companies to develop their clinical plans.
- **THERE IS NO STANDARDISED REIMBURSEMENT PATHWAY FOR DTx IN MOST COUNTRIES.** This means that DTx may not be reimbursed, be subject to long delays, or be reimbursed by individual providers, resulting in uncertainty over requirements for reimbursement.
- **DTx DO NOT RECEIVE ADEQUATE FUNDING, AND DISTINCT REIMBURSEMENT PATHWAYS DO NOT GUARANTEE DTx UPTAKE IN PRACTICE.** Few countries provide funding so that DTx can be made available to patients. However, even with adequate funding, there are further uptake challenges due to a lack of readiness from physicians and patients to use them. For example, patients and HCPs are insufficiently educated in the potential of digital technologies. Given that they are a new approach to treatment, HCPs and patients will need more education and experience to better understand the potential of DTx and to secure trust in their value and quality.

Several of the key barriers are not unique to DTx and reflect current or previous challenges in other areas of healthcare such as medicines and medical devices. Progress in those areas in clarifying requirements and improving harmonisation is much more developed than for DTx, and so it is crucial that this progress is learnt from.

LACK OF HARMONIZATION IN REGULATORY REQUIREMENTS ACROSS EU MEMBER STATES DUE TO DIFFERENCES IN INTERPRETATION

Given the definition of DTx set out above, DTx will be considered medical devices and consequently are governed by the European Regulation on Medical Devices 2017/745 (MDR). DTx are considered Medical Device Software. For DTx to be evaluated or reimbursed by national payers, a conformity assessment is conducted, and a CE Mark is granted by a designated regulatory authorized Notified Body.‡ As with all software, medical device software has fast cycles of innovation and development that can result in many version upgrades to the software in quick secession. Medical device legal frameworks and related authorities were not necessarily developed with novel and swift-moving software changes in mind. Improvements to the existing regulatory pathway that would allow a flexible risk-based approach to regulation would foster innovation and minimize risks to patients by not inhibiting the pace of changes while maintaining high safety, efficacy and quality standards.

The EU MDR came into force in 2021, replacing the existing Medical Devices Directive and Active Implantable Medical Devices Directive. As per the European Commission's Medical Device Coordination Group (MDCG), Medical Device Software (MDSW) is categorised into four classes based on inherent risks associated with the intended use – Class I (low risk), Class IIa (medium risk), Class IIb (medium/high risk) and Class III (high risk).[29] At the moment, as there are few DTx products that have undergone a conformity assessment, there is little regulatory precedent in determining the appropriate risk classification. It is anticipated that as regulatory agencies and DTx developers continue to learn and gain experience on the risk posed to patients, more precedent will be established. As a general matter, DTx products are highly innovative and novel in nature, and so it will be essential that notified bodies continue to prioritize obtaining the necessary expertise and knowledge to be able to effectively evaluate these products. There is concern that a lack of capacity within the notified bodies will negatively impact the scientific advice and review processes.

In addition to the MDR, as DTx products are medical devices, they must also comply with data protection requirements, as they relate to the General Data Protection Regulation (EU GDPR). However, in addition to EU GDPR, several Member States have additional regulatory requirements related to security and privacy. For example, Germany has implemented data protection laws that go beyond GDPR requirements, and the UK's National Health Service (NHS) launched its Digital Technology Assessment Criteria (DTAC) including criteria around safety, data protection, technical assurance, interoperability, and usability.[30,31] A lack of harmonization across Member States in these areas poses an additional challenge for DTx developers.

CHALLENGES IN EVIDENCE REQUIREMENTS AND LACK OF VALUE ASSESSMENT PROCESSES FOR DTx

DTx need to deliver health benefits and value for money.[32,33] This is the primary rationale for health technology assessment (HTA) of pharmaceuticals, which are used to inform decision-making, particularly on reimbursement, as to the value of new health technologies. However, a key challenge for DTx is that there is no standardised framework for value assessment, meaning that the evidence requirements a developer needs are uncertain and are likely to vary between markets.

