Personalised medicine

Position of the

European Social Insurance Platform (ESIP)

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Executive Summary

Personalised medicine is hailed as having the potential to provide major benefits to patients and healthcare systems by enabling more effective targeted therapy, avoiding side effects and unnecessary treatment and even offering the possibility of a cure (e.g. for rare diseases). To date however, there have been few examples of targeted therapies that have demonstrated any major patient benefit, and at the same time the very high prices demanded for such therapies can be expected to have a huge impact on the sustainability and equity of healthcare systems.

In this paper the statutory social insurers present some of the important practical and ethical challenges that the complexity of targeted therapies (based on a biomarker, a diagnostic test and a medicinal product) raise for our current systems of market access, HTA and pricing and reimbursement, as well as patients and healthcare professionals. The challenges underlined in this paper are addressed with a series of policy recommendations.

1. **A robust scheme of market access at EU level that addresses the complexity of personalised therapies**
   Current market access schemes are being challenged by these new therapies **targeted at small populations** identified by biomarkers and diagnostic tests. The combination of these elements calls for an **EU regulatory framework** that is **comprehensive, consistent and transparent**, and that continues to demand **strong clinical evidence** of safety and efficacy **prior to marketing authorisation**. **Early access schemes,** in particular, should **remain an exception** and be subject to strict conditional market authorisation rules and high standards for post-market studies.

2. **Strong pricing & reimbursement policies to ensure the sustainability of healthcare systems in the context of expensive personalised therapies**
   The high expectations for personalised medicine have yet to be realised as significant breakthroughs remain limited to only a few disease areas. At the same time, experience shows that **personalised therapies have a high price label**. Therefore, **strong pricing and reimbursement policies** are necessary to ensure the **sustainability of healthcare systems and patients' access to care**. Appropriate **evidence** on the added therapeutic benefit and/or cost effectiveness of a personalised therapy based on robust clinical studies needs to be **available prior to its admission for reimbursement**. In this context, **enhanced cooperation on HTA at EU level** should aim to develop **specific methodologies** appropriate to personalised medicine and share information between competent authorities to inform decision making at Member State level. To address the issue of the **affordability of personalised medicine** further **specific policy measures** should be envisaged around the use of centres of expertise, voluntary cooperation and exchange of best practice between the relevant competent bodies and Member States.

3. **Access to comparable data, data protection and patients' privacy**
   Personalised medicine implies **intensive use of patients' data** including genetic data. It raises challenges in terms of data protection and patients' privacy, accessibility to data

and their reliability. In this respect the new EU Regulation on data protection should be fully respected to protect patients against the use of their data for commercial interest. Early and full **access to clinical trial data and international registries** by **competent authorities** is essential for assessment and reassessment purposes**,** while **quality standards for registries** developed at EU level will facilitate the exchange and comparability of data.

4. Patient empowerment and healthcare provider information to make the best use of personalised medicine

Finally, patient empowerment has a special importance in the field of personalised medicine. This requires that **both patients and healthcare providers are well informed**. Appropriate information should be provided to patients, specifically on the lack of strong evidence of efficacy, the possible beneficial effects and the risks of side effects as well as the requirements for use of their healthcare data. In addition, **guidelines for healthcare providers** need to be developed in a collaborative way to inform decisions on the appropriate use of personalised therapies.

See page 15 for our full set of Policy Recommendations.

Contents

About the European Social Insurance Platform (ESIP)

The European Social Insurance Platform (ESIP) represents over 40 national statutory social insurance organisations (covering approximately 240 million citizens) in 15 EU Member States and Switzerland, active in the field of health insurance, pensions, occupational disease and accident insurance, disability and rehabilitation, family benefits and unemployment insurance. The aims of ESIP and its members are to preserve high profile social security for Europe, to reinforce solidarity-based social insurance systems and to maintain European social protection quality. ESIP builds strategic alliances for developing common positions to influence the European debate and is a consultation forum for the European institutions and other multinational bodies active in the field of social security.

Statement regarding positions submitted by ESIP: ESIP members support this position in so far as the subject matter lies within their field of competence.

