Package Leaflet - Tabular presentation of proposed changes

Initial Proposed PL plus proposed revisions (using track-changes function)	Objections/Points for consideration raised by Member States	Company response (with cross reference to the response document when applicable)
Package leaflet: Information for the user **[Nationally approved name] 100 micrograms/ml concentrate for solution for infusion** **Dexmedetomidine** **Read all of this leaflet carefully before you are given 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 or nurse. - If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.	--	--
What is in this leaflet What [Nationally approved name] is and what it is used for 1. What you need to know before you are given [Nationally approved name] 2. How [Nationally approved name] will be given 3. Possible side effects 4. How to store [Nationally approved name] **5.** Contents of the pack and other information	--	--
1. What [Nationally approved name] is and what it is used for [Nationally approved name] contains an active substance called dexmedetomidine, which belongs to a medicine group called sedatives. It is used to provide sedation (a state of calm, drowsiness or sleep) for adult patients in hospital intensive care settings or awake sedation during different diagnostic or surgical procedures.	--	--

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2. What you need to know before you are given [Nationally approved name] **You must not be given [Nationally approved name]:** - if you are allergic to dexmedetomidine or any of the other ingredients of this medicine (listed in section 6). - if you have some disorders of heart rhythm (heart block grade 2 or 3). - if you have very low blood pressure which does not respond to treatment. - if you have recently had a stroke or other serious condition affecting blood supply to the brain.	--	--
Warnings and precautions <u>Before you are given this medicine, tell your doctor or nurse if any of the following apply as [Nationally approved name] should be used cautiously:</u> - if you have an abnormally slow heart rate (either due to illness or high levels of physical fitness) - if you have low blood pressure - if you have low blood volume, for example after bleeding - if you have certain heart disorders - if you are elderly - if you have a neurological disorder (for instance head or spinal cord injury or stroke) - if you have severe liver problems - if you have ever developed a serious fever after some medicines, especially anesthetics	--	--

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Other medicines and [Nationally approved name] Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. The following medicines may enhance the effect of [Nationally approved name]: - medicines that help you sleep or cause sedation (e.g. midazolam, propofol) - strong pain medicines (e.g. opioids such as morphine, codeine) - anesthetic medicines (e.g. sevoflurane, isoflurane) If you are using medicines which lower your blood pressure and heart rate, co-administration with [Nationally approved name] may enhance this effect. [Nationally approved name] should not be used with medicines that cause temporary paralysis.	--	--
Pregnancy and breast-feeding [Nationally approved name] should not be used during pregnancy or breast-feeding unless clearly necessary. Ask your doctor for advice before having this medicine. **Driving and using machines** [Nationally approved name] has major impact on the ability to drive and use machines. After you have been given [Nationally approved name] you must not drive, operate machinery, or work in dangerous situations.. Ask your doctor when you can start doing these activities again and when you can go back to this kind of work. **[Nationally approved name] contains sodium** ~~Each ml of [Nationally approved name] contains less than 1 mmol (approximately 3.5 mg) sodium.~~This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially 'sodium-free'.	**(CMS):** Content of sodium should be in line with Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'	The text is adapted to the respective recommendation

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3. How [Nationally approved name] will be given *Hospital intensive care* [Nationally approved name] is administered to you by a doctor or nurse in hospital intensive care. *Procedural sedation/awake sedation* [Nationally approved name] is administered to you by a doctor or nurse prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation. Your doctor will decide on a suitable dose for you. The amount of [Nationally approved name] depends on your age, size, general condition of health, the level of sedation needed and how you respond to the medicine. Your doctor may change your dose if needed and will monitor your heart and blood pressure during the treatment. [Nationally approved name] is diluted and it is given to you as an infusion (drip) into your veins.	--	--
After sedation/wake-up • The doctor will keep you under medical supervision for some hours after the sedation to make sure that you feel well. • You should not go home unaccompanied. • Medicines to help you sleep, cause sedation or strong painkillers may not be appropriate for some time after you have been given [Nationally approved name]. Talk to your doctor about the use of these medicines and about the use of alcohol.	--	--

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If you have been given more [Nationally approved name] than you should If you are given too much [Nationally approved name], your blood pressure may drop, your heartbeat may slow down and you may feel more drowsy. Your doctor will know how to treat you based on your condition. If you have any further questions on the use of this medicine, ask your doctor.		
4. Possible side effects Like all medicines, this medicine can cause side effects, although not everybody gets them. **Very common** (~~*affects more than 1 user in 10*~~*may affect more than 1 in 10 people*) - slow heart rate - low or high blood pressure - change in breathing pattern or stopping breathing **Common** (~~*affects 1 to 10 users in 100*~~*may affect up to 1 in 10 people*) - chest pain or heart attack - fast heart rate - low or high blood sugar - nausea, vomiting or dry mouth - restlessness - symptoms after stopping the medicine - high temperature *(possible side effects continued on next page)*	**(CMS):** Frequency convention should be in line with last revision of QRD template	The text is adapted to the respective recommendation

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Initial Proposed PL plus proposed revisions (using track-changes function)	Objections/Points for consideration raised by Member States	Company response
(continued) **Uncommon** (~~*affects 1 to 10 users in 1,000*~~*may affect up to 1 in 100 people*) - a condition where there is too much acid in the body - low albumin level in blood - hallucinations - reduced heart function - shortness of breath and transient cessation of respiration - the medicine is not effective enough. - swelling of the stomach - thirst Reporting of side effects If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V*. By reporting side effects, you can help provide more information on the safety of this medicine.		
5. How to store [Nationally approved name] Keep this medicine out of the sight and reach of children. Do not use this medicine after the expiry date which is stated on the label and carton after EXP. This medicine does not require any special temperature storage conditions. Keep the ampoules or vials in the outer carton in order to protect from light.	--	--