This is particularly problematic for DTx due to the different types of evidence that are expected to be relevant in demonstrating their value. While randomised controlled trials have already been used for DTx, real-world evidence (RWE) is expected to play a role in the evaluation of DTx.[34] This is because RCTs may not always be the most appropriate approach for evidence generation given that DTx require new methods that allow continuous assessment of effectiveness in real-world settings, especially as software updates result in regular changes to the technology.[35] DTx also have unique capabilities for measuring patient-level data to support this. A related issue is that current HTA frameworks assess products within specific indications with a separate evidence package and trials per indication. Many DTx, by contrast, take a more patient-holistic approach, such as by supporting patients with several conditions. A

‡ Combination DTx will go through the EMA regulatory pathway for pharmaceuticals, but the DTx component will still require a CE mark.

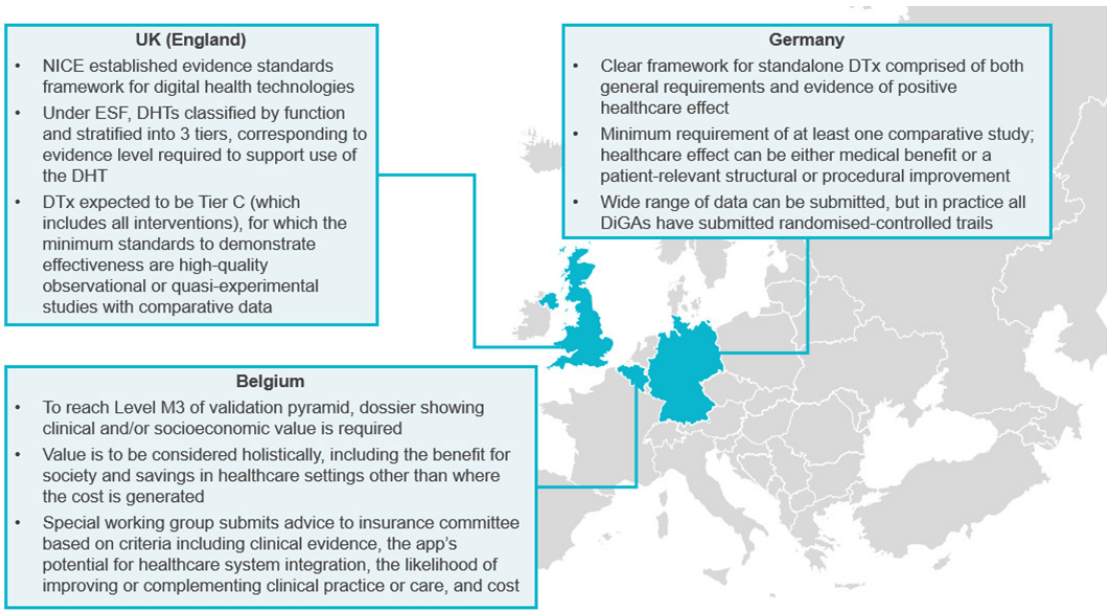
switch from indication-based HTA to a more patient-holistic approach to value assessment (including acceptance of evidence supporting a patient-holistic view) is equally important.

The lack of a value assessment process for DTx is likely to delay their uptake. Firstly, developing value assessment practices is necessary for payers to be willing to reimburse DTx. In addition, value assessment can contribute to building HCP trust in DTx. Currently, only Belgium, Germany, and England have developed a value assessment process for DTx, which are summarised in Figure 2.[§] To date, these value assessment processes have been commissioned and conducted at the national level, and the requirements for clinical evidence that DTx developers need to submit for value assessment vary between the Member States. So far, national evaluations have been based on clinical trials in a given country without mutual recognition of evidence between countries. For example, in Germany, the BfArM require local clinical studies (or transferability to the German healthcare situation if conducted outside Germany).[36] The industry has therefore faced the difficulty of designing studies and the increasing cost of developing local evidence. There have also been challenges around national capacity for DTx value assessment: despite the growing number of DTx that have been approved, only a small number have been successfully assessed as eligible for reimbursement.

