



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Communicating benefits and risks of medicines within the EU Regulatory Network

Joint PCWP/HCPWP Workshop on benefit-risk communication

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An agency of the European Union



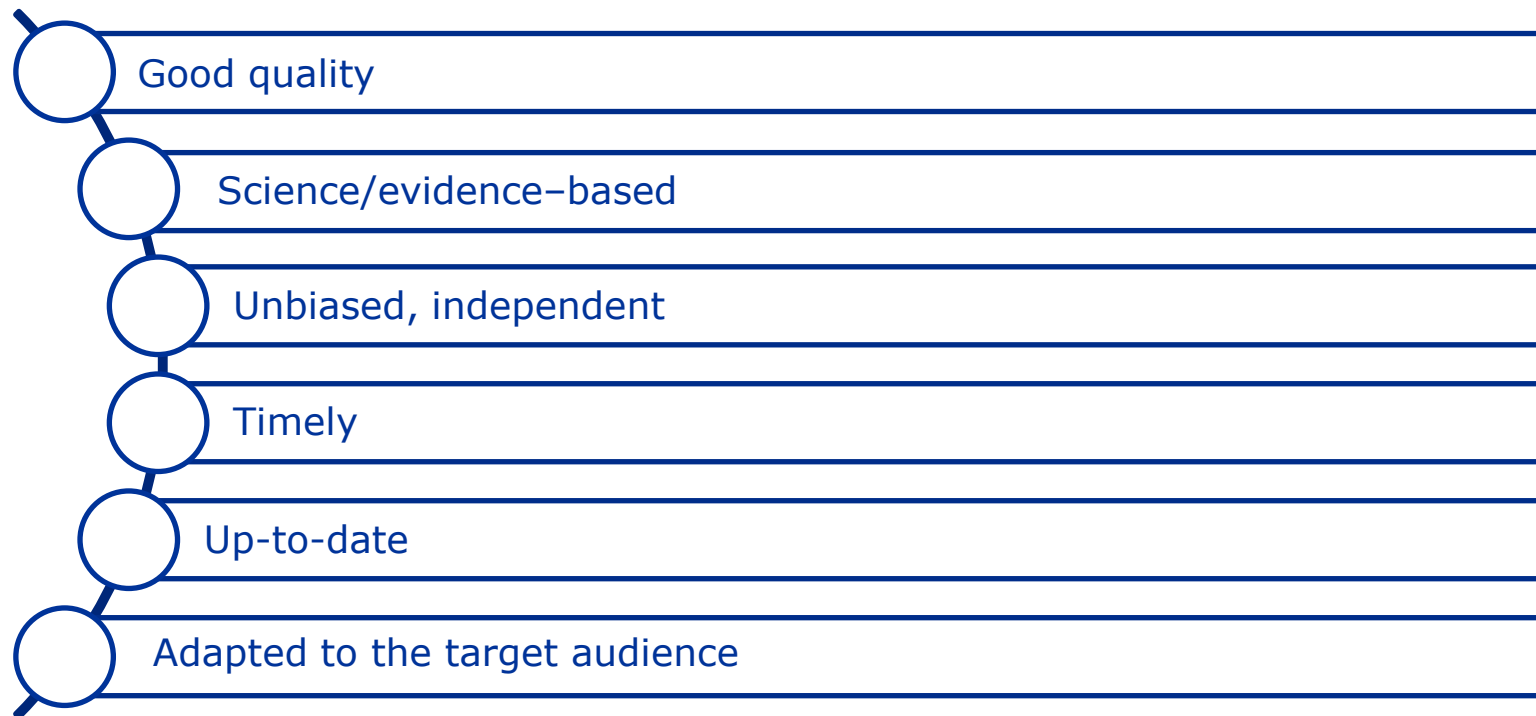


- Evolving role of regulatory authorities in benefit-risk communication:
 - Post-trust environment
 - New legislation
 - Higher demands from society and stakeholders
 - Today, a major outcome of regulatory process
- Refocusing our target audiences:
 - From industry and regulators
 - To patients, consumers and healthcare professionals
- Adapting and using different tools;
- Built as an interactive, conversational process.

