

## **Annex I**

**Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)**

## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR(s) for lenograstim, the scientific conclusions are as follows:

The MAH(s) have performed a comprehensive review of glomerulonephritis as part of this PSUR procedure. A total of 8 cases were retrieved. Taking into account the available evidence and the class effect already labelled for other human granulocyte colony-stimulating factors (G-CSF), glomerulonephritis should be added as new adverse drug reaction in section 4.8 of EU SmPC for lenograstim with a frequency "unknown". In addition, a warning on the risk of glomerulonephritis should be included in section 4.4 of the SmPC with recommendations to perform urinalysis as part of medical work up. The package leaflet will be updated accordingly.

In addition, arthralgia, myalgia and pain in extremities were also frequently reported in this PSUR interval. Therefore, the current wording should be revised in the EU SmPC and package leaflet with the addition of musculoskeletal pain including arthralgia, myalgia and pain in extremity (in addition to the already listed bone pain and back pain). The frequency should be listed as very common. The package leaflet will be updated accordingly.

The CMDh agrees with the scientific conclusions made by the PRAC.

## **Grounds for the variation to the terms of the Marketing Authorisation(s)**

On the basis of the scientific conclusions for lenograstim the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing lenograstim is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing lenograstim are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

## **Annex II**

**Amendments to the product information of the nationally authorised medicinal product(s)**

**Amendments to be included in the relevant sections of the Product Information** (new text **underlined and in bold**, deleted text ~~strike through~~)

**Summary of Product Characteristics**

- Section 4.4

**Other Special Precautions**

**Glomerulonephritis has been reported in patients and donors receiving lenograstim. Generally, events of glomerulonephritis resolved after dose reduction or withdrawal of G-CSF. Urinalysis monitoring is recommended.**

- Section 4.8

The following adverse reactions:

- **Glomerulonephritis** should be added under the SOC “Renal and urinary disorders” with a frequency unknown as follows :

Medra System Organ Class	Very common	Common	Uncommon	Rare	Very rare	<u>Not known</u>
<b><u>Renal and urinary disorders</u></b>						<b><u>glomerulonephritis</u></b>

- **Musculoskeletal pain** should be added under the SOC musculoskeletal and connective tissue disorders with a frequency very common (with a footnote below the table “includes bone pain, back pain, arthralgia, myalgia and pain in extremity) as follows:

Medra System Organ Class	Very common	Common	Uncommon	Rare	Very rare
Musculoskeletal and connective tissue disorders	<del>Bone pain</del> <del>Back pain</del> <b><u>Musculoskeletal pain</u></b> <sup>6</sup>	Pain (1)			

1,2,3...

<sup>6</sup> **includes bone pain, back pain, arthralgia, myalgia and pain in extremity**

## Package Leaflet

### Section 2

(...)

#### Take special care with <PRODUCT NAME>

Check with your doctor before having this medicine if

- You have ever had any illness, especially allergies, infections, kidney or liver problems

#### **Please tell your doctor immediately during the treatment of < PRODUCT NAME >, if you :**

- **Experience puffiness in your face or ankles, blood in your urine or brown-coloured urine or notice you urinate less than usual**

### Section 4 Possible side effects

#### Other side effects includes:

- Pains in your bones, ~~and~~ muscles, **joint, back and in legs and arms** and a headache. This is **very** common side effect. If it happens the pain can be controlled by normal painkillers.

(...)

#### Tell your doctor immediately if

(...)

- **You experience kidney injury (glomerulonephritis). Kidney injury has been seen in patients who received < PRODUCT NAME >. Call your doctor right away if you experience puffiness in your face or ankles, blood in your urine or brown-coloured urine or notice you urinate less than usual.**

(...)

#### Other side effects includes :

- **Damage to the tiny filters inside your kidneys (glomerulonephritis).**

#### Tell a doctor if you have any of the following very common side effects:

- You may have pain, pain in your bones, **muscle, joint, back and in legs and arms**, headache, fever, and/or feel sick (nausea).

### **Annex III**

#### **Timetable for the implementation of this position**

## Timetable for the implementation of this position

Adoption of CMDh position:	July CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	02 September 2017
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	01 November 2017