Impact of EU HTA regulation on DTx

In the long term, the value assessment of DTx will be impacted by the implementation of EU HTA for medical devices. In January 2022, the EU's Health Technology Assessment Regulation (2021/2282) entered into force and will apply from January 2025.[38] Starting in 2025, Joint Clinical Assessment (JCA) will include oncology therapies, advanced therapy medicinal products (ATMPs), and selected medical devices, with the scope of products to be expanded thereafter.[39] The use of EU HTA for DTx will depend on three factors: their type, that is, whether they are a standalone, companion, or combination product; their medical device risk class; and whether they are selected for JCA, if eligible.** These factors are summarised in Figure 3. The number of DTx that undergo JCA is expected to be limited.

FIGURE 2: European countries with value assessment frameworks for DTx[37]



[§] As noted above, France is implementing an early access reimbursement programme that includes DMTs with a therapeutic purpose, which will require CNEDiMTS to consider the DMT innovative, however implementation decrees are yet to be published (as of January 2023)

** The criteria for selection as one or more of: unmet medical needs; first in class; potential impact on patients, public health or healthcare systems; incorporation of software using artificial intelligence, machine learning technologies or algorithms; significant cross-border dimension; major Union-wide added value

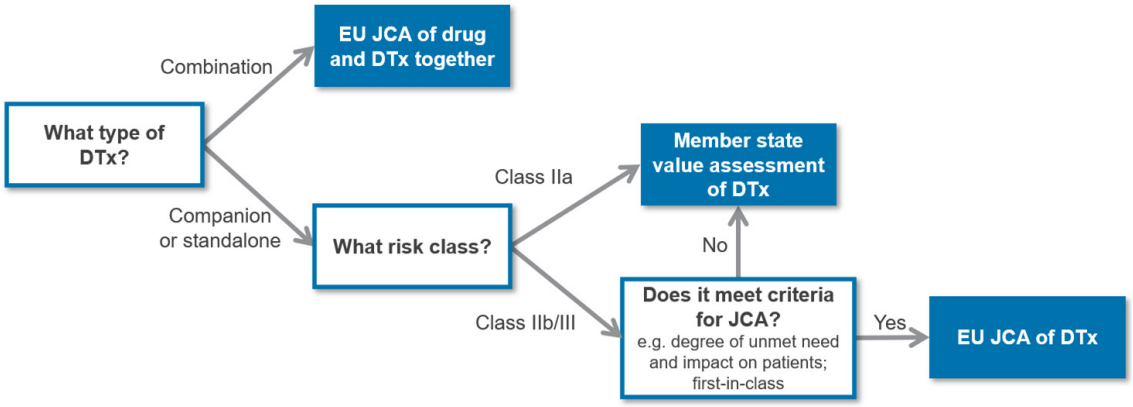
THERE IS NO STANDARDISED REIMBURSEMENT PATHWAY FOR DTx IN MOST COUNTRIES

Given their clinical benefits and the potential to apply methodical value assessment processes to them, DTx, which have been positively evaluated, should be reimbursed by health systems. However, the requirements for reimbursement are unclear in most countries, and there is no standardised access pathway. As a result, the time taken for reimbursement decisions is too long. In some countries, this means that there is unlikely to be any reimbursement of DTx, while in others, individual providers have been willing to reimburse DTx – such as in the Netherlands – but resulting in uncertainty over the requirements due to this decentralised approach.

