DA	A
VARIAZIONE TIPO II N. B.II.B.1 C), TIPO IA_{IN} N. B.II.B.1.A), TIPO II B.II.b.2.b.3),	
MANUFACTURER(S)	
• **Glaxo Wellcome Production** 1, rue De L'Abbaye Notre Dame De Bondeville France Fasi di produzione: Tutte le fasi di produzione, incluso controlli e rilascio dei lotti. • **Italfarmaco S.p.A.** Viale F. Testi, 330 - 20126 Milano Italy Fasi di produzione: Rilascio dei lotti di prodotto finito • **DHL Supply Chain (Italy) S.p.A** Viale Delle Industrie, 2-20090 Settala (MI) Italy Fasi di produzione: confezionamento secondario.	• **Glaxo Wellcome Production** 1, rue De L'Abbaye Notre Dame De Bondeville France Fasi di produzione: Tutte le fasi di produzione, incluso controlli e rilascio dei lotti. • **Italfarmaco S.p.A.** Viale F. Testi, 330 - 20126 Milano Italy Fasi di produzione: Tutte le fasi di produzione compreso confezionamento secondario, controllo e rilascio dei lotti. • **DHL Supply Chain (Italy) S.p.A** Viale Delle Industrie, 2-20090 Settala (MI) Italy Fasi di produzione: confezionamento secondario.
VARIAZIONE TIPO IB N. B.II.B.4.F)	
BATCH(S) SIZE	
IIB.1 MANUFACTURING FORMULA (all presentations) Batch size: 500 L of solution	**3.2.P.3.2 BATCH FORMULA (all presentations)** Batch size: 500 L of solution (Glaxo Wellcome Production) **Batch size: 184 L of solution (Italfarmaco S.p.A only)**

DA	A
VARIAZIONE TIPO IB N. B.II.e.6.a) Presentata come tipo IB forseen in quanto la condizione n.1 non viene rispettata essendo modificata la modalità di utilizzo della siringa dopo l'uso.	
CONTAINER CLOSURE SYSTEM	
Container Closure System *Immediate packaging (Syringes)* *Description* Seledie drug product consists of single dose prefilled syringes. Each pre-filled syringe consists of a barrel with a needle, needle shield and a plunger stopper and is equipped with a safety device. *Con.ed*	**Container Closure System** *Immediate packaging (Syringes)* **Manufacturer: Italfarmaco S.p.A** *Description* Seledie drug product consists of single dose prefilled syringes. Each pre-filled syringe consists of a barrel with a needle, needle shield and a plunger stopper ~~**and is equipped with a safety device**~~. *Con.ed* **Manufacturer: Glaxo Wellcome Production** Unchanged

Con.ed Type of Materials The medicinal product is packaged in a single dose, pre-filled syringe, equipped with a safety device. *Material in contact with the finished product* • Syringe Barrel: graduated type I glass barrel of 1 ml capacity. • Plunger Stopper in chlorobutyl elastomer (or other validated elastomer). • Needle: stainless steel needle secured to the syringe body with a single component adhesive polymerisable under UV light. • Needle Shield in styrene butadiene (or other validated elastomer) *Material not in contaact with the finished product* • Polypropylene plunger rod (or other validated material) • Safety Device in transparent styrene butadiene copolymer (or other validated material) allowing the needle to be covered after use.	*Con.ed* Type of Materials **Manufacturer: Italfarmaco S.p.A** The medicinal product is packaged in a single dose, pre-filled syringe~~**, equipped with a safety device**~~. *Material in contact with the finished product* • Syringe Barrel: graduated type I glass barrel of 1 ml capacity. • Plunger Stopper in chlorobutyl elastomer (or other validated elastomer). • Needle: stainless steel needle secured to the syringe body with a single component adhesive polymerisable under UV light. • Needle Shield in styrene butadiene (or other validated elastomer) *Material not in contact with the finished product:* • Polypropylene plunger rod (or other validated material) • ~~**Safety Device in transparent styrene butadiene copolymer (or other validated material) allowing the needle to be covered after use.**~~ **Manufacturer: Glaxo Wellcome Production** Unchanged

DA	A
VARIAZIONE TIPO IB N. B.II.D.2.D), E TIPO IB N. B.II.D.2.D)	
STABILITY TEST ON THE FINISHED PRODUCT	
STABILITY TEST ON THE FINISHED PRODUCT **DESCRIPTION OF TEST PROCEDURES** **Free sulfates** Examine by ion-exchange chromatography using an apparatus equipped with a conductimetric detector. Based on Ph Eur monograph. **Molecular distribution** Examine by size-exclusion chromatography (Ph. Eur. 2.2.30). The method refers to the method of the European Pharmacopoeia monograph „Heparins, Low Molecular Mass“ (Ph. Eur. 0828), section „Identification C“	**3.2.P.8 STABILITY** **DESCRIPTION OF TEST PROCEDURES** **Free sulfates** Method 1 Examine by ion-exchange chromatography using an apparatus equipped with a conductimetric detector. Based on Ph Eur monograph. **Method 2 (alternative only for Italfarmaco S.p.A.)** **Examine by ion-exchange liquid chromatography based on USP monograph.** **for details see Module 3 Section 3.2.P.5.2** **Molecular distribution** Method 1 Examine by size-exclusion chromatography (Ph. Eur. 2.2.30). The method refers to the method of the European Pharmacopoeia monograph „Heparins, Low Molecular Mass“ (Ph. Eur. 0828), section „Identification C“ **Method 2 (alternative only for Italfarmaco S.p.A.)** **Examine by size-exclusion chromatography (HPLC/UV/RID as equipment) through an in house method based on USP monograph.** **for details see Module 3 Section 3.2.P.5.2**

relativamente alla specialità medicinale indicata in oggetto e alle confezioni sotto elencate:

034668018 - «11.400 UI ANTIXA/0,6 ml soluzione iniettabile» 2 siringhe preriempite 0,6 ml

034668044 - «15.200 UI ANTIXA/0,8 ml soluzione iniettabile» 2 siringhe preriempite 0,8 ml

034668071 - «19.000 UI ANTIXA/1 ml soluzione iniettabile» 2 siringhe preriempite 1 ml

I lotti già prodotti possono essere mantenuti in commercio fino alla data di scadenza indicata in etichetta.

La presente determinazione ha effetto dal giorno successivo a quello della sua pubblicazione nella *Gazzetta Ufficiale* della Repubblica italiana.

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