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4 Electronic product information for human medicines in the 5 EU – draft key principles

6 A joint EMA–HMA–EC collaboration

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Comments should be provided using the online form: https://ec.europa.eu/eusurvey/runner/ePI_Public_Consultation

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30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5545
Send a question via our website www.ema.europa.eu/contact

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List of abbreviations

EC	European Commission
EEA	European Economic Area
EHR	Electronic health record
EMA	European Medicines Agency
ePI	Electronic product information
EU	European Union
HCP	Healthcare professional
HMA	Heads of Medicines Agencies
IDMP	Identification of Medicinal Products
ISO	International Organization for Standardization
MAH	Marketing authorisation holder
NCA	National competent authority
PDF	Portable document format
PI	Product information
PL	Package leaflet
SME	Micro, small or medium-sized enterprises
SmPC	Summary of product characteristics
SPOR	Substance, product, organisation and referential (EMA implementation of ISO IDMP standards)

Background

In the European Union (EU), a medicine's product information (PI), which includes the summary of product characteristics (SmPC, intended for healthcare professionals), labelling (outer and inner packaging information) and package leaflet (PL, for patients/consumers and generally included as a printed copy in the medicines package[1]), is the pivotal source of regulated and scientifically validated information that assists healthcare professionals in prescribing and dispensing the medicine and informs patients and consumers about its safe use.[2]

A report from the European Commission (EC) in March 2017, and a subsequent EMA action plan, identified areas where the SmPC and PL could be improved to meet the needs of patients and healthcare professionals and proposed actions to address these shortcomings. These wide-ranging actions relate to enhancing readability, improving patient input in development and testing, promoting best practices and developing an electronic format. Throughout 2018, a joint EMA-HMA-EC collaboration has worked on the latter: identifying stakeholder needs from a future electronic PI for medicines (ePI) and mapping ongoing initiatives in the field to create an overview of the current landscape. The electronic format is the most pressing priority out of the actions from a public health perspective as it will ensure patients have timely access to up-to-date information and coordination among the many initiatives ongoing in the EU. The current scope of this work is all human medicines authorised in the EU.

A workshop held at EMA on 28 November 2018 brought together patients/consumers, healthcare professionals, industry stakeholders, academia, not-for-profit organisations and regulators to discuss stakeholder needs and concerns, give an overview of the main ePI initiatives ongoing in the EU and decide how to move forward with a common approach. The outcome of the workshop is the following proposal for 'key principles' on ePI to be released for public consultation. These key principles do not represent final guidance from EMA on ePI; they are intended, following the outcome of public consultation, to form the basis of follow-up implementation plans for ePI.

[1] The legal requirement to include the PL in the packaging is laid down in Article 58 of the Directive 2001/83/EC which states: "The inclusion in the packaging of all medicinal products of a package leaflet shall be obligatory unless all the information required by Articles 59 and 62 is directly conveyed on the outer packaging or on the immediate packaging."
[2] The content of the SmPC, labelling and PL is described in Articles 11, 54, 55 and 59 of Directive 2001/83/EC.

Draft key principles on ePI in the EU

The following key principles are intended, following a period of public consultation, to be agreed by EMA, HMA, EC and representatives of patients, consumers, healthcare professionals and the pharmaceutical industry. Future work on ePI will progress in alignment with these principles.

1. Definitions

Definitions of 'ePI' and 'common electronic standard' are intended to explain the meaning of these terms as they are used in this initiative.

1.1. ePI

Statement

The following definition of ePI is proposed:

ePI is authorised, statutory product information for medicines (i.e. SmPC, PL and labelling[3]) in an organised format created using the common EU electronic standard.[4] ePI is adapted for electronic handling and allows dissemination via the world wide web, e-platforms and print.

Rationale

There are many different interpretations of 'electronic product information.' Therefore, it is important to clarify that for the purposes of this collaboration, ePI refers to a semi-structured format suitable for electronic handling. Semi-structured means that ePI contains some structured elements (e.g. fixed headings and vocabularies), and some unstructured elements (i.e. free text). Unstructured formats such as PDF, Word or other unstructured text are not considered to be ePI because these do not deliver the benefits to stakeholders outlined in these principles.

ePI refers to the structure of the PI and not its content.

Implication

By agreeing on an EU definition of ePI, there will be a harmonised understanding across the EU, which will guide collaborative work to create ePI that meets the definition.