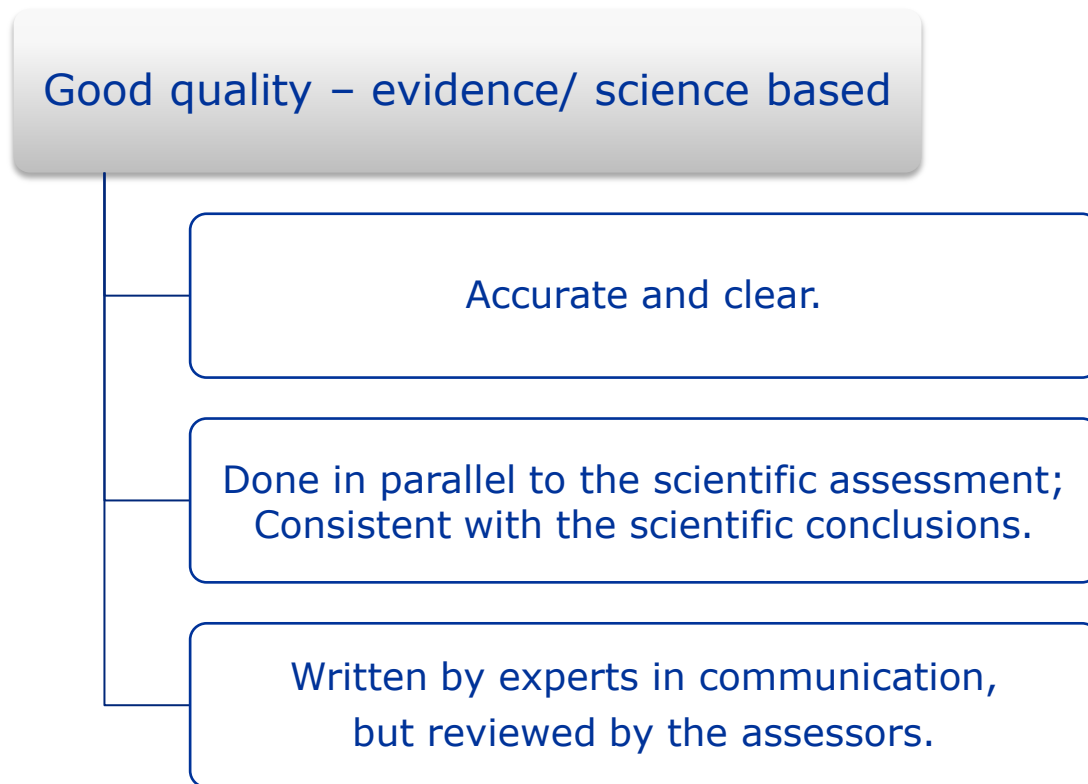
Good information and communication on benefit-risk

- Allows to choose the right treatment and to make informed decisions on medicines;
- Contributes to the safe and appropriate use of medicines;
- Describes the risks, in the context of the benefits, and explains how to manage them;
- Key, intrinsic element of the regulatory process, redounding to patient safety.

Elements of good benefit-risk communication



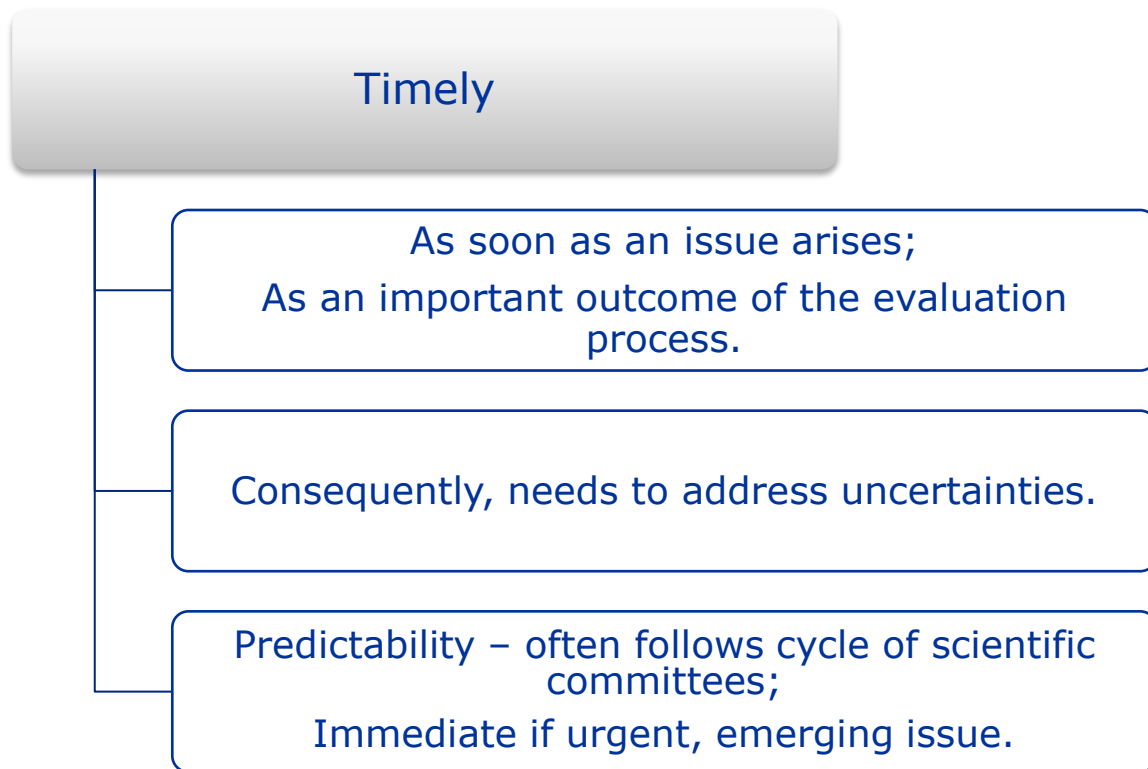
Elements of good benefit-risk communication



