EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EPAR summary template

Proposed updates

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Background

- Legal requirement to publish public summary of full EPAR
- All official EU languages; kept updated
- Available in pdf and html – integrated in EMA website

Naglazyme

galsulfase

This is a summary of the European public assessment report (EPAR) for Naglazyme. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Naglazyme.

Collapse all items in this list

What is Naglazyme?

Naglazyme is a solution for infusion (drip into a vein) that contains the active substance galsulfase (1 mg/ml).

What is Naglazyme used for?

Naglazyme is used to treat patients who have mucopolysaccharidosis VI (MPS VI or Maroteaux-Lamy syndrome). This disease is caused by the lack of an enzyme called N-acetylgalactosamine 4-sulfatase, which is needed to break down substances in the body called glycosaminoglycans (GAGs). If the enzyme is not present, GAGs cannot be broken down and they build up in the cells. This causes the signs of the disease, the most noticeable being a short body, a large head and difficulty moving about. The disease is usually diagnosed in infants between one and five years of age.

Because the number of patients with MPS VI is low, the disease is considered 'rare', and Naglazyme was designated an 'orphan medicine' (a medicine used in rare diseases) on 14 February 2001.

AUTHORISED
This medicine is approved for use in the European Union

Naglazyme RSS feed

Related information

Naglazyme: Orphan designation

Background

- Template based on extensive consultation - reflection paper January 2006
- Current format since start of 2010 – new website
- Writers use template + other tools (guidance, glossary) to write summaries: structure, content, style

Reasons to update template

- Experience of medical writers + internal/external feedback: improvements, not radical changes
- User testing results
- Regulatory developments:
  - Summaries for MRP/DCP products to be published
  - Risk management plan summaries to be published

➢ Proposals from medical writers for consultation

(1) Main proposals

Revise wording of introduction

- Simplify wording – less regulatory
- Summary not intended to give practical advice; refer to PL (or doctor or pharmacist) for practical information on how to use medicine

Justification

- Clarify better what summary is and what it is not; refer to PL at start, in case this meets reader's needs better.
- Supported by user testing findings

(1) Before…

Xalkori

crizotinib

This is a summary of the European public assessment report (EPAR) for Xalkori. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Xalkori.

Other information about Xalkori

The European Commission granted a marketing authorisation valid throughout the European Union for Xalkori on < date of issue of the Marketing Authorisation>.

The full EPAR for Xalkori can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Xalkori, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 08-2012.

(1) …and after

Xalkori

crizotinib

This is a summary of the European public assessment report (EPAR) for Xalkori. 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 Xalkori.

For practical information about using Xalkori, patients should read the package leaflet or contact their doctor or pharmacist.

(2) Main proposals

Revise 1st question to: 'What is <X> and what is it used for?'

- Merge content of '*What is <X>'* and '*What is <X> used for'*
- State type of medicine in lay terms; active substance; indication(s)

Justification

- Place information where reader expects to find it; most relevant information (indication) first; secondary information (pharmaceutical form, strength) moved down.
- Supported by user testing findings

(2) Before…

What is Xalkori?

Xalkori is a medicine that contains the active substance crizotinib. It is available as capsules (200 mg and 250 mg).

What is Xalkori used for?

Xalkori is used to treat adults with a type of lung cancer called non-small cell lung cancer (NSCLC), when the disease is advanced and has already been treated before. It is only used if the NSCLC is 'ALK-positive', which means that the cancer cells contain certain defects affecting the gene responsible for a protein called ALK (anaplastic lymphoma kinase).

The medicine can only be obtained with a prescription.

(2) …and after

What is Xalkori and what is it used for?

Xalkori is an anticancer medicine which contains the active substance crizotinib. It is used to treat adults with a type of lung cancer called non-small cell lung cancer (NSCLC), when the disease is advanced and has already been treated before. It is used only for NSCLC that is 'ALK-positive', which means that the cancer cells contain certain defects affecting the gene responsible for a protein called ALK (anaplastic lymphoma kinase).