Therefore, a key challenge for DTx is ensuring that there is a mechanism to enable their reimbursement. Removing barriers to reimbursement is a key step to ensuring the widespread adoption of DTx, and recent activity in some Member States demonstrates that progress is being made in this direction. For example, in September 2020, Germany announced that it would allow the reimbursement of prescription digital health applications (Digitale Gesundheitsanwendungen, DiGA). Germany's DiGA process provides a clear pricing and reimbursement pathway for standalone DTx, which has been essential in enabling patient access to DTx. As noted above, reimbursement pathways also exist or are being implemented in Belgium and France.[40,41]

In addition to the overall pathway for the pricing and reimbursement of DTx, some Member States have included additional principles in their pricing and reimbursement frameworks. For example, the German and Belgian reimbursement processes allow for provisional access for DTx to finance additional evidence generation (although it is unclear whether payers will still expect confirmative randomized controlled trials, as is the case with pharmaceuticals). The Belgian validation pyramid has demonstrated this principle by splitting Level M3 of the pyramid into M3- ("M3 light") and M3+. M3- apps are able to receive provisional access during data collection.[42]

FIGURE 3: Determining eligibility and selection of DTx for EU Joint Clinical Assessment

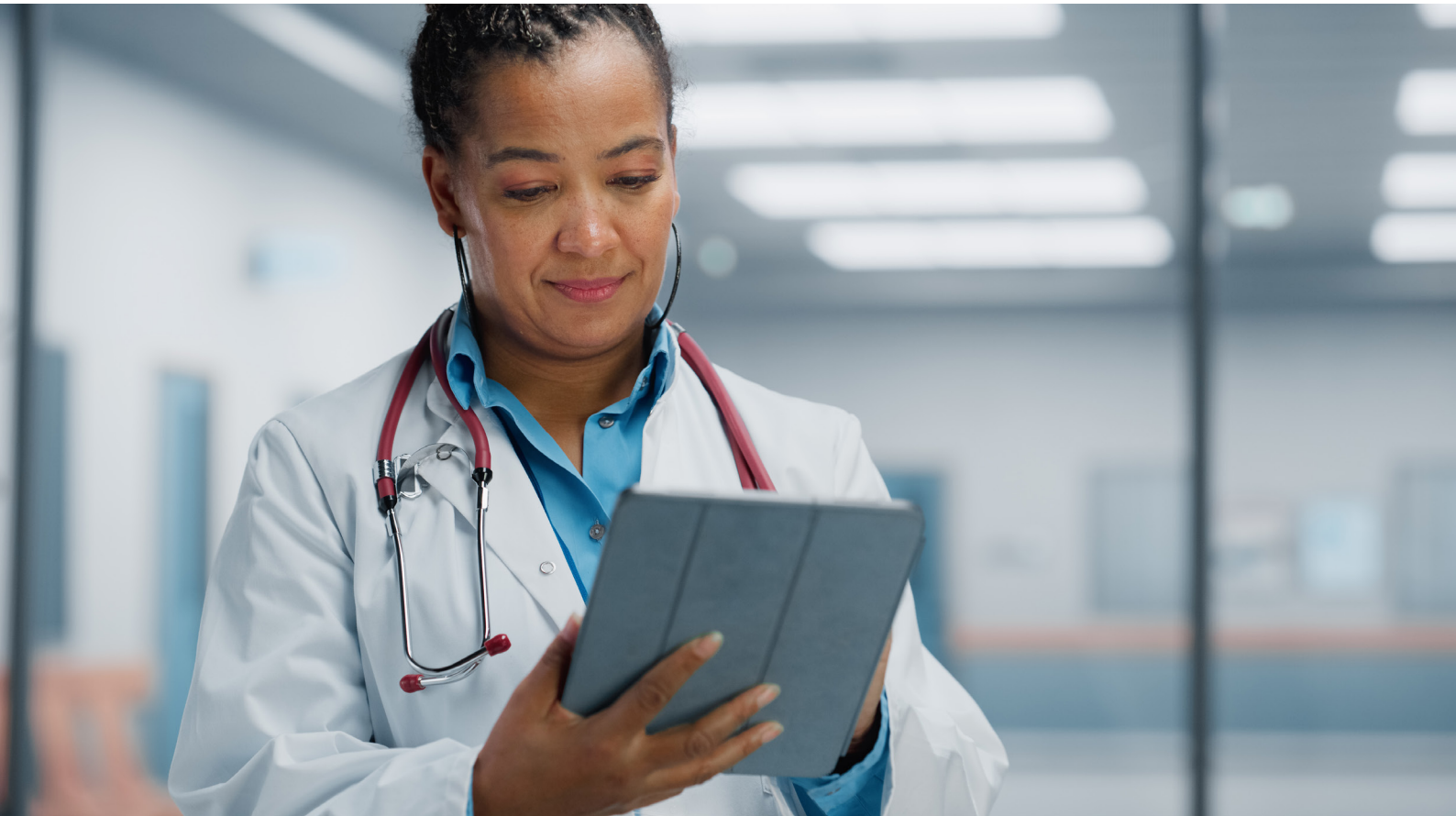


DTx DO NOT RECEIVE ADEQUATE FUNDING, AND DISTINCT REIMBURSEMENT PATHWAYS DO NOT GUARANTEE DTx UPTAKE IN PRACTICE

As with pricing and reimbursement, policy for the funding and uptake of DTx will be determined at the national level. In fact, there are already considerable differences in how DTx are funded between countries, reflecting differences in how health systems are structured. For example, in Germany DiGAs are prescribed at the expense of statutory health insurance (SHI) if listed in the DiGA directory, while in France, DTx will have to be listed on the LPPR list (medical device budget) or can receive experimental coverage for innovative products (Article 51[43] and Forfait Innovation[44]). In Belgium, DTx will be paid as part of the healthcare service from hospital budgets or budgets available from certain healthcare services (DRGs). Although these differences are to be expected, given variations in how healthcare budgets are organised between countries, there is nonetheless a common requirement to ensure that DTx are adequately funded. Currently, funding for DTx within the EU has been highlighted as a major challenge, with only a few countries making DTx available to patients. In fact, improving funding for DTx at the Member State level may simplify the market access pathways for new digital health products.