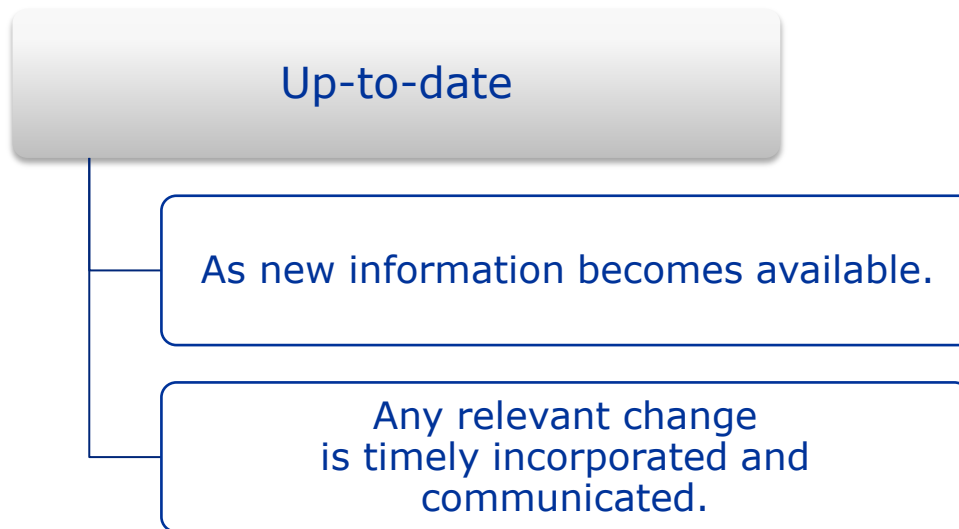
Elements of good benefit-risk communication



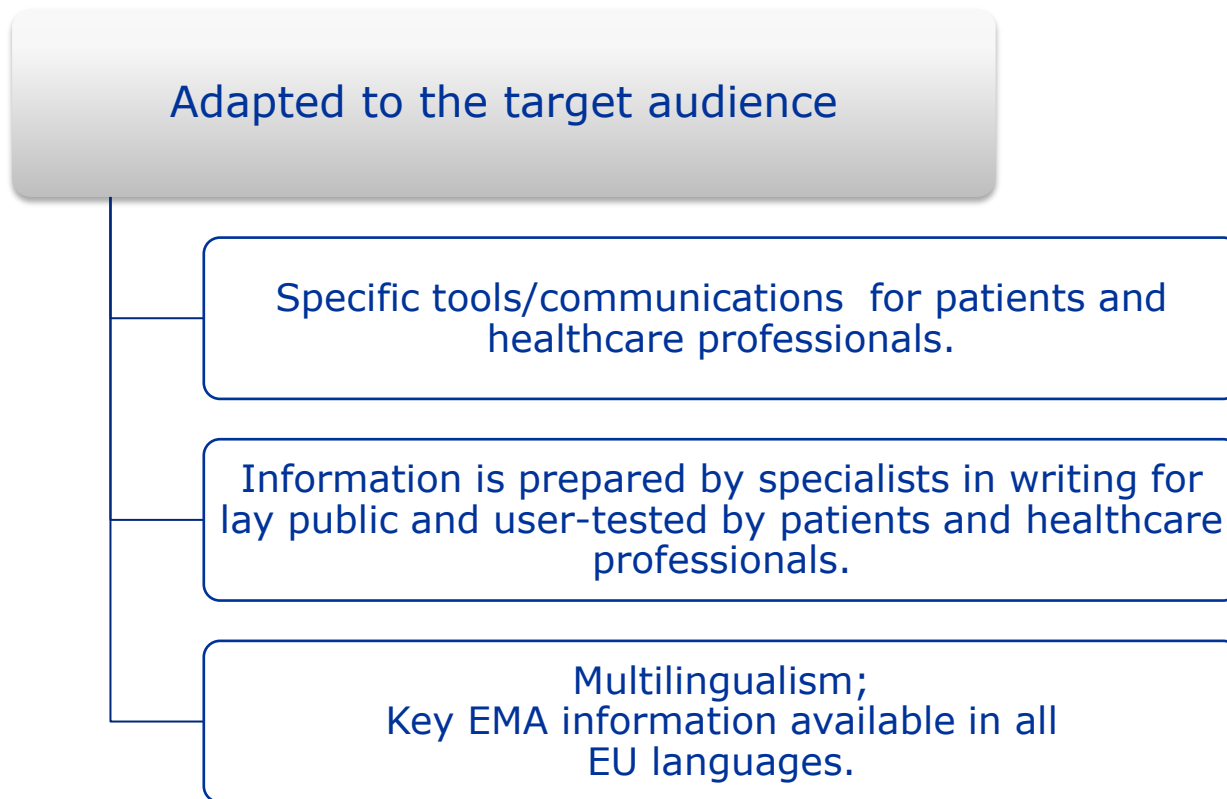
Elements of good benefit-risk communication



Elements of good benefit-risk communication



Elements of good benefit-risk communication



Coordination of information within the EU regulatory Network

- Aim of coordinating information: **clear, consistent messages for EU patients and healthcare professionals**
- Prior to the publication of a key (safety) announcement, the Member States, the EMA or the European Commission inform each other (not less than 24 hours in advance)
- Criteria for coordination have been defined
- The EMA is responsible for this coordination – ‘Early notification System’

Who provides information on benefit-risk within EU Regulatory Network?

Coordinated effort:

- EMA holds comprehensive multilingual information on benefit-risk of medicines authorised centrally (via EMA);
- EMA **DOES NOT** hold information on medicines authorised via decentralised/ national procedures – this is provided by NCAs at national level;
- EMA also communicates on emerging safety issues (for all medicines authorised in EU) – 2012 PhV legislation;
- EU medicines webportal – under development.

Means of benefit-risk communication

Tools and channels (currently used by EU Regulatory Network):

- Website and web-based communications
- Direct healthcare professional communications (DHPC)
- Press communications
- Documents in lay language for patients and dedicated information for health professionals
- Inter-authority communications (LTT)
- Public enquiries
- Bulletins and newsletters
- Others (e.g. scientific journals, etc)

What and when information on medicines is provided?