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Introduction

Personalised medicine (see definition below) raises challenges, risks and opportunities for existing systems and schemes in a comprehensive way. According to some, it has the potential to provide "major benefits [...], including increased efficiency and less adverse reactions to treatments, longer and healthier lives, and more sustainable healthcare systems"[1]. However, in practice only a very limited number of treatments had a major patient benefit and targeted therapies have been shown to be mostly associated with very high prices[2]. They potentially have an enormous impact on the sustainability and equity of healthcare systems and patients.

An important therapeutic area for personalised medicine is oncology. Since the number of cancer patients in the EU will continue to rise[3], the impact of new therapies in the field of oncology is significant for payers of healthcare services and for patients. There are some successful examples of targeted therapies with patient relevant benefits, but there are others yielding only limited or no improvements in patient outcomes and that can also cause severe side-effects. Therefore high level comprehensive evidence is necessary at time of market access to evaluate benefit-risk ratio.

In this context, European social insurers, representing the payers, invite the EU Institutions to consider measures to maximise the potential benefits of personalised medicine while minimising its risks. In this document, they express their concerns and formulate recommendations to tackle these challenges.

[1] EFPIA, in http://www.efpia.eu/topics/innovation/personalised-medicines
[2] Godman B, Finlayson AE, Cheema PK, Zebedin-Brandl E, Gutiérrez-Ibarluzea I, Jones J, et al. Personalizing health care: feasibility and future implications. BMC Med. BioMed Central Ltd; 2013;11(1):179
[3] See: http://www.who.int/mediacentre/factsheets/fs297/en/

Definitions

Personalised medicine: in this paper, personalised medicine is defined as "a medical model using characterisation of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, and lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time"[4].
This paper focuses on therapy in terms of medicinal products and does not address screening and prevention.
Personalised medicine is based on the sub-division (or stratification) of patients into groups based on their molecular profile, that is to say on the presence or absence of a predictive marker (e.g. biomarker) in the body, which indicates the presence of a disease or predicts the risk of developing a disease, its evolution or the response to and toxicity of certain therapies. The marker can be identified with a diagnostic test, which is called a "companion diagnostic" test in the case where it leads to the decision to administer a corresponding "targeted" therapy. For patients this can lead to a better health outcome through a better response to existing treatments, the avoidance of unnecessary treatment if the therapy is not effective for their specific profile, the avoidance of side effects, and/or to the possibility of a cure through new drugs (e.g. for rare diseases without adequate therapy so far).
Although we use the wording "personalised medicine", we recall that the approach using predictive biomarkers is population/statistics-based, not individual-based. The targeted therapy is therefore aimed at a sub-population of patients identified by a predictive marker (using a companion diagnostic).

Biomarker: a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses to a therapeutic intervention.

Companion diagnostic: a device or a procedure that is used to measure or analyse the status of a biomarker.

Market entry agreements: Market entry agreements (MEA) are national schemes that may facilitate a structured introduction of therapies with drug price as one of the components. They can be regarded as "conditional" reimbursement schemes for instance in a context of scientific and/or financial uncertainty. There are different types of market entry agreements, e.g. performance based, but MEAs are not feasible in all Member States.

Joint Horizon scanning: Joint Horizon Scanning is defined as the „assessment of future introduction of new medicinal products with a possibly significant financial impact on health systems at an early stage"[5]

[4] Council conclusions on Personalised Medicine for patients, 7 December 2015.
[5] Council conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States, 17 June 2016.

1. Market access

Market access schemes are challenged by the specificities of personalised medicine. The regulatory framework needs to be reviewed in order to strengthen the approval pathway and the generation of evidence on safety, efficacy and a positive risk-benefit balance before market access.