Even if DTx are adequately funded, their uptake is not guaranteed. This will depend on the readiness of HCPs to prescribe them, which may be an obstacle to their use, given low awareness and recognition of the potential value of DTx and a lack of attempts to educate physicians. Although the acceptance of DTx is improving, the current evidence suggests that HCPs are reluctant to prescribe DTx: a study from Germany found that within the first 12 months after DiGA's implementation, only 14% of eligible HCPs had prescribed at least one DiGA, which were heavily concentrated in three medical specialities. The education and training of physicians are likely to require collaborative initiatives involving policymakers, professional organisations, and the DTx developers themselves.

There are also challenges around healthcare infrastructure, which may delay the adoption of DTx and the realisation of their potential benefits. Although the utilisation of data generated is expected to be a benefit of broader access to DTx, many countries have underdeveloped basic digital health infrastructure, such as issues around the implementation of electronic health records. As such, there are difficulties around integrating DTx data into healthcare infrastructure so that their use can be scaled up rapidly and their potential benefits in terms of data generation can be capitalised on.[46]



POLICY RECOMMENDATIONS

Despite their potential benefits, most countries have taken limited action to address the significant challenges in existing access pathways. While EFPIA welcomes the initiatives already made in promoting access to DTx in some countries, there is a clear opportunity for policy change across the EU, both within the individual Member States and with regards to harmonisation across all Member States. To that end, EFPIA recommends the following actions to be considered at the national and European level to improve access to DTx:

HARMONIZED REGULATORY REQUIREMENTS WITH CLEAR GUIDANCE ARE REQUIRED TO ENSURE STREAMLINED ACCESS TO THE MARKET

EFPIA supports a high standard of safety, efficacy and quality for DTx products while providing patients with timely access. DTx are covered by EU regulation 2017/745 on medical devices and are considered medical device software. Improvements to the existing regulatory pathway that would allow a flexible risk-based approach to regulation would foster innovation and minimize risks to patients by not inhibiting the fast pace of software changes while maintaining high safety, efficacy and quality standards. In addition to the EU MDR, DTx must comply with relevant EU and national-level regulations, including GDPR and some Member State specific regulatory requirements related to security and privacy. Harmonization of regulatory requirements across the Member States would facilitate development and commercialisation for developers, leading to faster access for patients and HCPs. In fact, lack of harmonisation can increase uncertainty for DTx developers and their investors, which can reduce investment in European health start-ups and leave companies without the resources and financial power to bridge the "valley of death" between incubation and commercialisation. To avoid regulatory delays and uncertainties, there is a need for clarity over the level of clinical evidence that needs to be provided (depending on the risk class) to obtain the CE mark. Finally, EU stakeholders and Member States should develop capacity to ensure timely marketing approvals. This would ensure that patients are provided with timely access while maintaining high standards.