Implementation of the use of ePI, as described in the definition, will allow delivery of the benefits to stakeholders as explained in the key principles 2.1 and 2.2. Such implementation will be carried out in accordance with applicable European legislation. The development of ePI will not create new requirements with regard to the content of the PI or a new legal obligation to use ePI. In addition, this initiative should not be understood to change the interpretation of European legislation.

[3] In certain procedures, Annex II of the marketing authorisation (manufacturer(s) responsible for batch release, conditions and requirements of the marketing authorisation, other conditions or restrictions as applicable) is provided electronically together with ePI.
[4] See '1.2. Common EU electronic standard.'

1.2. Common EU electronic standard

Statement

ePI in the EU for all human medicines, including both centrally and nationally authorised medicines, will be created using a common electronic standard. The following definition of a common EU electronic standard for ePI is proposed:

A common standard for ePI in the EU refers to the technical features (including mark-up language, controlled vocabularies and interoperability specifications) agreed by regulators and stakeholders. The standard will be used to generate ePI that fulfils the agreed key principles.

Rationale

A common standard is necessary to provide consistent functionality of ePI for all medicines throughout the EU. This will reflect the reality of interlinked medicines' regulatory systems among the European medicines regulatory network as well as meeting the expectations of patients and healthcare professionals who travel and work in several EU countries.

A common standard enables the generation and dissemination of electronic authorised information for patients and consumers of medicines in the EU/EEA. It will not lead to a change in the interpretation of applicable European legislation nor will it create new requirements with regard to the content of the PI as described in EU legislation.

The aims of the common standard are:

- to create the technical foundation for the dissemination of trusted information in the electronic world, which will allow patients/consumers and healthcare professionals an additional and tailored approach on information for medicines according to his/her need and/or wish by using suitable (electronic) output forms and platforms;
- to offer possibilities to streamline, simplify and speed up the regulatory process in the creation and updating process (variation) of PI by using existing data of the SPOR (substance, product, organisation and referential) process, both for regulators and the pharmaceutical industry.

Agreement of a common standard will avoid a situation where multiple different standards are developed and used in different parts of the EU, which would generate unnecessary complexity, impede access to information and require multiple interfaces between standards, restricting flow of data.

Implication

The first step and pre-requisite for ePI implementation is the agreement of a common standard that fulfils the requirements outlined in the key principles and is compatible with use at centralised and national (through national competent authorities [NCA]) levels.

The common standard will be established considering the available technical features, including those from EU Telematics projects. Further features, such as vocabularies and interoperability specifications yet to be developed, may be added in later releases.

2. Benefits for public health

Regulators and stakeholders wish to work towards ePI in the EU because of the benefits this format can offer for public health. While acknowledging that many future applications of ePI cannot currently

be predicted, the following principles outline the key benefits which constitute the fundamental reasons underpinning this initiative.

2.1. Expanding access to information on medicines as a public health imperative

Statement

ePI is a public health priority because it will expand the dissemination of unbiased, up-to-date, regulator-approved PI for all medicines in the EU. ePI will support, among other functions:

- provision of the latest information on a medicine's safety, benefits and its conditions of use;
- better delivery of information so that the right information is available to the right patient/consumer at the point of need;
- informed decision-making by patients/consumers and healthcare professionals.

Rationale

Unlike paper PLs contained in medicine packages, which are updated gradually as stocks of medicines turn over, it will be possible to rapidly update ePI with the latest authorised information. Patients/consumers and healthcare professionals using ePI can be fully confident that they hold the latest information about benefits, risks and use.

In contrast to current PDF and unstructured text formats, ePI will enable wider availability on a range of platforms. ePI is thereby expected to increase support to patients/consumers in informed decision-making about their treatment and help them to adhere to their medication regimes, ultimately contributing to optimal outcomes. ePI should also facilitate patient/consumer–healthcare professional interactions and discussions about medicines.

The structured nature of ePI will offer new opportunities to better tailor product information to the needs of individual patients/consumers. Also, because ePI can be handled electronically and read by machines, ePI information can flow to other systems, such as electronic health records and e-prescribing systems, facilitating targeted delivery of the right information to the right patient/consumer at the point of need.

Availability of regulator-validated ePI will counterbalance unreliable and spurious claims about medicines, often widely spread through online and other forums, by giving EU citizens an authoritative source of scientific and evidence-based information on medicines.

