EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Optimising the use of the EURD list – the key to the single assessment: Procedural aspects

Periodic Safety Update Report Information Day
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An agency of the European Union

Disclaimer

Legal bits: Basis

DIR Article 107c (paragraphs 4 and 7), and REG Article 26(g)

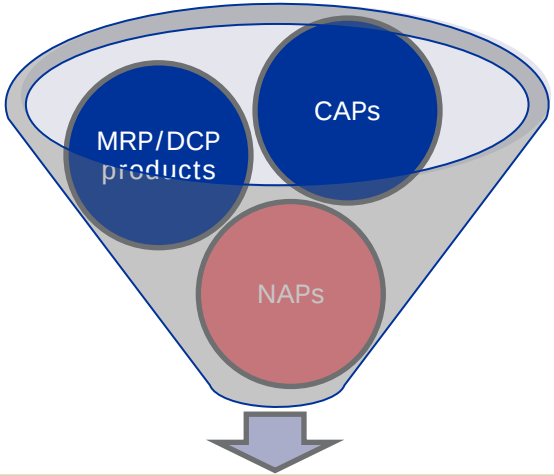
1. Active substance in the “List of European Union reference dates and frequency of submission of Periodic Safety Update Reports” (EURD list): PSUR Submission as part of a PSUSA procedure
2. AS not in the EURD list & MA contains a condition for the PSUR frequency: Submission nationally
3. MA contains no condition, and AS not on EURD list: Submission nationally , frequency follows article 107c (2) of Directive 2001/83/EC:

   - at least every 6 months following authorisation and until the placing on the market;
   - at least every 6 months during the first 2 years following the initial placing on the market
   - once a year for the following 2 years and at three-yearly intervals thereafter.

Legal bits: Scope

- Substances/combinations subject to the **EU single assessment of PSURs** as defined in Art 107e of Directive 2001/83/EC

Substances or combinations contained in…



Substances or combinations authorised in more than 1 MS

- Single Assessment procedure involving **CAPs only** → Started in July 2012
- Single Assessment procedure of **CAPs + NAPs** → Started in April 2013 (EURD list entered into force)
- Single Assessment procedure involving **NAPs only** → Started in January 2015

Information from the EURD list

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16 January 2015
EMA/630645/2012 Rev.26 Corr*
Business Data and Support Department

List of Union reference dates and frequen

Related Information:
Introductory cover note to the List of European Union reference dates and frequency of Requests for amendments of the EU reference dates list
The PSUR assessment procedure will start according to the Timetables published on EMA
Single Assessment Reports of PSURs are shared among all Marketing Authorisation Holders involved in the concerned procedure

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/10/WC500133157.pdf
http://www.ema.europa.eu/docs/en_GB/document_library/Template_or_form/2012/10/WC500133160.xls
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/07/

PSUR Submission according to the EURD List

Changes take effect 6 months after

Procedure Numbers Rapporteur (CAPs) /LMS (NAPs)

Active substances and combinations of active substances	European Union reference date (EURD) Not Available* = EURD not provided during the consultation phases	PSUR Submission Frequency	DLP	Submission date (According to the timelines defined in GVP Module VII, Section A)	Are PSURs required for products referred to in Articles 10(1), 10a, 14, 16a of Directive 2001/83/EC as amended? Yes/No	Publication Date (in accordance with Article 107c(7) Directive 2001/83/EC as amended)	Notes	Procedure number of the PSUR single assessment (DLP)	PRAC representative of the PSUR single assessment procedure	(Lead) Member State of the PSUR single assessment procedure	Centrally authorised product(s) (CAP)	Nationally authorised product(s) (NAP)
(18F) fludeoxyglucose	14/11/1994	3 years	30/11/2014	28/02/2015	No		Lead MS was added on 22/12/2014	PSUSA/00001437/201411	Arnaud Batz	France		NAP
1,3-butanediol, cinchocaine hydrochloride,	23/09/1983	13 years	15/05/2025	13/08/2025	No	01/10/2012		PSUSA/00000759/202505				NAP
125i-human serum albumin	15/12/1989	13 years	15/12/2025	15/03/2026	No	01/10/2012		PSUSA/00000003/202512				NAP
131i-6-iodo-norcholesterol	21/06/1990	13 years	21/06/2025	19/09/2025	No	01/10/2012		PSUSA/00000004/202506				NAP
^{13}C-urea	14/08/1997	5 years	15/01/2018	15/04/2018	No	01/10/2012		PSUSA/00000006/201801			CAP	
5 fluorouracil (i.v. application)	16/12/1977	3 years	16/12/2014	16/03/2015	Yes	01/10/2012	Lead MS was added on 22/12/2014	PSUSA/00000007/201412	Nectaroula Cooper	Cyprus		NAP
5 fluorouracil (topical application)	Not Available*	3 years	16/12/2014	16/03/2015	Yes	01/10/2012	Lead MS was added on 22/12/2014	PSUSA/00010000/201412	Nectaroula Cooper	Cyprus		NAP
5 fluorouracil, salicylic acid	25/05/1994	3 years	25/05/2015	23/08/2015	No	01/10/2012		PSUSA/00000008/201505				NAP
5-aminolevulinic acid (glioma)	07/09/2007	3 years	07/03/2015	05/06/2015	Yes	01/10/2012		PSUSA/00000009/201503			CAP	
5-aminolevulinic acid (keratosis)	07/09/2007	1 year	14/06/2014	23/08/2014	No	31/01/2014		PSUSA/00010006/201406	Martin Huber	Germany	CAP	NAP
abacavir	29/06/1998	3 years	31/12/2013	31/03/2014	Yes	01/10/2012		PSUSA/00000010/201312	Arnaud Batz	France	CAP	
abacavir, lamivudine	14/11/2003	3 years	31/12/2013	31/03/2014	Yes	01/10/2012		PSUSA/00000011/201312	Arnaud Batz	France	CAP	
abacavir, lamivudine, zidovudine	28/12/2000	3 years	31/12/2013	31/03/2014	Yes	01/10/2012	PSUSA procedure published on 01/04/2014	PSUSA/00003144/201312	Arnaud Batz	France	CAP	NAP
abarelix	Not Available*	13 years	01/01/2025	01/04/2025	No	01/10/2012		PSUSA/00000012/202501				NAP
abatacept	22/12/2005	3 years	22/12/2016	22/03/2017	No	08/08/2014	Correction of DLP was done on 02/05/2014	PSUSA/00000013/201612			CAP	