1.1. The need for a comprehensive, consistent and transparent regulatory framework at EU level

Currently at EU level no comprehensive legislative approach exists as regards the approval of targeted therapies, despite the high interdependency of the stratifying tool (e.g. biomarkers), the companion diagnostic and the corresponding drug.
Three different parallel processes exist at EU level: a) a voluntary opinion of the EMA concerning biomarker-qualification and validation, b) a certification granted by notified bodies for the companion diagnostic test approval, where the notified body "considers" the EMA's opinion and c) a separate drug approval with unclear rules on labelling information concerning the diagnostic tests. Fragmented and non-transparent initiatives and projects (e.g. the adaptive pathway approaches) aim to address some of the challenges that are raised by personalised medicine, but without a comprehensive, clear and transparent political approach to the problem.

Past experience has shown that **a comprehensive regulatory approach at EU level is urgently needed** to address the risks and the opportunities for development. Therefore we recommend that:

- The existence of a **« qualified / validated biomarker »** is a **prerequisite** to the approval of the therapy;
- To allow new technological developments in the field of diagnostics, there should be **no fixed combinations of diagnostic tests and drugs** and the drug label should not mention the commercial denomination of any diagnostic test;
- **Commercialised companion diagnostic tests** are subject to an **independent authorisation process**, e.g. by an expert committee, as the optimal performance of the test, when performed properly, determines the safety, efficacy and positive risk-benefit ratio of the corresponding drug;
- **European standards** on **external quality assessment** programmes and **procedural standards** for laboratories performing the tests must be developed to guarantee uniform and reproducible outcomes
- The **"orphanisation" of personalised medicine is avoided** i.e. the orphan drug regulation should not apply to sub-populations of broader patients groups.

1.2. The need for strong clinical evidence before accessing the market

It is sometimes argued that collecting clinical evidence in order to demonstrate the safety and efficacy of targeted therapies is challenging, as they often target small populations. One proposed solution is to "soften" the requirements for the demonstration of safety and efficacy before marketing authorisation, in exchange for more demanding post-authorisation monitoring of the effects of the therapy, in the so called "real life" setting.

Yet, we think that part of a comprehensive regulatory approach must be that the promise of a better targeting of the population potential benefits in this subgroup must be **proven before marketing authorisation**, not when the drug is already on the market. The very fact that biomarkers are a means of selecting patients, i.e. including / excluding people from therapies, is a highly sensitive medical and ethical issue. Therefore, the biological rationale of the marker needs to be proven by data about the efficacy of the new drug. The **design of the study** will be **case specific** and needs to **involve** the **national competent authorities**, **payers** and **patients**.

In addition, **randomised clinical trials** should remain the **gold standard to demonstrate clinical utility**, i.e. that the treatment is more effective (and/or less toxic) among the patients with the specific biomarker and not/less effective among patients without the biomarker - who have the specificity that makes them eligible for the treatment - than among patients who do not have this specificity. Experience has shown that clinical trials for some commercialised therapies did/could not confirm that the treatment was more effective for patients with the marker[6].

1.3. Early access must remain the exception and must be subject to strong rules

In the exceptional case of early access schemes with limited evidence at the moment of marketing authorisation, **standards should be developed for post market studies** and:

- Any given **authorisation** should **only be temporary**, with conditional approval and conditional use
- Studies are payed by the manufacturer/marketing authorisation holder.
- **Sufficient evidence on** both **efficacy** and **safety** must be **generated during the conditional approval period** in a transparent way. The feasibility of high level evidence studies or randomised controlled trials begun prior to authorisation should be evaluated during the approval process. The marketing authorisation applicant / holder should be responsible for the data generation which can be facilitated by national MEA (managed entry agreement) schemes

[6] Terasawa T, Dahabreh I, Castaldi PJ, Trikalinos TA, Systematic Reviews on Selected Pharmacogenetic Tests for Cancer Treatment: CYP2D6 for Tamoxifen in Breast Cancer, KRAS for anti-EGFR antibodies in Colorectal Cancer, and BCR-ABL1 for Tyrosine Kinase Inhibitors in Chronic Myeloid Leukemia, Agency for Healthcare Research and Quality (US); 2010 Jun.

