RAPID ALERT NOTIFICATION OF A QUALITY DEFECT/RECALL

IMPORTANT - DELIVER IMMEDIATELY **Ref. IT/_ /2/01**

1.To: see list attached

2.Product Recall Class of Defect: to be assigned	**3.Falsified / Counterfeit / Fraud (specify)*:** suspected falsified
4.Product: see the attached file	**5.Marketing Authorisation Number:*** see the attached file
6.Brand/Trade Name: see the attached file	**7.INN or Generic Name:**
8. Dosage Form: see the attached file	**9. Strength:** see the attached file
10.Batch/Lot Number: see the attached file	**11.Expiry Date:** see the attached file
12. Pack size and Presentation: see the attached file	**13. Date Manufactured:**

14. Marketing Authorisation Holder:

15. Manufacturer:	**16. Recalling Firm (if different):**

17. Recall Number Assigned (if available): Ref. IT/_ /2/01

18. Details of Defect/Reason for Recall: Following the FMD ALERT MDR 123-05/19 issued by MHRA on June 27, 2019, where medicines have been suspected to be taken out of the regulated medicines' supply chain during distribution and later re-introduced, on Falsified documentation and without the "bollino" stickers, the Italian authorities ask for additional checks on the products object of the MHRA Alert.

19.Information on distribution including exports (type of customer, e.g. hospitals): not available

20. Action taken by Issuing Authority: NUI on Falsified "bollino" stickers issued by AIFA on February 6th, 2019

21.Proposed Action: In order to prevent the distribution of falsified medicines through the parallel distribution channel, it is considered useful to communicate any anomalies with regard to the offer of medicinal products missing the "bollini" labels or showing different features from those described in the AIFA NUI dated February 6th, 2019. Note that Italian medicinal products WITHOUT the "bollino" sticker (i.e. with the serialized lower layer on the box, but missing the sticker – see image below and refer to the NUI in annex for details) are to be considered non-compliant with Italian requirements, and can potentially be linked to fraud in the "national health system" or to other illegal practices.

LEFT. A bollino sticker with upper (sticking) level and lower level.
RIGHT. The lower, serialized level of the bollino sticker: packages seized in UK were missing the upper level.

As some of the medicinal products listed in the MHRA's FMD ALERT are among those currently in "short supply" in Italy we kindly ask you to check **in particular the packages of Neupro, Vimpat, Clexane and Spiriva** imported from Italy, due to the risk that the supply of these medicines could have originated from not authorised sources.

Please contact in writing the office at the e-mail addresses medicrime@aifa.gov.it and d.digiorgio@aifa.gov.it in order to ascertain the legitimacy of the products.

22.From (Issuing Authority): Italian Medicines Agency - AIFA	**23.Contact Person:** Domenico Di Giorgio – d.digiorgio@aifa.gov.it, medicrime@aifa.gov.it	
24.Signed:	**25.Date: July 3rd, 2019**	**26.Time:***

Annexes:

- MHRA FMD ALERT MDR 123-05/19 (EL__19_A15_final_.pdf)
- AIFA NUI on Falsified "bollino" stickers Feb/2019 (Non Urgent Information - Fake Italian traceability stickers + annex - Feb 2019.pdf)

Medicines & Healthcare products Regulatory Agency

FMD ALERT*

CLASS 2

Action Within 48 Hours
Pharmacy / Patient Level Recall

Date: 27 June 2019 EL (19) A/15 Our Ref: MDR 123-05/19

Dear Healthcare Professional,

B & S Healthcare

Please see Appendix 1 for list of products and batch numbers

Brief details of issue:

It has recently come to our attention that medicines have been taken out of the regulated medicines' supply chain during distribution and later re-introduced. This means that the correct transport and storage conditions cannot be guaranteed during this period and, while unlikely, could impact their effectiveness. The products have been parallel imported into the UK by B & S Healthcare from Italy and have been re-labelled in B & S Healthcare livery. The same batches of products may have been parallel imported legitimately into the UK by other importers. Only those packs in B & S Healthcare livery are within the scope of this Alert. The products are believed to be legitimate. There is no evidence that they have been tampered with and these medicines are stable at room temperature.