(3) Main proposals

Simplify content of 'How is <X> used?'

- Only provide: pharmaceutical form(s), main dose recommendations, method of administration, prescription status (if mentioned: treatment duration, specific monitoring/diagnostic tests)
- *Add standard sentence referring to PL for more information*

Justification

- Reduce potential for confusion with PL; not possible to give full information from SmPC 4.2
- User testing findings

(3) Before…

How is Xalkori used?

Treatment with Xalkori should be started and supervised by a doctor who is experienced in using anticancer medicines. The presence of the genetic defect affecting ALK ('ALK-positive' status) has to be confirmed in advance by appropriate methods.

The recommended dose is 250 mg twice per day, until the disease progresses or treatment cannot be tolerated due to side effects. If certain side effects develop the doctor may decide to interrupt or reduce the dose to 200 mg twice per day then to 250 mg once per day. In certain cases treatment should be permanently stopped, including if the patient has a severely prolonged QT interval (an alteration of the electrical activity of the heart).

The capsules should not be taken with grapefruit juice or St John's wort, as these can alter the amount of active substance in the patient's blood.

(3) …and after

How is Xalkori used?

Xalkori is available as capsules (200 mg and 250 mg). The recommended dose is 250 mg twice per day, until the disease progresses or treatment cannot be tolerated due to side effects. If certain side effects develop the dose may be interrupted or reduced. In certain cases treatment should be permanently stopped, including if the patient has a severely prolonged QT interval (an alteration of the electrical activity of the heart).

Xalkori can only be obtained with a prescription. Before treatment, the presence of the genetic defect affecting ALK ('ALK-positive' status) has to be confirmed by appropriate tests.

For further information, see the package leaflet.

(4) Main proposals

Studies: 'What benefits of <X> have been shown in studies?'

- Merge *'How has <X> been studied'* and *'What benefit has <X> shown during the studies'*
- Give primary endpoint results directly after study description. Bullet points if helpful (e.g. multiple indications)

Justification

- Address criticism that information harder to follow when results given separately
- Supported by user testing findings

(4) Before…

How has Adcetris been studied?

The effects of Adcetris were first tested in experimental models before being studied in humans.

In Hodgkin lymphoma, Adcetris has been studied in one main study in 102 patients with CD30-positive HL, who had previously received an autologous stem cell transplant and whose cancer had come back or had not responded to previous treatment. In addition, the company provided data on 40 patients with CD30-positive HL, whose cancer had come back or had not responded to at least two prior therapies and who are not eligible for autologous stem cell transplant or multi-agent chemotherapy.

In sALCL, Adcetris has been studied in one main study in 58 sALCL patients whose cancer had come back or had not responded to treatment.

In both studies the main measure of effectiveness was the percentage of patients who responded completely or partially to treatment. Response to treatment was assessed using body scans and patients' clinical data. A complete response is when a patient has no signs of the cancer.

What benefit has Adcetris shown during the studies?

In the study in HL, 75% of patients (76 out of 102) responded partially or completely to treatment. A complete response was observed in 33% of patients (34 out of 102). The data on the 40 patients showed that 55% of patients (22 out of 40) responded to treatment. For 23% of these patients (9 out of 40) a complete response was observed.

In the sALCL study, 86% of patients (50 out of 58) responded partially or completely to treatment and this response was complete for 59% of them (34 out of 58).

(4) …and after

What benefits of Adcetris have been shown in studies?

