Annex III

Amendments to the relevant sections of the product information

Note:

This product information is the outcome of the referral procedure to which this Commission decision relates.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the Reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

Amendments to the relevant sections of the product information

The valid product information is the final version achieved during the Coordination group procedure with the following amendments (marked as **insertion** or ~~deletion~~ of the text as appropriate) to reflect the agreed wording as provided below:

A. Summary of Product Characteristics

Section 4.2 Posology and method of administration

Posology
Standard dosages are provided in the table 1 below. Additional details are provided in the text following the table.

Table 1

Age/Body weight range	**First dose**	**Second dose** At least 10 min after first dose
Conscious sedation and premedication		
12 kg to 43 kg	2.5 mg	2.5 mg
≥ 44 kg and < 60 years	5 mg	2.5 mg or 5 mg*
≥ 60 years	2.5 mg	2.5 mg
Treatment of prolonged, acute, convulsive epileptic seizures		
12 kg to 18 kg	2.5 mg	2.5 mg
19 kg to 39 kg	3.75 mg	3.75 mg
≥ 40 kg or ≥ 12 years **to < 60 years**	5 mg	5 mg
> 60 years	**3.75 mg**	**3.75 mg**

* depending on desired level and duration of sedation

(…)

Treatment of prolonged, acute, convulsive seizures dosage

- [Product name] must only be used by parents/care givers where the patient has been diagnosed to have epilepsy
- [Product name] prescribers should consider the following prior to ~~initiation of~~ **starting** treatment:
  1. for patients at increased risk of respiratory depression from benzodiazepines, administration of [Product name] under healthcare professional supervision should be considered prior to **starting** treatment with [Product name]. This administration may be performed in the absence of a seizure.
  2. prior to **starting** treatment, the healthcare professional should instruct the patient and patient's parents, caregivers on:
     - how to identify (convulsive) seizures
     - how to use [Product Name] appropriately

- when to administer a second dose and when not
- the risk of concomitant use of opioids/alcohol/CNS depressants/other benzodiazepines;
- the risk of respiratory depression, the symptoms and what to do if it occurs

- [Product name] can be administered in any position, including lying or sitting patients
- The **first** dose indicated in table 1 should be administered intranasally in one nostril.
- ~~If the patient does not respond to the initial dose, one subsequent dose may be administered intranasally in the opposite nostril of the first dose, at least 10 minutes after the initial dose, only after obtaining medical advice. This subsequent dose should not be administered if the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure, in these cases medical assistance must be sought immediately.~~
- ~~If the seizure has not stopped after administration of the 2 doses of midazolam (see table 1), emergency medical assistance must be sought immediately and the empty devices should be given to the healthcare professional to provide information on the dose received by the patient.~~
- ~~The maximum dose to treat a prolonged, acute convulsive seizure is 10 mg~~
- ~~After receiving midazolam, patients should be kept under supervision by a carer who remains with the patients.~~

- **Carers should only administer a single dose of midazolam. If the seizure has not stopped within 10 minutes after administration of midazolam, emergency medical assistance must be sought, and the empty single-dose container should be given to the healthcare professional to provide information on the dose received by the patient.**
- **A second or repeat dose when seizures continue or re-occur after an initial response should not be given without prior medical advice. In particular, young children, patients with respiratory impairment and elderly patients should receive a second dose only in the presence of a health care professional. This second or repeat dose should be administered into the opposite nostril of the first dose.**

Use in Special Populations

(…)

Elderly
In patients from 60 years and in elderly patients [Product name] should be used with caution and dose reduction is recommended (see Table 1). Elderly patients should receive a second dose only in the presence of a health care professional. See also the text following table 1 and section 4.4.

Paediatric patients
For children < 12 kg: [Product name] should not be used. The safety and efficacy of midazolam in these children, has not been established. No data are available.
For children ≥ 12 kg: [Product name] should be used according to table 1. **In particular, young children should receive a second dose only in the presence of a health care professional**. See also the text following table 1 and section 4.4.

B. Package Leaflet

Section 3

(…)
Recommended dose to STOP a SUDDEN, PROLONGED, ACUTE SEIZURE (table 2):

Age/Body weight range	First dose	Second dose Only upon guidance of 112/emergency number/ medical advice and at least 10 min after first dose	Maximum dose
12 kg to 18 kg	1 spray of 2.5 mg	1 spray of 2.5 mg	5 mg
19 kg to 39 kg	1 spay of 3.75 mg	1 spay of 3.75 mg	7.5 mg

40 kg and more or 12 years ~~and older~~to **less than 60 years**	1 spray of 5 mg	1 spray of 5 mg	10 mg
60 years and older	**1 spray of 3.75 mg**	**1 spray of 3.75 mg**	**7.5 mg**

- [Product name] must only be administered by parents/care givers to stop a sudden, prolonged, acute seizure, where the persons have been diagnosed with epilepsy
- Always have 2 unused nasal devices available for administration, in case a second dose is required
- The **first** dose indicated in Table 2 should be administered **in one nostril** ~~intranasally~~.
- If the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure, [call 112/emergency number/seek medical advice] immediately (see after Method of administration). ~~If the seizure does not stop within 10 minutes after administration of the first dose, always [call 112/emergency number/seek medical advice] to obtain guidance if a second dose should be given.~~
- **Carers should only administer a single dose of midazolam. If the seizure has not stopped within 10 minutes after administration of midazolam, emergency medical assistance must be sought to obtain guidance if a second dose should be given, and the empty single-dose container should be given to the healthcare professional to provide information on the dose received by the patient.**
- **A second or repeat dose when seizures do not stop or re-occur should not be given without prior medical advice. In particular, young children, patients with respiratory impairment and elderly patients should receive a second dose only in the presence of a health care professional.**
- This second dose should NOT be administered if the patient has trouble breathing or if there is excessive sedation that is uncharacteristic of the patient during a seizure - in these cases seek medical advice immediately (see after Method of administration).
- A second dose must be administered into the other nostril than the first dose.
- After administration of [Product name], you should be kept under supervision by a carer who remains with the patient

(…)
Method of administration

(…)

7. If another spray is needed, use a new single-dose container and follow the instructions again from step 1 to 5, but administer the second spray in the other nostril than the one that was used for administering the first [Product name]. The second dose of [Product name] may only be administered if the first spray has been administered at least 10 minutes ago and the seizure did not stop or re-occurred ~~and~~ **AND** you have obtained medical advice [e.g. by calling 112/emergency number/prescribing physician] to do so. **Young children, elderly and patients with respiratory impairment should only get a second dose in the presence of a health care professional.**

(…)

- ALWAYS call an ambulance /emergency number 112 or seek medical advice immediately, when:
  - The seizure does not stop within 10 minutes after the recommended dose~~s~~ (see table 2) of [Product name]; show the empty devices to the healthcare professionals who can assess how much [Product name] was administered.

(…)