Advice for healthcare professionals:

- Please check your stocks of all the listed products for the relevant batches in B & S Healthcare livery. If any relevant packs are identified, please quarantine and return it to your supplier using your supplier's approved process.
- The MHRA has undertaken a medical assessment to determine whether there is any risk to patients. As a precautionary measure, three medicines are being recalled to a patient level because in the very unlikely event that these medicines are not fully effective there is a potential risk to patient safety. For these three particular medicines, whilst the likelihood of their effectiveness being compromised is low (because they are stable legitimate medicines), the consequences of a lack of effectiveness could be serious which is why we are treating them differently. If patients have any of these affected products, you should advise that they should continue taking their medicines and contact their GP practice to arrange a new prescription. Once they have a new prescription, patients should return the affected batches to their pharmacist.

- The three products that are being recalled to **patient level** are **Clexane 8000iu Injection 0.8ml; Neupro 4mg/24 hr patches; and Vimpat 100mg tablets**. We will use media, social media and will contact patient groups and charities, to help draw the attention of patients to the affected batches of these products.

- As a precaution, all other affected medicines are being recalled at **pharmacy level**. Again, you should advise patients to continue taking their medicines. If they have any of these affected products, they do not need to arrange a new prescription, but if they have any questions, they should speak to their GP or healthcare professional. The products being recalled at **pharmacy level** are: **Dovobet Gel, Incruse Inhaler, Provisacor (Crestor) 10mg Tablets, Seebri Breezhaler, Spiriva Inhalation Powder.**

Contacts for further information:

For general enquiries please contact B & S Healthcare customer services:
Email customerservice@bnshealthcare.com
For medical information enquiries please contact the B & S Healthcare medical information team:
Email medinfo@bnshealthcare.com

Recipients of this Alert should bring it to the attention of relevant contacts by copy of this letter. NHS Regional teams are asked to forward this to relevant clinics, general practitioners and community pharmacists.

Yours faithfully

Defective Medicines Report Centre
10 South Colonnade
Canary Wharf
London
E14 4PU
Telephone +44 (0)20 3080 6000

*Falsified Medicines Directive Alert

Falsified Medicines Directive (FMD) 2011/62/EU introduced new requirements to enhance the security of the European supply chain. Where the MHRA has identified risks to the security of the supply chain, FMD Alerts will be issued.

For further information about FMD and safety features, please see this link on GOV.UK.