Given the need for further clarity on how to interpret and implement regulatory requirements for DTx, the Medical Device Coordination Group can play a role in clarifying the interpretation of regulatory requirements across the EU to standardise regulatory approval, potentially including guidelines related to interpretation of classification rules and evidence generation. Furthermore, with the emergence of EU legislation on artificial intelligence – which is often used by DTx – there is a need for alignment between these different regulations.

VALUE ASSESSMENT REQUIREMENTS NEED TO BE TAILORED AND FIT-FOR-PURPOSE FOR DTX AND MORE PREDICTABLE AND CONSISTENT, AND INVOLVE A PORTFOLIO OF EVIDENCE THAT CAN INCLUDE REAL-WORLD EVIDENCE

There is a need for a holistic, risk-category based approach to value assessment to increase the predictability, clarity, and consistency of evidence requirements across Member States. The value assessment of DTx should incorporate a broad portfolio of evidence that includes clinical data, consumer data, real-world evidence (RWE), and accessibility data, leveraging the particular capabilities of DTx to generate patient-reported outcomes data.

These requirements should be clearly defined and transparent. The NICE Evidence Standards Framework provide one benchmark. In particular, there is the potential for RWE to have a significant role in DTx value assessment, given the data generated through the use of DTx. RWE should be accepted to support access but should not

be required for positive outcomes. Furthermore, a switch from indication-based HTA to a more patient-holistic approach to value assessment is important, given that existing processes conduct evaluations only within specific indications. This is because indication-by-indication assessment does not support a patient-centric approach enabled by DTx whereby patients may be treated with a unique mix of modules depending on the individual's indications and comorbidities. Finally, as DTx have significant capabilities to collect patient reported outcome measures (PROMs), the acceptance of PROMs in value assessment is also important.

MEMBER STATES AND THE EUROPEAN COMMISSION SHOULD CONSIDER SUPPORTING COLLABORATION BETWEEN COUNTRIES TO ENABLE HARMONISATION OF EVIDENCE REQUIREMENTS

The European Commission should facilitate mutual recognition of evidence and collaboration between countries to enable consistent and timely value assessment of DTx. Member States should explore mutual recognition of clinical evidence by establishing a minimum set of requirements that are common across the Member States. Furthermore, the Commission could support collaboration between Member States by facilitating knowledge sharing and supporting the exchange of best practices and clinical evidence recognised by national / sub-national HTA bodies and payers between the Member States. A positive first step towards evidence harmonisation has been the establishment of the European Taskforce for Harmonised Evaluation of Digital Medical Devices, coordinated by EIT Health and co-funded by the EU. The work of the taskforce focuses on three themes of harmonisation: taxonomy for different types of digital medical device (DMD); clinical requirements to assess DMDs; and socioeconomic evaluation of DMDs.[47]

EUROPEAN COMMISSION AND MEMBER STATE COLLABORATION WILL BE NEEDED TO SUPPORT DATA SHARING AND BUILD INFRASTRUCTURE TO REALISE THE POTENTIAL OF DATA GENERATED BY DTx

The Commission and Member States should support evidence generation. If successful, the European Health Data Space (EHDS) will facilitate health data exchanges throughout the patient journey and strengthen cooperation across Member States. To ensure this, appropriate data governance is fundamental to realise the potential of health data in a trusted and secure way. EHDS will promote health data system interoperability by further developing common interoperability standards. Interoperability will allow the exchange of health data across borders and enable citizens to have more continuous, well-informed healthcare regardless of their point of interaction with healthcare system in Member States. The EU's proposed Data Governance Act aims to promote trusted data sharing and may facilitate the sharing of health data across Member States.[48]