Comprehensive information on the medicine's:

- Benefit-risk evaluation;
- Conditions of use.



- Any variation/change;
- Other relevant (safety) info.

Benefit-risk communication at the time of authorisation

EPAR summary	• Information in lay language on the benefits and risks of medicine and how it was assessed
Product Information	• SmPC - for health professionals • Package leaflet - for patients
Summary of risk management plan	• Summary of the medicine's safety profile and the measures taken to prevent or minimise its risks
Assessment report	• The full scientific evaluation

At time of authorisation

Product information

- Information on the benefit of the medicine is now included in the package leaflet;
- Summary of the safety profile is now included in the SmPC, and is the basis for the package leaflet's safety information:
 - List the most serious side effects first
 - Followed by a list of all other side effects ordered by frequency
 - With advice on what to do



Product information

European public assessment reports
Patient safety
Pending EC decisions
Withdrawn applications
Paediatrics
Rare disease designations
Medicines under evaluation

Plegridy
peginterferon beta-1a

About
Authorisation details
Product information
Assess

[« Previous tab](#)
Product information
18/07/2014 Plegridy -EMA/H/C/002827 --

Name	Language	First published
	EN – English	

Package leaflet: Information for the user

Plegridy 63 micrograms solution for injection in pre-filled syringe
 Plegridy 94 micrograms solution for injection in pre-filled syringe
 Plegridy 125 micrograms solution for injection in pre-filled syringe
 Peginterferon beta-1a

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Plegridy is and what it is used for
2. What you need to know before you use Plegridy
3. How to use Plegridy
4. Possible side effects
5. How to store Plegridy
6. Contents of the pack and other information
7. Instructions for injecting Plegridy

How Plegridy works

Plegridy seems to work by stopping the body's immune system from damaging your brain and spinal cord. This can help to reduce the number of relapses that you have and slow down the disabling effects of MS. Treatment with Plegridy can help to prevent you from getting worse, although it will not cure MS.

Please note that the size of the above document can exceed 50 pages.
 You are therefore advised to be selective about which sections or pages to print.

How Plegridy works

Plegridy seems to work by stopping the body's immune system from damaging your brain and spinal cord. This can help to reduce the number of relapses that you have and slow down the disabling effects of MS. Treatment with Plegridy can help to prevent you from getting worse, although it will not cure MS.



Product information

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

and discontinuation of therapy should be considered (see section 5.3). In patients with a high relapse rate before treatment started, the risk of a severe relapse following discontinuation of Plegridy in the event of pregnancy should be weighed against a possible increased risk of spontaneous abortion.

Pregnancy

There is limited information on the use of Plegridy in pregnancy. Available data indicates that there may be an increased risk of spontaneous abortion. Initiation of treatment is contraindicated during pregnancy (see section 4.3).

Breast-feeding

It is not known whether peginterferon beta-1a is secreted in human milk. Because of the potential for serious adverse reactions in breast-feeding infants, a decision should be made either to discontinue breast-feeding or Plegridy therapy.

Fertility

There are no data on the effects of peginterferon beta-1a on human fertility. In animals, anovulatory effects were observed at very high doses (see section 5.3). No information is available on the effects of peginterferon beta-1a on male fertility in animals.

4.7 Effects on ability to drive and use machines

Central nervous system-related adverse events associated with the use of interferon beta (e.g. nausea) might influence the patient's ability to drive or use machines (see section 4.8).

4.8 Undesirable effects

Summary of safety profile

The most common adverse drug reactions (ADR) (at a higher incidence than placebo) for Plegridy 125 micrograms subcutaneously every 2 weeks were injection site erythema, influenza like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus, and arthralgia. The most commonly reported adverse reactions leading to discontinuation in patients treated with Plegridy 125 micrograms subcutaneously every 2 weeks was influenza-like illness (<1%).

Tabulated list of adverse reactions

In clinical studies 1468 patients received Plegridy for up to 177 weeks (overall exposure equivalent to 4937 person-years). 1093 patients received at least 1 year, and 415 patients have received at least 2 years of treatment with Plegridy. The experience in the randomised, uncontrolled phase 3 (see 2) of the ADVANCE study and in the 2 year safety extension study ATTAIN was consistent with the experience in the 1 year placebo-controlled phase of the ADVANCE study.

The table summarizes ADRs (incidence above placebo and with a reasonable possibility of causality) from 512 patients treated with Plegridy 125 micrograms subcutaneously every 2 weeks and 500 patients who received placebo for up to 48 weeks.

The ADRs are presented as MedDRA preferred terms under the MedDRA System Organ Class. The incidence of the adverse reactions below are expressed according to the following categories:

- Very common ($\geq 1/10$)
- Common ($\geq 1/100$ to $< 1/10$)
- Uncommon ($\geq 1/1,000$ to $< 1/100$)
- Rare ($\geq 1/10,000$ to $< 1/1,000$)
- Very rare ($< 1/10,000$)
- Not known (cannot be estimated from the available data)



Product information

Serious side effects

- Liver problems

(common - may affect up to 1 in 10 people)

If you get any of these symptoms:

- Yellowing of your skin or the whites of your eyes
- Itching all over
- Feeling sick, being sick *(nausea and vomiting)*
- Easy bruising of the skin
- **Call your doctor immediately.** They may be signs of a possible liver problem.