Appendix 1: Table of Products / batches

Product and Pack Size	Italian Batch Number	B & S Batch Number	Expiry Date	Date of First Distribution
Clexane 8000iu 0.8ml 1 x 10	7CK98A	04N0078	30-OCT-20	18-APR-18
Clexane 8000iu 0.8ml 1 x10	7CH63B	04N0016	30-JUN-20	11-APR-18
Clexane 8000iu 0.8ml 1 x 10	7CL23B	03N1722	30-OCT-20	22-MAY-18
Clexane 8000iu 0.8ml 1 x10	7CH36C	03N1721	30-JUN-20	11-APR-18
Clexane 8000iu 0.8ml 1 x 10	7CH77B	03N1721	30-JUN-20	11-APR-18
Clexane 8000iu 0.8ml 1 x 10	7CL82B	03N1720	30-NOV-20	11-MAY-18
Clexane 8000iu 0.8ml 1 x 10	7CL37D	03N1722	30-OCT-20	22-MAY-18
Clexane 8000iu 0.8ml 1 x 10	8CA66C	03N1716	30-DEC-20	10-MAY-18
Dovobet Gel 1 x 30g	A80960	11N0735	30-JUL-20	06-DEC-18
Dovobet Gel 1 x 30g	A79729	11N0734	30-JUN-20	05-DEC-18
Dovobet Gel 1 x 30g	A85747	01P0222	30-OCT-20	09-JAN-19
Dovobet Gel 1 x 30g	A78018	01P0850	30-MAY-20	16-JAN-19
Dovobet Gel 1 x 30g	A80960	01P0221	30-JUL-20	09-JAN-19
Dovobet Gel 1 x 30g	A87671	02P1199	30-OCT-20	02-APR-19
Dovobet Gel 1 x 30g	A85936	02P1206	30-OCT-20	19-MAR-19
Dovobet Gel 1 x 30g	A85747	02P1207	30-OCT-20	29-APR-19
Dovobet Gel 1 x 30g	A88301	02P1205	30-NOV-21	15-MAY-19
Dovobet Gel 1 x 30g	A80960	02P1204	30-JUL-20	30-APR-19
Dovobet Gel 1 x 30g	A89721	04P0609	30-NOV-21	14-MAY-19
Dovobet Gel 1 x 30g	A90279	03P1677	30-DEC-21	12-APR-19
Dovobet Gel 1 x 30g	A85936	03P1679	30-OCT-20	14-MAY-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R829935	06N0036	30-JUN-19	07-JUN-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R834141	05N0506	30-SEP-19	21-MAY-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R839098	05N0750	30-OCT-19	23-MAY-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R838744	05N0659	30-OCT-19	22-MAY-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R844186	05N0657	30-DEC-19	21-MAY-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R851918	11N0754	30-MAR-20	27-NOV-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R856773	11N0753	30-JUL-20	21-NOV-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R853231	11N0755	30-MAR-20	21-NOV-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R849465	11N0752	28-FEB-20	22-NOV-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R853231	01P0344	30-MAR-20	09-JAN-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R851918	01P0345	30-MAR-20	09-JAN-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R856773	12N0071	30-JUL-20	07-DEC-18
Incruse Inhaler 55Mcg 1 x 30 Doses	R858970	01P0343	30-AUG-20	09-JAN-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R856773	12N0808	30-JUL-20	31-DEC-18
Incruse Inhaler 55MCg 1 x 30 Doses	R852223	01P0344	30-MAR-20	09-JAN-19

Incruse Inhaler 55Mcg 1 x 30 Doses	R858970	02P1201	30-AUG-20	11-APR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R856773	02P1200	30-JUL-20	18-APR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R851918	02P1209	30-MAR-20	18-APR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R861997	03P0530	30-SEP-20	28-MAR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R860226	03P0991	30-AUG-20	27-MAR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R861997	03P0955	30-SEP-20	03-APR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R860226	03P1676	30-AUG-20	05-APR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R861997	03P1675	30-SEP-20	11-APR-19
Incruse Inhaler 55Mcg 1 x 30 Doses	R861997	04P1150	30-SEP-20	29-APR-19
Neupro 4mg/24hrs 1 x 28 Patches	56688403	05N0469	28-FEB-20	01-JUN-18
Neupro 4mg/24hrs 1 x 28 Patches	56679402	06N0592	30-JAN-20	14-JUN-18
Neupro 4mg/24hrs 1 x 28 Patches	56712404	10N1295	30-JUN-20	31-OCT-18
Neupro 4mg/24hrs 1 x 28 Patches	56722401	10N1292	30-JUL-20	02-NOV-18
Neupro 4mg/24hrs 1 x 28 Patches	56728403	10N1296	30-AUG-20	26-OCT-18
Neupro 4mg/24hrs 1 x 28 Patches	56722401	11N0650	30-JUL-20	23-NOV-18
Neupro 4mg/24hrs 1 x 28 Patches	56712403	11N0649	30-JUN-20	22-NOV-18
Neupro 4mg/24hrs 1 x 28 Patches	56742401	11N0651	30-NOV-20	06-DEC-18
Neupro 4mg/24hrs 1 x 28 Patches	56728403	11N0647	30-AUG-20	26-NOV-18
Neupro 4mg/24hrs 1 x 28 Patches	56712404	11N0648	30-JUN-20	26-NOV-18
Neupro 4mg/24hrs 1 x 28 Patches	56699404	04P1286	30-APR-20	14-MAY-19
Neupro 4mg/24hrs 1 x 28 Patches	56728403	01P0366	30-AUG-20	14-JAN-19
Neupro 4mg/24hrs 1 x 28 Patches	56742401	01P0314	30-NOV-20	09-JAN-19
Neupro 4mg/24hrs 1 x 28 Patches	56757104	04P1278	30-JAN-21	03-MAY-19
Neupro 4mg/24hrs 1 x 28 Patches	56763103	04P1279	30-JAN-21	03-MAY-19
Provisacor (Sold as Crestor) 10Mg Tabs 1 x 28	U733A	04N1584	30-APR-20	08-MAY-18
Provisacor (Sold as Crestor) 10Mg Tabs 1 x 28	U571A	05N0155	28-FEB-20	29-MAY-18
SEEBRI BREEZHALER 44mg 1 x 30 Doses	BFD79	04PO113	30-JUL-20	18-APR-19
Spiriva Inhalation Powder 18mcg Cap 1 x 30	802223	01P0226	28-FEB-20	09-JAN-19
Spiriva Inhalation Powder 18mcg Cap 1 x 30	804102	01P0227	30-MAY-20	09-JAN-19
VIMPAT 100MG TABS 1 X 56	254265	01P0324	30-APR-23	11-JAN-19
VIMPAT 100MG TABS 1 X 56	255279	02P1067	30-APR-23	19-MAR-19
VIMPAT 100MG TABS 1 X 56	258582	02P0892	30-JUN-23	25-MAR-19
VIMPAT 100MG TABS 1 X 56	254265	02P0893	30-APR-23	25-MAR-19