Implication

EMA and NCAs should work towards ePI to fulfil their mission to protect public health. Implementation will have as a goal the creation of ePI for all authorised human medicines in the EU/EEA.

ePI will be rapidly and continually updated as soon as changes to the SmPC and PL are authorised by the regulatory authorities. The most up-to-date ePI version should be always easily available.

To achieve this principle, ePI should be made available through various technologies and applications, including mobile scanning technology (such as a 2D barcode) on the medicine package.[5] Correct ePI depends on the medicine batch: some parts of the ePI may be applicable to all batches and some only

[5] EMA and CMDh guidance on use of barcodes is available at: https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/product-information/product-information-reference-documents-guidelines and http://www.hma.eu/90.html

to specific batches (e.g. when excipients change). Therefore the need for the correct ePI to be supplied for the medicine batch should be taken into consideration.

2.2. Accessibility to patients/consumers with diverse abilities

Statement

ePI will facilitate creation of PI that is accessible to everyone, including patients/consumers with print impairments such as blind and partially sighted people (e.g. use of large font size) and those with low literacy levels (e.g. audible formats). ePI on the web will be accessible to screen readers, convertible to large font and amenable to other accessible formats.

Rationale

Current PDF and print copy formats of PI do not well serve all citizens equally, given the wide range of abilities throughout society.

In contrast with current PDF and print copy formats of the PI, the availability of ePI will allow third-parties, such as companies, not-for-profit organisations or patient/consumer groups, to convert the PI into accessible formats.

Implication

ePI will be accessible by design.

3. Existing legislative framework

Implementation and use of ePI must comply with the legislation in force. These principles underline some of the legislation relevant to ePI.

3.1. Complementing paper package leaflet

Statement

ePI will not supersede or negate the requirement of the pharmaceutical legislation (Article 58 of Directive 2001/83/EC[1]) to include a PL in the packaging of all medicines or directly convey all information required (by Articles 59 and 62 of the Directive) on the outer or immediate packaging.

Since the current legislation does not require the use of an electronic version of PI, the use of ePI will not constitute a new legal obligation.

Rationale

The ePI is intended to expand the formats in which PL is available and not to remove or substitute the currently available paper format. PLs are a valuable tool presented directly in the medicines package and therefore provided to all patients/consumers when they open their medicine. The paper PL is particularly important for patients/consumers with low digital literacy (low ability to use digital devices effectively) or limited internet access.

Implication

Generation of ePI does not involve any change to the content of the PI. ePI generation will be performed in addition to the current inclusion of the PL in the medicine package. The use of ePI will be a recommended innovation; however it is not mandatory.

The paper PL should include a statement directing to the ePI as the most up-to-date version of the PL.

3.2. Open access to regulator-approved information only

Statement

ePI is intended for the delivery of regulator-approved medicine PI only. The content of ePI should be identical to the latest version of the PI approved by regulatory authorities. ePI will not be used for delivery of promotional information.

ePI should always be published as open data, freely accessible for use and reuse.

Rationale

The development and implementation of ePI will be carried out in accordance with applicable EU legislation; therefore the content of ePI will be approved as a result of regulatory procedures currently prescribed in the legislation (or as will be amended by any future legislation). Accordingly, no additional information — either for promotional or other purposes — can be included in the ePI.

The European Interoperability Framework (underlying principle 2: openness) describes the principle of openness as the idea that all public data should be freely available for use and reuse by others, unless restrictions apply.

Implication

Since, by use of ePI, stakeholders must comply with the applicable EU legislation, which strictly regulates the content of PI and excludes any element of a promotional nature, the rights of patients and consumers to have access to validated, non-promotional information will be maintained.

3.3. Data protection

Statement

ePI itself will not include any personal data.

In any event where processing (e.g. collecting or handling) of personal data may occur in relation to the implementation and use of ePI, for example in the context of a mobile application developed for the use of patients to access ePI, personal data processing must be in accordance with applicable European data protection legislation. This includes, in particular Regulation (EU) 2016/679 (GDPR) and Regulation (EU) 2018/1725 applicable to EU institutions.

Rationale

All parties involved in the development and use of ePI including the members of the European medicines regulatory network, MAHs, other companies and healthcare professionals are reminded of their obligation to comply with applicable European data protection legislation, which includes Regulation (EU) 2016/679 (GDPR) and Regulation (EU) 2018/1725.

Implication

All stakeholders processing personal data in relation to ePI must ensure full compliance with the applicable European data protection legislation.