MEMBER STATES SHOULD CREATE CLEAR AND TRANSPARENT NATIONAL PATHWAYS FOR DTx PRICING AND REIMBURSEMENT

Countries should implement a separate national pathway for the reimbursement of standalone and companion DTx, while for combination DTx, combined reimbursement of the DTx and pharmaceutical together is more appropriate. New pathways should draw on lessons from existing pathways – particularly DiGA – but the limitations of the DiGA process need to be considered, such as that only standalone DTx are eligible. Combination DTx, by contrast, must be used with specific therapy and so combined reimbursement of the DTx and pharmaceutical together is expected to be more appropriate. Reimbursement systems must recognise that a broad range of DTx exist, including digital solutions with multiple components that include a medical device or associated services with the software.

PAYERS SHOULD PERMIT FLEXIBLE APPROACHES ALLOWING PROVISIONAL ACCESS WHILE ADDITIONAL DATA IS GENERATED

In both Belgium and Germany, the specific DTx pathways permit provisional access to be on the market and used by HCPs and patients for a limited period of time, and in France innovative products can receive experimental coverage through Article 51 and Forfait Innovation. The real-world evidence this generates can be used to support clinical and health economic assessments. This has the benefit of accelerating patient access to innovative technologies while allowing payers to incorporate RWE into their finalised reimbursement decisions. Implementing provisional access in the nearer term would be particularly beneficial in areas with demonstrated unmet clinical or resource-related needs.

PAYERS SHOULD BE WILLING TO IMPLEMENT NOVEL PAYMENT MODELS TO MANAGE EVIDENCE UNCERTAINTIES

Given that there is often uncertainty in the data package for DTx due to lack of comparators and the nature of the technology, DTx value assessments should be adaptive and efficient enough to incorporate real-world data collected before and after the value assessment. Novel payment models, such as outcome-based agreements leveraging patient-reported outcome measures, could be attractive when payers are not convinced that clinical evidence represents real-world patient care. Products that are subject to an outcomes-based agreement can request developers to collect additional data as part of the conditions for provisional access.

TO ENSURE THAT DTx ARE ADEQUATELY FUNDED, FUNDING NEEDS TO BE EXPLICIT AND BUDGETED, AND SHOULD NOT HAVE A FINANCIAL BURDEN ON PATIENTS

DTx funding has been highlighted as a major challenge, with only a few countries making DTx available to patients. To ensure that DTx are adequately funded, funding needs to be explicit and budgeted. It should not pose a financial burden on patients and should be adequate and sustainable to allow healthcare providers and patients to adopt DTx without fear of financial repercussions. Member States need to ensure sufficient budget for DTx that deliver benefits to patients and healthcare systems, potentially by using funding models which support value-based approaches. In addition to general healthcare budgets, the implementation of DTx should be supported by budgets allocated to digital health.

INCREASING DTx UPTAKE WILL REQUIRE COLLABORATIVE EFFORTS BETWEEN POLICYMAKERS, HCPs, AND COMPANIES. TO DEVELOP TRUST IN DTx, STAKEHOLDERS MUST BE PREPARED TO WORK TOGETHER TO ENHANCE THE EDUCATION AND EXPERIENCE OF HCPs AND PATIENTS

Even if DTx are reimbursed and adequately funded, there is no guarantee of their uptake due to further challenges in terms of HCP readiness to prescribe and patient willingness to use them. As a result, national-level policymakers should explore solutions to improving digital health literacy and information around DTx. This could include investment in digital infrastructure, support for digital training, and ensuring that HCP time receives adequate reimbursement that reflects the effort in monitoring, communication, patient education, and documentation. DTx developers should be ready to collaborate with other stakeholders to enable this, particularly to improve education and awareness among healthcare providers. This education, along with experience, will be critical for building trust for all stakeholders with the emerging technology of DTx.

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