Follow-up and Non-urgent Information for Quality Defects

	ITALIAN MEDICINES AGENCY – (AIFA)		
1.	To: (see list attached, if more than one)		
2.	Recall Number Assigned: **German RAs of October 08 and November 21, 2018**	2a	National reference Number **Ref.** **DE_BW_01_FD Pharma_2018_001** **DE_BW_01_Allomedic_2018_001** **DE_BW_01_Allomedic_2018_002**
4.	Product: **Seebri Breezehaler** **Abstral** **Palexia**	5.	Marketing Authorisation number: **042306035** **038736031** **040422661** **For use in Humans**
6.	Brand/Trade name: **Seebri Breezehaler** **Abstral** **Palexia**	7.	INN or Generic Name: **Glycopyrronium-bromid** **Fentanyl** **Tapentadol**
8.	Dosage form: **capsule with powder for inhalation** **sublingual tablets** **modified release tablet**	9.	Strength: **44 mcg** **150 mg** **150 mg**
10.	Batch number (and bulk, if different): **BCE98 - BCJ73** **607717701** **681N01**		Expiry Date: **12/2019 – 11/2019** **01-2020** **12-2020**
14.	Marketing Authorisation holder: Novartis Europe Limited (UK) Kyowa Kirin Services Ltd, EC3M 6BN, London, GB Grunenthal Italia Srl (Italy)		
15.	Manufacturer[1]: Novartis Aescia Queenborough Ltd, GB Grunenthal GmbH (Aachen, D)	16.	Contact Person:

[1] The holder of an authorisation to under Article 40 of Directive 2001/83/EC and Article 44 of Directive 2001/82/EC and the holder of the authorisation on behalf of whom the Qualified Person has certified the batch for release in accordance with Article 51 of Directive 2001/83/EC or Article 55 of Directive 2001/82/EC, if different

17. SUBJECT – Falsified "bollino" stickers

BACKGROUND INFORMATION

Following the reports issued by Germany (October 08 and November 21, 2018), where bollini labels have been suspected to be manipulated and then confirmed as falsified, upon further investigation, the Italian authorities detected additional cases of bollini labels falsification related to hospital medicinal products, in particular

a. Standard pharmacy medicines bought by wholesalers in "hospital package", and sold to pharmacies or exported after having substituted the stamped bollino with a fake one bearing the same unique code, but no indication regarding the hospital use;

b. Anti-cancer drugs, sold without bollini stickers on the outer box/carton:

In both cases, the products should be considered as possibly falsified medicines, as for the EU definition:

a. Products bearing a falsified "bollino" bear a counterfeit component in the packaging;

b. Products with no "bollino" could have been sourced via theft, and sold via fake credentials.