Adcetris was investigated in three main studies, where the main measure of effectiveness was the percentage of patients who responded completely or partially to treatment. This was assessed using body scans and patients' clinical data to look for signs such as a reduction in the size of the cancer (a complete response is when a patient has no signs of the cancer):

- In Hodgkin lymphoma, Adcetris was studied in a main study involving 102 patients who had received an autologous stem cell transplant and whose cancer had come back or not responded to treatment. 75% (76 out of 102) responded to treatment, and response was complete for 33% (34 out of 102). Adcetris was also studied in a further 40 patients who were not eligible for autologous stem cell transplant or multi-agent chemotherapy, whose cancer had come back or not responded to at least two prior treatments. 55% (22 out of 40) responded to treatment and response was complete for 23% (9 out of 40).
- In systemic anaplastic large cell lymphoma, Adcetris was studied in one main study involving 58 patients whose cancer had come back or had not responded to treatment. 86% (50 out of 58) responded to treatment and response was complete for 59% (34 out of 58).

(5) Main proposals

B/R discussion: 'Why is <X> approved?'

- Changed from *'Why has <X> been approved'*
- Still summarise benefit-risk discussion using lay language
- Update text for major variations which can result in important changes such as restriction of indication (e.g. safety referrals)

<u>Justification</u>

- Summarise initial benefit-risk discussion in lay language; can be updated if benefit-risk profile changes over time (difficult with current template)

(5) Some time ago…

Why has Prolia been approved?

The Committee for Medicinal Products for Human Use (CHMP) decided that Prolia's benefits than its risks and recommended that it be given marketing authorisation.

(5) …more recently…

Why has Sancuso been approved?

The Committee considered that Sancuso transdermal patch showed a similar benefit to granisetron taken by mouth but that it may have a slower onset of action. The CHMP considered however that Sancuso would be of benefit for patients with difficulty swallowing, who might otherwise need to be given daily intravenous injections. Therefore, the CHMP decided that Sancuso's benefits are greater than its risks and recommended that it be given marketing authorisation.

(5) …and after

Why is Dacogen approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Dacogen's benefits are greater than its risks and recommended that it be approved for use in the EU. In particular, the CHMP noted that the improvement in survival seen in patients with AML was modest but relevant, as the benefits of currently available treatments are limited in adults aged 65 years or older. In addition, there were no major safety concerns with Dacogen and the overall safety profile was similar to that of low-dose cytarabine, with the exception of some side effects such as infections and neutropenia, which were more common with Dacogen.

Other minor changes

See table listing all changes + justification

No.	Proposed change	Justification
1	**Revise wording of introduction** In addition to describing what the EPAR summary is, this now also states that the summary is not intended to provide practical advice on how to use the medicine, and refers patients to the package leaflet (or their doctor or pharmacist) for practical information about using it.	Clarify better what the summary is and what it is not; clarify relationship to PL; provide reference to PL at the start in case this is what the reader needs. This is a main recommendation from user testing.
2	**Revise the 1st question to: 'What is <X> and what is it used for?'** This now mentions the type of medicine if easily expressible in lay terms (e.g. anticancer medicine, antibiotic, contraceptive, vaccine), active substance and indication(s). It merges content previously contained in two questions, 'What is <X>' and 'What is <X> used for'. Information on pharmaceutical form and prescription status, which was previously given in these two questions, now comes under 'How is <X> used'. We need to reflect the full indication(s) without this section getting too long or detailed. For multiple indications we will need to use bullet points. For complex indications, we may outline the main indication and then use a separate paragraph to describe the details (e.g. second/third line, co-administration with other medicines, restricted patient populations, etc.).	This will put the most relevant information up front (concerning the indication), while secondary information (concerning pharmaceutical form and prescription status) is moved down.
3	**'How is <X> used?' becomes the 2nd question, and the content is less detailed.** This now only contains information on: pharmaceutical form(s); main dosing recommendations; route/method of administration; duration of treatment if specified; need for any specific monitoring of certain parameters or for diagnostic tests; prescription status.	By not giving too much detail we should reduce overlap/confusion with the package leaflet, while describing the main conditions of use in the EPAR summary.

Next steps

- Consultation/information:
  - EMA secretariat, **PCWP/HCP WG,** CHMP, CMD(h), Commission
- See template + table of changes for feedback
- Test template on more summaries
- Finalise and implement for new summaries + updates from: October/November 2012

Thank you!