- If the product doesn't show significant patient benefit and/or shows increased risk, the **marketing authorisation** should be **withdrawn**
- **Financial penalties** should be applied if the **holder of the marketing authorisation fails to adhere to the obligations** laid down in the **conditional marketing authorisation** in a timely manner (e.g. additional data generation), as proposed by the Commission[7]. If these obligations are not met the marketing authorisation should be withdrawn.
- The **patient population** must be **clearly defined** and the centres that administer these drugs must demonstrate **explicit patient consent** to the **therapy** and to the **collection and use of their data**
- Potentially negative consequences due to side-effects during the conditional approval period should be covered by the **liability insurance** of the manufacturer
- Observational data (sometimes referred to as "real world data") on therapies generated during the post-authorisation stage must be **evaluated and made public** (with appropriate protection of personal data).

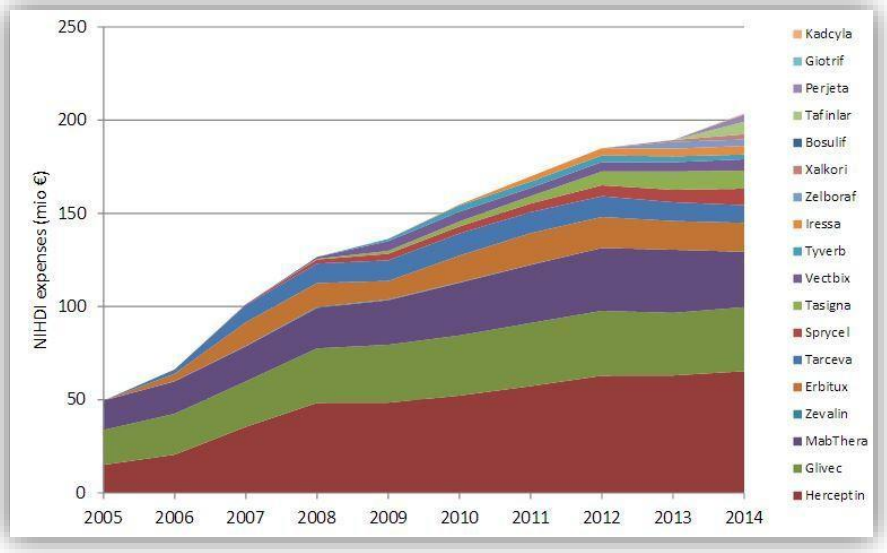
We note here that the "Adaptive pathways" approach as currently considered potentially presents even greater risks when applied to personalised therapies than to traditional medicines since personalised therapies involve three interdependent elements (clinical utility of the biomarker, performance of the companion diagnostic test and safety and effectiveness of the drug).

2. Pricing and reimbursement (P&R)

One big challenge for health systems as regards personalised medicine is the very high price demanded by industry for therapies that have little significant patient relevant benefit (for example very expensive cancer therapies which prolong life by just a few weeks). The problem is becoming more and more critical, as very expensive medicines are more frequently used in combination. It is argued that these therapies might help to avoid or replace ineffective healthcare, or that better selection improves the effectiveness of existing therapies, leading to cost reductions. Nevertheless, the **budget impact caused by targeted therapies is not compensated by the theoretical cost reductions**, primarily because lines of therapy are added instead of replaced, and also because expensive prices negotiated for initially small patient populations tend to be retained when new indications are authorised and the target patient population increases in size. Therefore, a substantial increase in healthcare costs can be expected as illustrated by the graph below.

[7] Proposal for a regulation of the European Parliament and the Council amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, COM(2014) 557 final, 10.09.2014, Article 1 (17).

Evolution of annual clear RIZIV / INAMI spending (hospitals and public pharmacies 2005-2014) for anti-cancer personalised therapies in Belgium.



Source: *Monitoring of Reimbursement Significant Expenses*, INAMI, 2014.

If no corrections are made, this will result in:

- Increasing inequity as many public systems in EU countries are not able to pay for personalised medicine
- Problems of sustainability for the healthcare systems in Member States that reimburse personalised therapies.