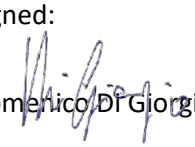
PROPOSED ACTION

In order to prevent the distribution of falsified medicines through the parallel distribution channel, it is considered useful to widespread the guide attached to this NUI, describing the essential characteristics of genuine Bollini labels which should and could be checked by the parallel importers within their incoming goods inspection.

It is also considered useful to underline that the Italian bollino label has always to be present on the outer carton of exported medicines of Italian origin. Furthermore, the exported packages should bear a "bollino" with a nullification mark (e.g., an "**ANNULLATO**" stamp or a cross over the barcode).

For medicines classified as hospital product (class H), the packs distributed should have the bollino with the specific wording "**Confezione Ospedaliera/Ambulatoriale**" stamped on the label, in order to invalidate reimbursement out of the hospital channel.

If there be any anomalies with regard to the offer of medicinal products with bollini labels showing different features from those described, please contact the writing office at the e-mail address medicrime@aifa.gov.it, to allow any check to ascertain the legitimacy of the products.

22.	From (issuing Authority): **Product Quality and Pharmaceutical Crime Counteracting Office** **AIFA – Italian Medicines Agency**	23.	Contact person: **Dr. Domenico Di Giorgio,** **medicrime@aifa.gov.it**
24.	Signed:  Domenico Di Giorgio	25. 26.	Date: February 6th, 2019 Time:

Ministero della Salute

AIFA
Agenzia Italiana del Farmaco

Bollino

The Italian Security Label
for
Pharmaceutical Products

POLIGRAFICO
E ZECCA
DELLO STATO
ITALIANO

The Italian Security label for Pharmaceutical products (Bollino) is a two-layer paper label:

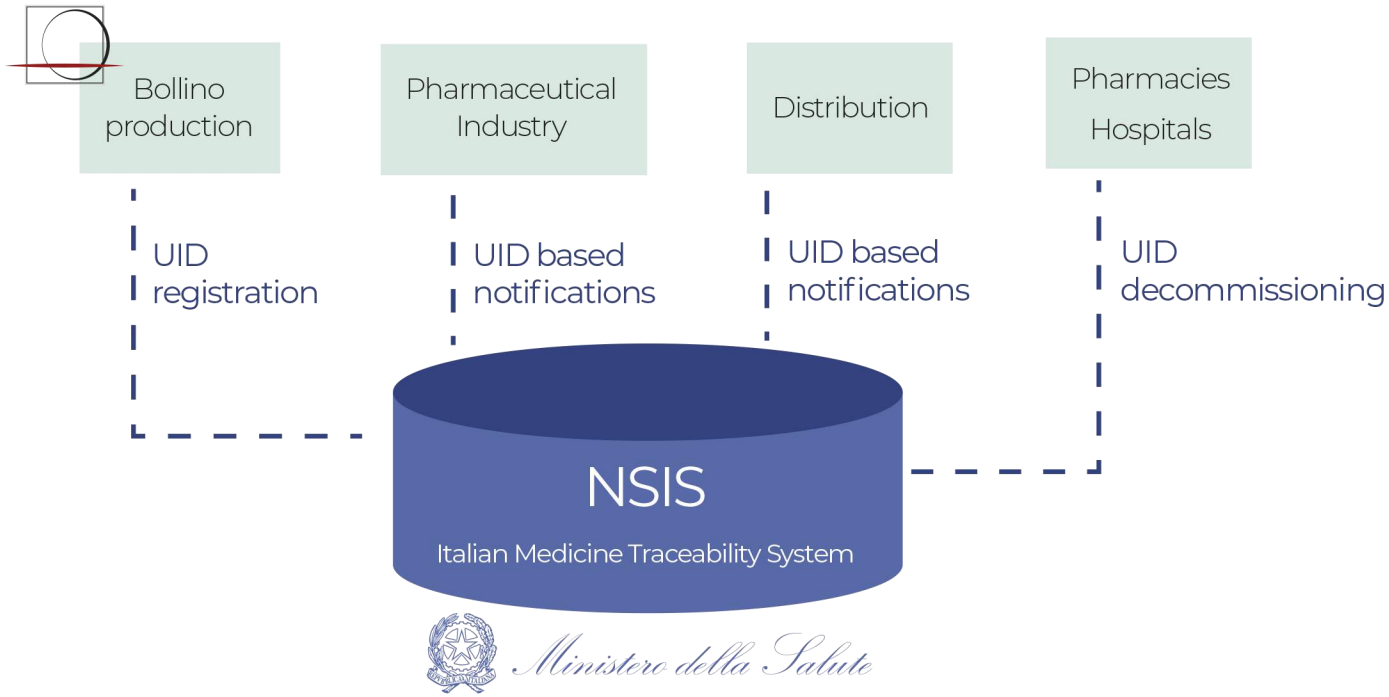
- The lower layer shows the unique serial number (UID). It will remain attached to the pack for the entire period of validity of the pharmaceutical product and in case of attempts of removal it acts as anti-tampering device;