Other side effects

Very common side effects

(may affect more than 1 in 10 people)

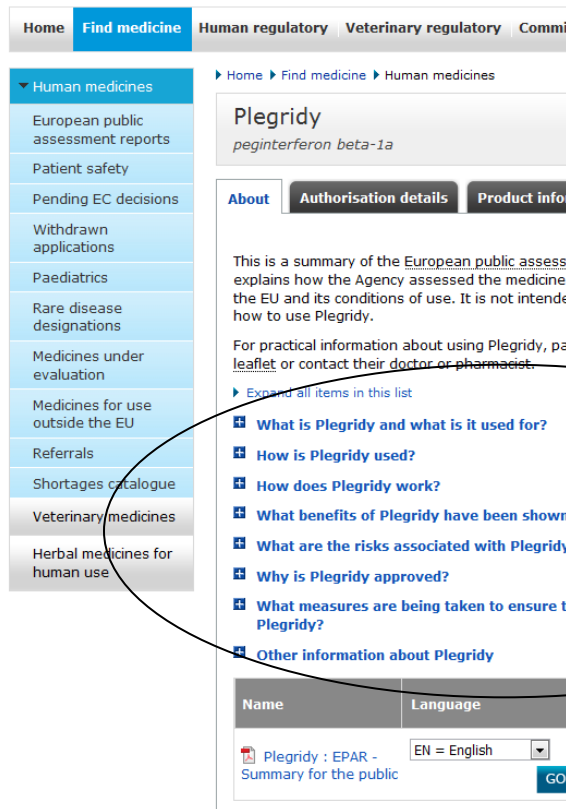
- Flu-like symptoms. These symptoms are not really flu, see below. You can't pass it on to anyone else.
- Headache
- Muscle pain *(myalgia)*
- Pain in your joints, arms, legs or neck *(arthralgia)*
- Chills
- Fever
- Feeling weak and tired *(asthenia)*
- Redness, itching or pain around the place you have injected
- **If any of these effects trouble you, talk to your doctor.**

At time of authorisation

EPAR summary

- EMA 'landing' page for each medicine (centrally) authorised;
- Written in lay language for lay audience;
- Available in all EU languages;
- Constantly kept updated;
- Provides access (links) to other information (e.g. product information)
- Summarises the evaluation of each medicine:
 - Explains the reasons why the medicine is approved (why its benefit/risk is positive).

EPAR summary



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Human medicines

- European public assessment reports
- Patient safety
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- Paediatrics
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- Shortages catalogue
- Veterinary medicines
- Herbal medicines for human use

Home Find medicine Human medicines

Plegridy

peginterferon beta-1a

About Authorisation details Product info

This is a summary of the European public assess explains how the Agency assessed the medicine the EU and its conditions of use. It is not intende how to use Plegridy.

For practical information about using Plegridy, p leaflet or contact their doctor or pharmacist.

Expand all items in this list

- What is Plegridy and what is it used for?
- How is Plegridy used?
- How does Plegridy work?
- What benefits of Plegridy have been show
- What are the risks associated with Plegridy
- Why is Plegridy approved?
- What measures are being taken to ensure t Plegridy?
- Other information about Plegridy

Name	Language
Plegridy : EPAR - Summary for the public	EN = English

GO

- + What is Plegridy and what is it used for?
- + How is Plegridy used?
- + How does Plegridy work?
- + What benefits of Plegridy have been shown in studies?
- + What are the risks associated with Plegridy?
- + Why is Plegridy approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that Plegridy's benefits are greater than its risks and recommended that it be approved for use in the EU. The CHMP considered that Plegridy given every two weeks has been shown to produce about a 30% reduction in the number of relapses in patients with relapsing-remitting MS compared with placebo, which is comparable to the effect of other MS medicines containing non-pegylated interferon beta, and is considered clinically relevant.

Also, the CHMP considered Plegridy to be of greater benefit to patients when given every two weeks as compared to less frequent injections tested in the study. When Plegridy was given every four weeks its beneficial effect was smaller, and it was not possible to identify a group of patients in whom this less frequent dosing was considered appropriate.

With regards to the safety profile, the most common adverse events observed during treatment with Plegridy are considered to be manageable and generally consistent with those seen with non-pegylated interferon products.

- + What measures are being taken to ensure the safe and effective use of Plegridy?

At time of authorisation

RMP summary

- First published in March 2014 - 1 year pilot phase;
- Increased transparency and access to relevant (safety) information;
- Complements and links to the EPAR summary and Product Information;
- Target audience:
 - Primarily – stakeholders with professional interest in medicines
 - Secondary – useful resource for any member of the public who wants to know more about his/her medicine

RMP summary – an example

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Plegridy
peginterferon beta-1a

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About Authorisation details Product information Assessment history

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This is a summary of the [European public assessment report \(EPAR\)](#) for Plegridy. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Plegridy.

For practical information about using Plegridy, patients should read the [package leaflet](#) or contact their doctor or pharmacist.

Expand all items in this list

- What is Plegridy and what is it used for?
- How is Plegridy used?
- How does Plegridy work?
- What benefits of Plegridy have been shown in studies?
- What are the risks associated with Plegridy?
- Why is Plegridy approved?
- What measures are being taken to ensure the safe and effective use of Plegridy?
- Other information about Plegridy

Name	Language	First published	Last updated
Plegridy : EPAR - Summary for the public	EN = English	31/07/2014	

Name	Language	First published	Last updated
Plegridy : EPAR - Risk-management-plan summary	(English only)	31/07/2014	

This EPAR was last updated on 31/07/2014 .