2.1 The need to collect evidence on patient-related benefit

Limited evidence regarding patient-relevant benefit at the time of market access poses problems for pricing and reimbursement decision-makers. If personalised medicine offers the promise for more effective healthcare, sufficient **evidence is needed on its added value, before the therapy is admitted to reimbursement**. Otherwise it will only result in higher costs with little or no added patient benefit.

Therefore, **robust clinical studies** need to be performed to demonstrate the **added therapeutic benefit** (including clinical utility of the biomarker) **and/or economic value** of the therapy **over and above that of existing therapies**. Good clinical studies can be designed and implemented even in small populations. Due to the difficulties in removing a therapy from the reimbursement list[8], and/or enforcing post- marketing monitoring, it is important

[8] Ermisch M, Bucsics A, Vella Bonanno P, Arickx F, Bybau A, Bochenek T, Casteele MV, Diogene E, Furst J, Garuoliene K, Graaff Mv, Gulbinovic J, Haycox A, Jones J, Joppi R, Laius O, Langner I, Martin A, Markovic-Pekovic V, McCullagh L, Magnusson E, Nilsen E, Selke G, Sermet C, Simoens S, Sauermann R, Schuurman A, Ramos R, Vlahovic-Palcevski V, Zara C and Godman B (2016). Payers' views of the changes arising through the possible adoption of Adaptive Pathways. Front. Pharmacol. 7:305. doi: 10.3389/fphar.2016.00305.
HAI, ISDB, IRCCS, Medicines in Europe Forum, Nordic Cochrane Center, Wemos, A PRIME example of how EMA is pushing for accelerated market approvals, but at what cost for patients?, 23 December 2015.

that this evidence is provided **before the assessment** for pricing and reimbursement decisions[9].

In order to improve the evidence base for decision making, **access to and transparency of the clinical data** submitted **for marketing authorisation** is critical.

"Early Dialogue"[10] procedures may contribute to the design of studies that allow the assessment of additional patient benefit compared to the standard of care. Early dialogue may be a win-win solution: allowing industry to reduce the uncertainty related to its R&D investment in a certain therapy, allowing patients to benefit from faster access to those therapies and streamlining the P&R decision-making processes. However, we would like to stress that "**measures to sufficiently guard against [...] potential conflict of interest**" [11]need to be **put in place**. Finally, it is important to recall that in any case, pricing and reimbursement procedures, including the **assessment of added patient benefit** (HTA), should **remain independent from** that of **marketing authorisation**.

2.2 The role of HTA for ensuring the patient relevant benefit of personalised medicine

The promise that personalised medicine will revolutionise medicine has not yet been realised. Breakthroughs have only been made for very few diseases (e.g. lung cancer, melanoma, gut cancer, breast cancer and chronic myelogenous leukaemia). Nevertheless, research in this field develops fast and health systems need to find ways to assess the additional benefits for patients and to reduce the risks as much as possible.

Voluntary cooperation on HTA at EU level will lead to synergies. Consideration should be given to **developing a specific, new methodology for personalised medicine**, for example in the framework of the EUnetHTA cooperation.

Also, as outlined in the ESIP-AIM position on access to innovative medicines published on 13 October 2015, **transparency** and sharing information in this area is **critical to maximise the benefits of EU cooperation on HTA**.

2.3 Policy measures for the sustainability of healthcare systems

Even if patient relevant benefit can be proven for a new personalised therapy, the question of affordability arises. While manufacturers must be rewarded for real innovations, affordability for the health systems has to be considered. Further, subsequent extension of a treatment to a broader patient group will increase the budgetary impact and exacerbate

[9] HAI, ISDB, IRCCS, Medicines in Europe Forum, Nordic Cochrane Center, Wemos, A PRIME example of how EMA is pushing for accelerated market approvals, but at what cost for patients?, 23 December 2015.

[10] « This procedure aims to allow medicine developers to gain feedback from regulators and HTA bodies at the same time, at any point in the developmental lifecycle of medicines. This helps them to establish the evidence that both parties will need to determine a medicine's benefit-risk balance and value as efficiently as possible », in http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000049.jsp.