4. Processes

The following principles relate to the implementation of ePI, including processes, roles and responsibilities.

4.1. Governance

Statement

It is envisaged that, eventually, ePI format will be used for the PI of all human medicines authorised in the EU by all EU authorities from the point of submission and throughout the evaluation process.

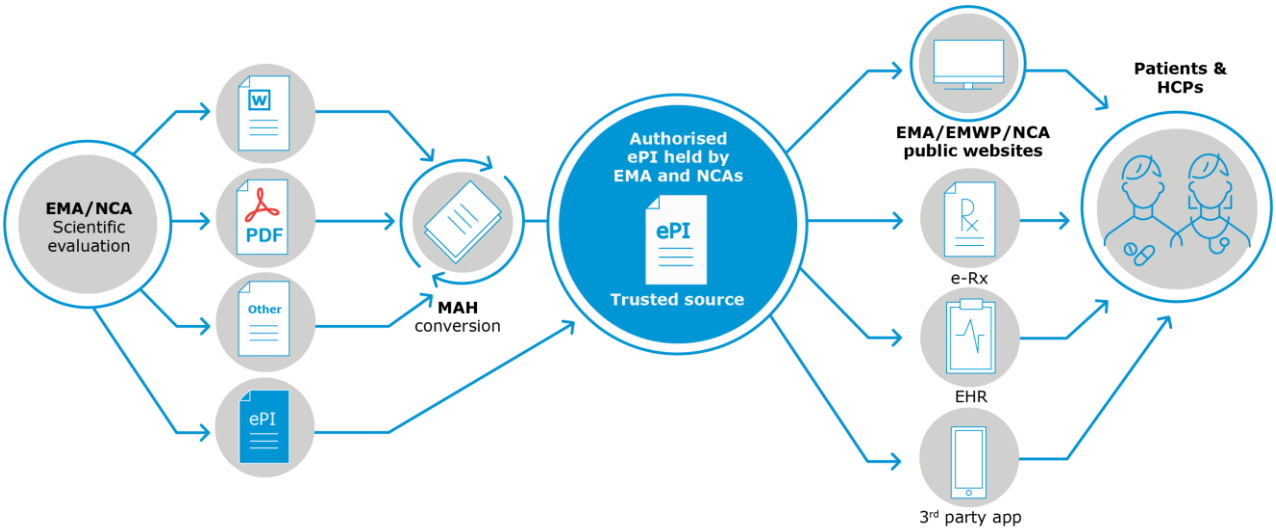
However, in the short and medium term, regulatory authorities may decide to implement ePI using a step-wise approach: ePI may either be used throughout the assessment, or alternatively, assessment may be performed as is done currently, and the PI converted to ePI once the regulatory procedure is complete.

ePI will be made available to users (patients/consumers and healthcare professionals) through websites at EMA level and if available, Member State level.

ePI data will be made available for use in other e-health systems, such as electronic health records and e-prescribing systems.

ePI will also be available for use by third-parties, who can reproduce ePI and make it available to patients and healthcare professionals.

Figure 1. Proposed model for ePI process (subject to change following feasibility analysis once ePI project is started). Following regulatory evaluation, if final PI is not already in ePI format, it is converted to ePI by the MAH using a conversion tool. As currently done for the final PI in PDF, the final ePI will be accompanied by a declaration from the MAH confirming that the converted version is identical in content to the one approved (in Word or other format). ePI for both nationally and centrally authorised products (NAPs and CAPs) can be accessed from the European medicines web portal (EMWP) and NCA public websites. ePI can be used with systems for e-prescribing (e-Rx) and electronic health records (EHR). Data can be accessed by third-party providers for example, for use in patient/consumer apps.



Rationale

Currently, the responsibility for creating the final PI files after the content is approved by the regulator lies with the MAH, and this will also be the case for ePI.

Where authorities are not using ePI throughout the assessment, conversion to ePI may take place once the evaluation is completed.

The regulator should hold ePI data, as a trusted source for reliable medicines information. The NCA in each country will store and handle ePI in their jurisdiction. In addition, it is envisaged that a pan-European medicines web portal could provide a central point for access of ePI for all centrally and nationally authorised medicines.

Implication

During implementation, it is anticipated that several scenarios will co-exist in the EU in the short to medium term.