More detail is available in the [summary of product characteristics](#)

EMA/329000/2014

Summary of the risk management plan (RMP) for Plegridy (peginterferon beta-1a)

This is a summary of the risk management plan (RMP) for Plegridy, which details the measures to be taken in order to ensure that Plegridy is used as safely as possible. For more information on RMP summaries, see [here](#).

This RMP summary should be read in conjunction with the EPAR summary and the product information for Plegridy, which can be found on [Plegridy's EPAR page](#).

Overview of disease epidemiology

Plegridy is used to treat the relapsing-remitting form of multiple sclerosis (MS). MS is a disease in which the body's immune system malfunctions and attacks parts of the central nervous system (the brain and spinal cord). This causes inflammation and destroys the protective sheath around the nerves, leading to progressive disability. Onset of MS is usually between the ages of 20 and 40 years, and rarely occurs in children or in adults 60 years and older. Approximately twice as many women than men have MS. About 85% of people with MS initially have the relapsing-remitting form, characterised by occasional flare-ups of the disease, called relapses, in between periods when the disease is inactive. About half of patients with MS relapses go on to develop progressive MS within 10 to 20 years after diagnosis. The total number of people with MS worldwide is estimated to be between 2 to 2.5 million, and approximately 93 of every 100,000 persons in Europe have MS.

Summary of treatment benefits

Plegridy is a medicine that contains the active substance peginterferon beta-1a. It is available as a solution for injection under the skin. The peginterferon beta-1a in Plegridy is a 'pegylated' interferon (a protein naturally produced by the body), which is removed from the body at a slower rate than other interferons, allowing the medicine to be given less often.

Plegridy was investigated in 1,516 patients in one main study, in which it was compared with placebo (a dummy treatment). Plegridy showed about a 30% reduction in the number of relapses in patients with relapsing-remitting MS compared with placebo, which is comparable to the effect of other MS



RMP summary – an example

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
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Important potential risks

Risk	What is known
Cardiac (heart) disorders	Worsening of cardiac disease has been reported in patients receiving interferon beta. If patients develop heart problems, which can cause symptoms such as chest pain (angina), particularly after any activity; swollen

Missing information

Risk	What is known
Use in paediatric patients	Plegridy has not been studied in patients under 18 years of age.
Use in older patients	Plegridy has not been studied in patients over 65 years of age.
Effects on pregnancy and use in breastfeeding women	Treatment with Plegridy should not be started in pregnant patients. Patients who could get pregnant should use contraception during treatment with Plegridy. Patients planning to have a baby, or who become pregnant while using Plegridy, should tell their doctor to discuss possible treatment discontinuation. Patients wishing to breastfeed while using Plegridy should speak with their doctor first.

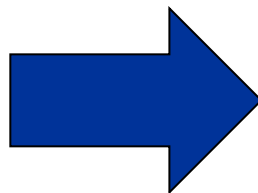
At time of authorisation

Assessment report

- Updated structure of the section describing benefit-risk, including:
 - Description of the beneficial effects
 - Uncertainty in the knowledge about the beneficial effects
 - Unfavourable effects
 - Uncertainty in the knowledge about the unfavourable effects
 - Importance of favourable and unfavourable effects
 - Discussion on the benefit-risk balance
 - Conclusion