[11] See ESIP answer to the Public consultation on a "Reflection paper on a proposal to enhance early dialogue to facilitate accelerated assessment of priority medicines (PRIME)" : http://esip.eu/index.php?q=node/1675.

the question of affordability. It is important that the price should not jeopardise the sustainability of healthcare systems and patients' access to the treatments they need.

Market entry agreements might be one solution to better support the sustainability of healthcare systems and patients' access. In this context, **prices must be set in relation to the level of evidence** regarding the patient benefit at the moment of market authorisation.

The **centralisation of expertise**, e.g. through centres in which companion tests are performed at national level (like in France) is **another possible solution to increase the quality and cost-effectiveness of personalised medicine**. Indeed, this would at the same time ensure efficient, professional use of diagnostic tests, high diagnostic quality and allow economies of scale, which is crucial where the quality and performance of the test is so decisive for the effectiveness of the therapy. **European funding** could be foreseen **to co-fund the infrastructure and / or research**, and **European networks** could be set up **to share the expertise**. European reference networks set up under the Directive on cross- border healthcare[12] could serve as an example.
Voluntary cooperation between European countries in order to influence the price of pharmaceuticals already exists and could be further explored, especially in the field of expensive therapies like personalised ones.
Initiatives already existing may include:

- The use of voluntary cooperation and tools **for joint negotiations and joint procurement** (e.g. the Benelux-Austria cooperation, southern Europe and Baltic initiatives….)
- Joint **horizon scanning**

In addition, **ESIP calls on the European Commission to continue to support the fora for exchange of information between competent authorities for pricing and reimbursement** (CAPR) and between these authorities and stakeholders including ESIP (under the Corporate Responsibility in the field of Pharmaceuticals initiative) facilitated by the European Commission DG GROW with the engagement of all relevant Directorate Generals.
Finally, the **exchange of best practices** e.g. on rational prescribing and guidelines on the interpretation of diagnostic test results (and thus the use of therapies) to promote good clinical practice **is necessary**. We advocate **closer cooperation between national bodies responsible for elaborating these guidelines**.

3. The importance of data, data protection & patients' privacy

Personalised medicine implies intensive use of patients' data. It raises challenges in terms of data protection and patients' privacy, accessibility to those data and their reliability. Those considerations will become more and more acute, when personalised medicine is associated with the use of "Big data".

[12] http://ec.europa.eu/health/rare_diseases/european_reference_networks/erf/index_en.htm

3.1 The protection of patients' data and privacy

Personalised medicine increasingly challenges data protection. It uses personal genetic information. Research on diseases can imply complete genetic profiling as well as the identification of biomarkers, which require the intensive use of (genomic) data. There must be the correct balance between the use of personal health data on the one hand and the respect of individual rights to data privacy on the other hand.

In this respect the new **EU Regulation on data protection** should be **fully respected** and in a way that is **clear enough to protect patients against commercial interests**. **Data** generated throughout the lifecycle of the product **must not be owned by commercial entities**.

3.2 Clinical data must remain accessible to competent authorities

Early and full access to clinical trial data and international registries is also important:

- for regulatory bodies **to assess the efficacy and the risk/benefit balance** and to be able to **withdraw a therapy from the market** in case of safety issues
- for HTA and P&R bodies for **reassessment purposes** and **to remove a therapy from the reimbursement list** if it does not demonstrate any patient relevant benefit, or **to issue recommendations** to health professionals, etc.
- to assess the effectiveness and safety in the healthcare system, for epidemiology studies, studies on the use of the medicines, etc.

Again, this **post-authorisation follow-up** is important but **should not replace the data from pre-authorisation randomised clinical trials** that is required to assess efficacy and safety, as well as added therapeutic benefit and / or cost-effectiveness.

3.3 Standards for the comparability & exchange of data

Reliability of data is crucial. In this regard we welcome the work done by the **PARENT Joint Action** to develop **quality standards for registries**, to **facilitate the exchange and comparability of data**.