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6. Contents of the pack and other information **What [Nationally approved name] contains** - The active substance is dexmedetomidine. - Each ml of concentrate contains dexmedetomidine hydrochloride equivalent to 100 micrograms dexmedetomidine. - The other ingredients are sodium chloride and water for injections. Each 2 ml ampoule contains 200 micrograms of dexmedetomidine (as hydrochloride). Each 2 ml vial contains 200 micrograms of dexmedetomidine (as hydrochloride). Each 4 ml vial contains 400 micrograms of dexmedetomidine (as hydrochloride). Each 10 ml vial contains 1000 micrograms of dexmedetomidine (as hydrochloride). The concentration of the final solution after dilution should be either 4 micrograms/ml or 8 micrograms/ml.	--	--
What [Nationally approved name] looks like and contents of the pack Concentrate for solution for infusion (sterile concentrate). The concentrate is a clear, colourless solution. <u>Containers</u> 2 ml colourless glass ampoules 2, 5 or 10 ml colourless glass vials <u>Pack sizes</u> 5 x 2 ml ampoules 25 x 2 ml ampoules 5 x 2 ml vials 4 x 4 ml vials *(possible side effects continued on next page)*	--	--

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Initial Proposed PL plus proposed revisions (using track-changes function)	Objections/Points for consideration raised by Member States	Company response
(continued) 5 x 4 ml vials 4 x 10 ml vials 5 x 10 ml vials Not all pack sizes may be marketed.		
Marketing Authorisation Holder and Manufacturer **Marketing Authorisation Holder:** to be completed nationally **Manufacturer:** to be completed nationally This medicinal product is authorised in the Member States of the EEA under the following names: < {Name of the Member State} > < {Name of the medicinal product} > < {Name of the Member State} > < {Name of the medicinal product} **This leaflet was last revised in <{MM/YYYY}>**		

Formatiert: Englisch (USA)

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The following information is intended for healthcare professionals only: **[Nationally approved name] 100 micrograms/ml concentrate for solution for infusion** **Method of administration** [Nationally approved name] should be administered by healthcare professionals skilled in the management of patients requiring intensive care or in the anaesthetic management of patients in the operating room. It must be administered only as a diluted intravenous infusion using a controlled infusion device.	--	--

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<table>
<tr><th>Initial Proposed PL plus proposed revisions (using track-changes function)</th><th>Objections/Points for consideration raised by Member States</th><th>Company response</th></tr>
<tr><td>
Preparation of solution
[Nationally approved name] can be diluted in glucose 50 mg/ml (5%), Ringers, mannitol or sodium chloride 9 mg/ml (0.9%) solution for injection to achieve the required concentration of either 4 micrograms/ml or 8 micrograms/ml prior to administration. Please see below in tabulated form the volumes needed to prepare the infusion.
<u>In the case the required concentration is 4 micrograms/ml:</u>
<table>
<tr><th>Volume of [Nationally approved name] 100 micrograms/ml concentrate for solution for infusion</th><th>Volume of diluent</th><th>Total volume of infusion</th></tr>
<tr><td>2 ml</td><td>48 ml</td><td>50 ml</td></tr>
<tr><td>4 ml</td><td>96 ml</td><td>100 ml</td></tr>
<tr><td>10 ml</td><td>240 ml</td><td>250 ml</td></tr>
<tr><td>20 ml</td><td>480 ml</td><td>500 ml</td></tr>
</table>
<u>In case the required concentration is 8 micrograms/ml:</u>
<table>
<tr><th>Volume of [Nationally approved name] 100 micrograms/ml concentrate for solution for infusion</th><th>Volume of diluent</th><th>Total volume of infusion</th></tr>
<tr><td>4 ml</td><td>46 ml</td><td>50 ml</td></tr>
<tr><td>8 ml</td><td>92 ml</td><td>100 ml</td></tr>
<tr><td>20 ml</td><td>230 ml</td><td>250 ml</td></tr>
<tr><td>40 ml</td><td>460 ml</td><td>500 ml</td></tr>
</table>
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The solution should be shaken gently to mix well. [Nationally approved name] should be inspected visually for particulate matter and discoloration prior to administration. [Nationally approved name] has been shown to be compatible when administered with the following intravenous fluids and medicinal products: Lactated Ringers, 5% glucose solution, sodium chloride 9 mg/ml (0.9%) solution for injection, mannitol 200 mg/ml (20%), thiopental sodium, etomidate, vecuronium bromide, pancuronium bromide, succinylcholine, atracurium besylate, mivacurium chloride, rocuronium bromide, glycopyrrolate bromide, phenylephrine HCl, atropine sulfate, dopamine, noradrenaline, dobutamine, midazolam, morphine sulfate, fentanyl citrate, and a plasma-substitute. Compatibility studies have shown potential for adsorption of dexmedetomidine to some types of natural rubber. Although dexmedetomidine is dosed to effect, it is advisable to use components with synthetic or coated natural rubber gaskets.	--	--
Shelf life *After dilution:* Chemical and physical stability of the diluted infusion (Infusion Solution Stability) has been demonstrated for 48 hours at 25°C and at refrigerated conditions (2 °C – 8 °C). From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to the use are the responsibility of the user and would not normally be longer than 24 hours at 2° to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.	--	--