Post-authorisation

- New therapeutic indications
- New contraindications
- Other variations

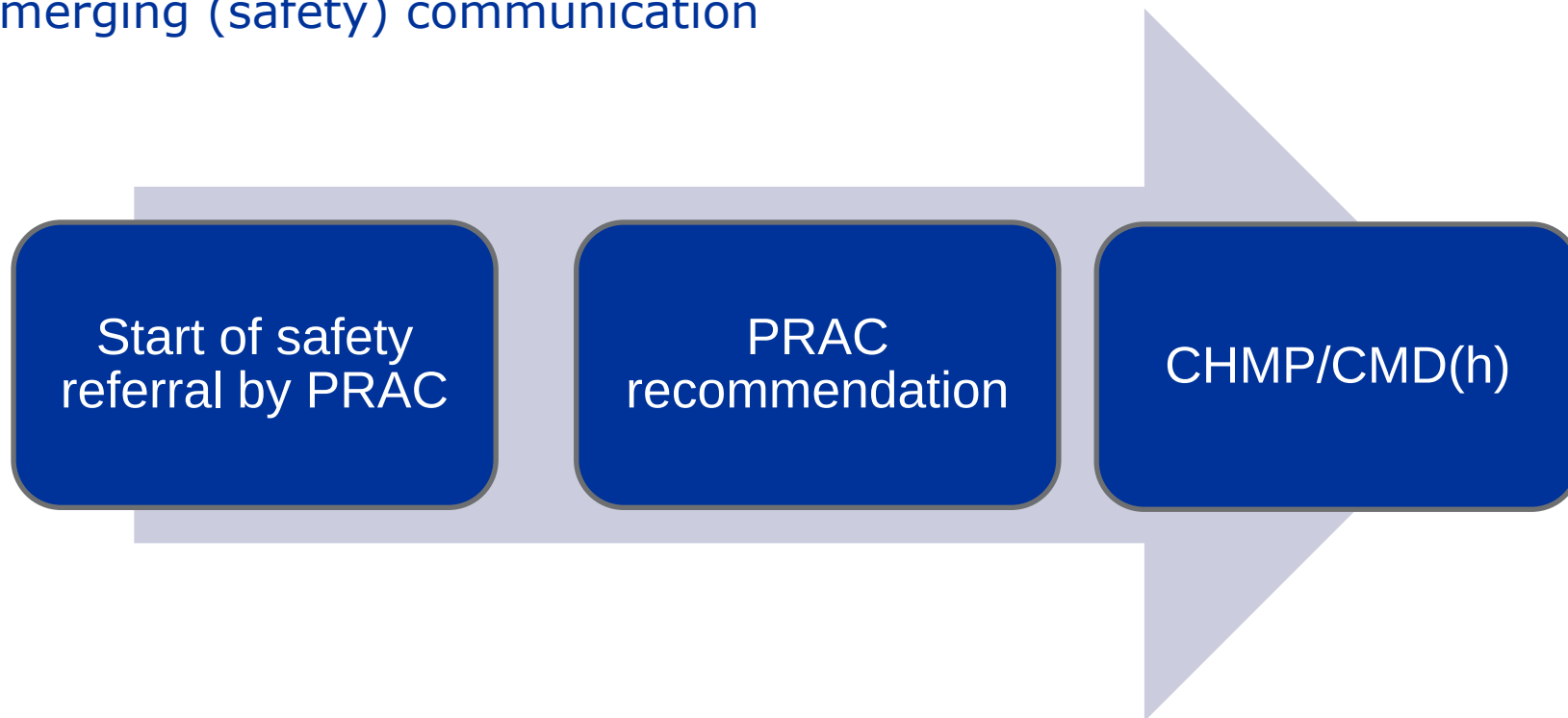


- Update of EPAR summary
- Update of Product Information
- Update of RMP summary
- Publication of relevant assessment report



Post-authorisation

Emerging (safety) communication





▼ Human medicines

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assessment reports

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Combined hormonal contraceptives

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Summary

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Benefits of combined hormonal contraceptives (CHCs) continue to outweigh risks

Product information updated to help women make informed decisions about their choice of contraception

On 21 November 2013, the European Medicines Agency completed its review of combined hormonal contraceptives (CHCs), particularly of the risk of venous thromboembolism (VTE or blood clots in veins) associated with their use. The European Medicines Agency's [Committee for Medicinal Products for Human Use \(CHMP\)](#) concluded that the benefits of CHCs in preventing unwanted pregnancies continue to outweigh their risks, and that the well-known risk of VTE with all CHCs is small.

The review has reinforced the importance of ensuring that clear and up-to-date information is provided to women who use these medicines and to the healthcare professionals giving advice and clinical care.

The [product information](#) of CHCs has been updated to help women make informed decisions about their choice of contraception together with their healthcare professional. It is important that women are made aware of the risk of VTE and its signs and symptoms, and that doctors take into consideration a woman's individual risk factors when prescribing a contraceptive. Doctors should also consider how the risk of VTE with a particular CHC compares with other CHCs (see table below).

The review also looked at the risk of arterial thromboembolism (ATE, blood clots in arteries, which can potentially cause a stroke or heart attack). This risk is very low and there is no evidence for a difference in the level of risk between products depending on the type of progestogen.

The CHMP opinion, in agreement with the previous recommendation by the [Pharmacovigilance Risk Assessment Committee \(PRAC\)](#), was sent to the European Commission, which adopted on 16 January 2014 a legally binding decision to update the [product information](#) of all CHCs throughout the EU.

Current status:
European
Commission final
decision

More information on combined hormonal contraceptives

- Evra: [EPAR](#)
- Ioa: [EPAR](#)
- Zoely: [EPAR](#)
- [Meeting highlights from the Committee for Medicinal Products for Human Use \(CHMP\) 18-21 November 2013 \(22/11/2013\)](#)
- [PRAC confirms that benefits of all combined hormonal contraceptives \(CHCs\) continue to outweigh risks \(11/10/2013\)](#)
- [Meeting highlights from the Pharmacovigilance Risk Assessment Committee \(PRAC\) 7-10 October 2013 \(11/10/2013\)](#)
- [Meeting highlights from the Pharmacovigilance Risk Assessment Committee \(PRAC\) 4-7 February 2013 \(08/02/2013\)](#)
- [European Medicines Agency starts safety review of Diane 35 and its generics \(08/02/2013\)](#)
- [Combined hormonal contraceptives](#)



► Expand all items in this list

Information to patients

- This Europe-wide review looked at the benefits and risks of combined hormonal contraceptives (CHCs), particularly the risk of blood clots associated with these medicines. It confirmed that the benefits of CHCs outweigh the risk of blood clots, which has been known for many years and is very low.
- If you have been taking CHCs without any problem, there is no reason for you to stop taking them on the basis of this review. But it is important that you are aware of the risk of blood clots associated with these medicines, even though it is very low.
- The risk of blood clots in the veins varies between CHCs, depending on the type of progestogen (a hormone) they contain, and ranges from 5 to 12 cases of blood clots per 10,000 women who use them for a year (see table below). This compares with 2 cases of blood clots in the veins each year per 10,000 women who are not using CHCs.
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- You should discuss with your doctor or nurse what is the most appropriate type of contraception for you.
- When taking CHCs, you should be alert for the signs and symptoms of blood clots, which may include severe pain or swelling in the legs, sudden unexplained breathlessness, rapid breathing or cough, chest pain, and weakness or numbness of the face, arm or leg. If you develop any of these signs and symptoms you should seek medical advice immediately.
- If you have any questions or concerns, speak with your doctor, pharmacist or nurse.