1. No ePI: authorisation is performed as is done today and ePI format is not yet generated for the authorised medicine;
2. Conversion to ePI: authorisation is performed as is done today and once the procedure is complete, PI is converted to ePI;
3. Submission of ePI: PI is submitted to the authorities in electronic format, evaluated in this format, and is therefore already in ePI format once the evaluation procedure is complete.

4.2. Flexibility in implementation

Statement

All stakeholders, including pharmaceutical companies and regulators, will commit to implementation of the common electronic standard for creation of ePI for all EU medicines. However, it is recognised that timelines and processes for implementation should be flexible to allow for variations in resources and priorities. A roadmap will be proposed by HMA and EMA to guide implementation.

Rationale

The size and complexity of the task of creating ePI for European medicines is such that it is unrealistic to envisage implementation throughout the EU simultaneously.

In addition, handling ePI may be a significant burden for some Member States as well as certain companies such as micro, small or medium-sized enterprises (SMEs) and companies producing generic medicines.

Implication

Once a common standard and governance process are established, stakeholders must plan for their implementation in their jurisdictions according to a roadmap, including timelines, determined at HMA and EMA level.

Some early-adopter Member States may begin using ePI for their authorised medicines as soon as possible, whereas other Member States may have different priorities for implementation. Also, some Member States may wish to implement ePI throughout the medicines authorisation process and use it as a vehicle for exchanges on the PI with the applicant during the assessment, whereas other Member States may wish to have the SmPC, labelling and PL converted to ePI format only once the evaluation process has been finalised.

Support and flexibility for pharmaceutical companies in implementation will also be considered.

Flexible implementation should also include planning for conversion of existing PIs of authorised medicines to the new ePI format. This could be incorporated into post-authorisation procedures.

Flexibility will allow for divergent mechanisms and timelines for implementation, as these will still ultimately allow a harmonised approach for ePI across the EU.

5. EU context

These principles describe how ePI fits into the multilingual EU environment and interacts with other ongoing initiatives.

5.1. Multilingual ePI

Statement

ePI should support all official EU languages and Icelandic and Norwegian so that EU citizens will be able to read ePI in their preferred language when authorised ePI in that language is available.

Rationale

The PI for a centrally authorised medicine is available in all official EU languages (plus Norwegian and Icelandic) and the PI for a nationally authorised medicine is available in one or more official language(s) of the Member State where the medicine is placed on the market.

National authorities decide in which official language(s) PI will be provided in their countries for nationally authorised products.

ePI should also be possible in these languages, as applicable. Availability of ePI in patients'/consumers' and healthcare professionals' own language, where available, facilitates full understanding.

PI may be needed in non-EU languages in some Member States. National authorities are responsible for additional non-EU languages and these are not currently in the scope of the ePI initiative.

Implication

ePI design and implementation must, from the start, ensure capability to provide PI in all official EU languages as well as Icelandic and Norwegian.

5.2. Interoperability with EU and global initiatives

Statement

ePI will interface and interact with many ongoing and foreseen eHealth initiatives. eHealth and related services should work together, within and across organisations or domains. ePI interoperability with cross-border prescription, electronic health records, the future European medicines web portal, pharmacovigilance systems, SPOR data management services, a future European common data model and national ePI systems must be considered in the design of EU ePI. Use of ePI in both an EU and global context should also be taken into account.

Rationale

This collaboration takes place in the context of today's ongoing digital transformation of healthcare. Digital tools and services such as electronic health records, e-prescribing, mobile platforms and wearables gather data and disseminate knowledge, yet maximising the benefits of digital technologies to public health will depend on ensuring the flow of data through interconnected health systems to deliver point-of-need access to the information that matters to patients/consumers and healthcare professionals.

The EC eHealth policy anticipates that 'person-centred approaches' can ensure improved patient well-being and quality of care and contribute to sustainable health systems. Patients/consumers and healthcare professionals need information from the PI at various points in the treatment journey, including information on use and administration of the medicine, how to recognise possible side effects and how to act in the light of new safety data. Interoperability will ensure that this information can be delivered to patients/consumers at the point of need through interaction of the ePI with electronic health records and e-prescriptions.

The European Interoperability Framework recommends (recommendation 9) ensuring data portability, namely that data is easily transferable between systems and applications supporting the implementation and evolution of European public services without unjustified restrictions, in accordance with the legal framework.

Implication

ePI will be interoperable by design with eHealth initiatives and EU Telematics projects, and will consider national infrastructures and global health standards.