4. Patient empowerment

Patient empowerment has a special importance in the field of personalised medicine. In this context, we welcome the Council conclusions on personalised medicine for patients, where it is stated that Member States should "put in place information and awareness strategies for patients, based on available, objective, balanced and non-promotional data in order to improve health literacy and access to reliable, relevant and understandable information on treatment options, including benefit and risks, thus enabling patients to actively cooperate with health care professionals in choosing the most appropriate treatment option."

4.1 Patient information & health literacy

New therapies, especially those that have only limited proof of their efficacy and safety must be introduced into healthcare in a managed way. This implies that **patients are informed** about **the lack of robust evidence, the possible beneficial effects** (e.g. likely extended survival period), **the risks of side effects** and the requirements for use of their healthcare data so that they can make an informed decision.

To this end, it is of crucial importance that **patients and healthcare professionals have access to clinical data relating to targeted treatments**. Measures should be carried out at European level in order to ensure and encourage the enforcement of the new pharmacovigilance rules (on the reporting of side effects and adverse events) and of the new clinical trials Regulation, especially the **obligation to publish data from clinical trials, including failed clinical trials**.

4.2 Guidelines for healthcare providers

Healthcare providers are important contributors to patient empowerment. Therefore they should be sufficiently informed and trained. The Council conclusions on personalised medicine for patients recommend that Member States "provide education, training and continuing professional development for health professionals in order to equip them with the necessary knowledge, skills and competences […]".
In this domain we advocate **closer cooperation between national bodies** (i.e. healthcare professionals' representatives and national public health authorities) responsible for elaborating guidelines, including therapeutic guidelines and guidelines for biomarker testing and reporting.

Conclusion

The role of the social health insurers (payer organisations) is to ensure equitable access to healthcare and high quality, safe and effective treatments for patients who need them. In this paper we have identified a number of challenges, risks and opportunities for patients and healthcare systems linked to the development of personalised medicine and have defined a series of recommendations aimed at maximising the potential benefits and minimising the risks of targeted therapies. As a key stakeholder in enabling sustainable access to safe and effective medicines ESIP would welcome the opportunity to share its expertise with decisions makers and other stakeholders in future discussions around access to safe and effective personalised medicine.
Finally ESIP takes the opportunity to recall that **prevention and public health measures** (e.g. anti-tobacco-campaigns and screenings) should **remain a priority of healthcare systems** and that **public research should be targeted towards public health needs**, personalised medicine for high unmet need being only one of these.

Policy recommendations

To maximise the potential benefits of personalised medicine while minimising the risks both to patients and healthcare systems, ESIP considers that the following are required:

1. A robust scheme of market access at EU level that addresses the complexity of personalised therapies, including:

- A comprehensive, consistent and transparent regulatory framework at EU level governing all components of targeted therapies
- A requirement for strong clinical evidence demonstrating safety and efficacy prior to market access
- Strong criteria limiting early access to exceptional cases only with strict enforcement of the obligations on the marketing authorisation holder
- Rules preventing fixed combinations of diagnostics with therapies
- European standards to guarantee uniform and reproducible outcomes of diagnostic tests

2. Strong pricing and reimbursement policies to ensure the sustainability of healthcare systems in the context of expensive personalised therapies, including:

- The collection of evidence on patient-relevant benefit / cost-effectiveness before admission to reimbursement, through robust clinical studies
- Voluntary cooperation on HTA, including joint horizon scanning
- Policy measures aimed at ensuring the affordability of available therapies
- Voluntary cooperation on joint procurement

3. Access to comparable data, data protection and patients' privacy, including:

- Strong measures to protect patients' data and privacy
- Early and full access to clinical trials data and international registries by competent authorities
- Continued support for EU level coordination on quality standards for registries to facilitate the exchange and comparability of data

4. Patient empowerment and healthcare provider information to make the best use of personalised medicine, including:

- Clear information to patients about any lack of robust evidence, the possible beneficial effects and the risks of side effects of personalised therapies
- Continued professional education to ensure healthcare providers have the necessary knowledge, skills and competences to help patients reach an informed decision
- Cooperation between national bodies responsible for elaborating guidelines for healthcare professionals (therapeutic guidelines and guidelines for biomarker testing and reporting) to inform appropriate use