Examples for entries

1 row in the EURD list = 1 PSUR Single Assessment (PSUSA) procedure

a) Separate entries specific to:

- Indications

zoledronic acid (indicated for cancer and fractures)
zoledronic acid (indicated for Osteoporosis)

- Formulations / Routes of administration

5 fluorouracil (i.v. application)
5 fluorouracil (topical application)
ketorolac (ophtalmic formulations)
ketorolac (systemic formulations)

b) Merged entries to indicate that substances or combinations will follow a single assessment:

hydrochlorothiazide / telmisartan, telmisartan

acetylsalicylic acid / clopidogrel, clopidogrel

Link with other EMA databases and systems

Principle: Products matching individual EURD list entry in Art.57 database (XEVMPD)

Fees

- fee cover note sent in advance of a PSUSA procedure
- at start of procedure: invoices

PSUR repository

- upload of product selection in PSUR repository: submission only for products in DB
- EURD list entry determines also submission deadline in repository

PSUSA Procedure

- Appendix to Assessment report

How to request changes

- Email to EURDlist@ema.europa.eu
- Structured template
- Request for one EURD entry per request

Examples for requests

- Addition of new NAPs not covered by EURD list yet
- Harmonisation with IBD (usually from MAHs after initial MA)
- Change/harmonisation of frequency (outcome of assessment or following request)
    - Mycophenolic acid harmonised with mycophenolate mofetil
- PSUR submission requirement for Generics
- Merging of entries (e.g. to allow submission of a single PSUR)
    - lisinopril/hydrochlorothiazide with lisinopril
    - atorvastatin (adult indication) with atorvastatin (paediatric indication)
- General queries (Scope of procedure, questions on how to submit queries etc.)

Maintenance of the list: processing of requests

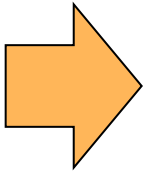
- Check of Article 57 database for overview of products authorised in EU
- EMA liaises with LMS (or P-RMS if LMS not appointed yet) e.g. on proposed DLP, frequency, requirement for generics.
- Alternatively MSs where the substance was identified as authorised in Art.57 DB are contacted for input.
- Consultation with Granularity and Periodicity Advisory Group (GPAG) as appropriate

1. Change to EURD list to be adopted by CMDh/CHMP after PRAC consultation;

2. Any changes to the EURD list come into force 6 months after its publication

Example : merging entries

Active substances and combinations of active substances	PSUR Submission Frequency	DLP
calcium chloride dihydrate, glucose monohydrate	15 years	01/01/2027
calcium chloride dihydrate, glucose monohydrate, sodium chloride	13 years	01/01/2025
calcium chloride dihydrate, glucose, potassium chloride, sodium chloride	13 years	22/03/2025
calcium chloride, glucose monohydrate, magnesium chloride hexahydrate	15 years	01/01/2027
glucose	13 years	01/01/2025
glucose, potassium chloride	5 years	17/04/2019
glucose, potassium chloride, sodium chloride, sodium citrate	13 years	01/01/2025
glucose, sodium chloride	13 years	01/01/2025



Active substances and combinations of active substances	PSUR Submission Frequency	DLP
glucose (apart from glucose1-phosphate) / glucose in combination with calcium chloride and/or sodium chloride and/or magnesium chloride and/or sodium citrate and/or potassium chloride (parenteral use)	13 years	01/01/2025

Maintenance of the list: routine work

- Inclusion of new CAPs (automatic following EC Decision)
- Bidding for LMSs (ca 10 months in advance of DLP) and subsequent reflection in list
- Removal of entries in case products are not authorised in >1 MS in Art. 57 DB
- Updates following PSUSA assessments and Referrals (CAPs & NAPs) and procedures involving CAPs (variations, renewals)
- Inclusion of next DLP/submission date once a PSUSA is finalised

The EURD list in summary…

- Supports the single EU assessment procedure by harmonisation of DLPs and frequency of PSURs for products with active substances authorised in >1 MS
- Periodicity defined on a risk-based approach: Optimisation of the management and assessment of PSUR for the same active substance;
- Increase of predictability in terms of PSUR submission.
- Linked with PSUR repository and fees through Art. 57 database
- MAHs and MSs can request changes to entries via email to EURDlist@ema.europa.eu, or as part of PSUSA (& other) procedures
- Updated on a monthly basis
- The Future: web-based interface, automatic entries based on new NAPs, database…

Thank you for your attention