Information to healthcare professionals

More about the medicine

More about the procedure

Information to healthcare professionals

- The EU-wide review of combined hormonal contraceptives (CHCs) has confirmed that the known risk of venous thromboembolism (VTE) with all low-dose CHCs (ethinylestradiol < 50 mcg) is small.
- Differences exist between CHCs in their risk of VTE depending on the type of progestogen they contain. Currently available data indicate that CHCs containing the progestogens levonorgestrel, norethisterone or norgestimate have the lowest risk of VTE (see table below).
- When prescribing a CHC, careful consideration should be given to the individual woman's current risk factors, particularly those for VTE, and the difference in risk of VTE between products. CHCs are contraindicated if a woman has one serious or multiple risk factors that put her at high risk of blood clots.
- There is no evidence for differences between low-dose CHCs in their risk of arterial thromboembolism (ATE).
- Because a woman's individual risk factors will change over time, there is a need to regularly re-assess the suitability of her contraceptive.
- It is also important to raise awareness of the signs and symptoms of VTE and ATE when prescribing a CHC.
- Healthcare professionals should always consider the possibility of a CHC-associated thromboembolism when presented with a woman who has symptoms.

Risk of developing a blood clot (VTE) in a year

Women not using a combined hormonal pill/patch/ring and are not pregnant	About 2 out of 10,000 women
Women using a CHC containing levonorgestrel, norethisterone or norgestimate	About 5-7 out of 10,000 women
Women using a CHC containing etonogestrel or norelgestromin	About 6-12 out of 10,000 women
Women using a CHC containing drospirenone, gestodene or desogestrel	About 9-12 out of 10,000 women
Women using a CHC containing chlormadinone, dienogest or nomegestrol	Not yet known ¹

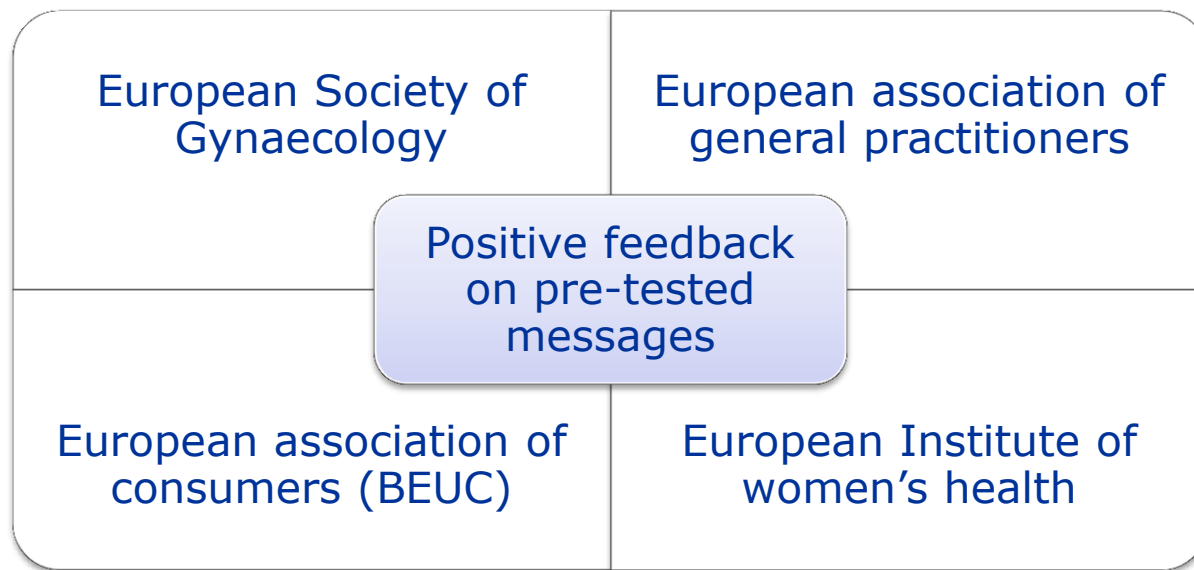
¹ Further studies are ongoing or planned to collect sufficient data to estimate the risk for these products.

Collaboration with EU patients, consumers and healthcare professionals

- Collaboration with individuals nominated by 'EU eligible organisations':
 - Actively through and with PCWP and HCP WP (EMA working parties with patients, consumers and healthcare professionals)
 - No financial support available
- Help us in:
 - Designing and adapting communication tools
 - Preparation of documents
 - Dissemination of key information timely among members
- Very useful feedback and experience.

Patient/healthcare professional involvement

Example: Combined Hormonal Contraceptives (CHCs)



Benefit-risk communication: conclusions

- Is an integral part of the regulatory process, necessary to carrying out the EU regulatory network's objective of protecting public health effectively;
- Communication vs transparency (avoid 'data dump');
- Patients, consumers and healthcare professionals – key audience for benefit-risk communication;
- Coordination, especially for new emerging information on benefit-risk is paramount in EU:
 - among regulatory authorities while involving patients and healthcare professionals
- Must be evaluated to ensure optimal effectiveness.



Thank you for your attention