- The upper layer shows the following information:
  - The AIC code in both clear and code 39 barcode form;
  - The company that holds the AIC in the Italian regulation system;
  - The name of the medicine with pharmaceutical form, dosage indication and number of dose units;
  - The unique serial number (UID) in both clear and barcode form.

AIC — Medecine marketing authorization code issued by A.I.F.A. (Agenzia Italiana del Farmaco) the Italian National Authority responsible for human drugs regulation.

UID — Unique serial number is issued by Poligrafico e Zecca dello Stato, the Italian National Printing House, and represents both the traceability unique identifier and the unique reimbursement code.

NSIS — National Traceability System owned and managed by the Ministry of Health.



Security printing technical features

Upper layer:

- Size: 35 mm X 25 mm;
- Watermarked paper with rhombus shape;
- UV dull paper treatment;
- Security fibers in light blue and yellow colours.

Lower layer:

- Size: 40 mm X 25 mm;
- Printed text “SICUREZZA” and symbol of the caduceus, red ink.

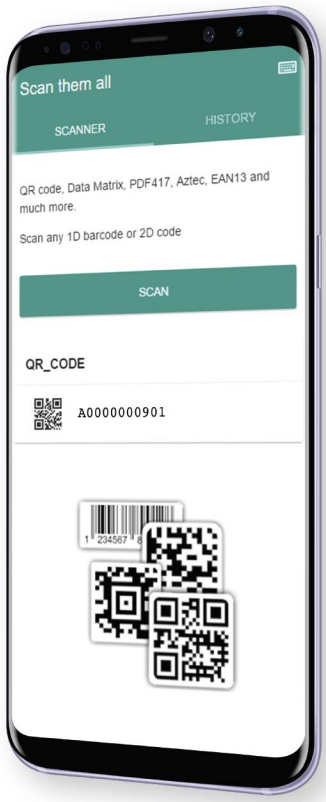
Security checks

1. UV lamp exposal:
   a. Security fibers reaction to UV light;
   b. Paper surface reaction to UV light (UV Dull security element);
2. Watermark shapes visible when the upper layer is held against the light.

Barcode check with smartphone's app:

Using a general purpose code scanner app for smartphone (e.g. Scan them all) scan the barcodes and check:

1. The AIC number in code 39 form
2. The UID (correspondent to the two clear versions printed on the lower and the upper layer)
3. The combination of the UID and AIC number in code 39 form



Poligrafico provides Bollino on behalf of the Italian Authorities, with the following responsibilities:

- Production under the GMP and ISO standards, including ISO-14298 Intergraph for security printing (Governmental Level).
- 100% quality control on the total amount of Bollino produced.
- Collaboration with all the national control bodies to support investigations.
- Sworn and certified testimony of authenticity required by the investigation authorities.

Any further check on UID validity and Bollino's physical authenticity can be requested to the Italian authorities

MINISTERO DELLA SALUTE
Viale Giorgio Ribotta, 5 - 00144 - Roma
Tel. +39 06 59941
www.salute.gov.it

AGENZIA ITALIANA DEL FARMACO
Via del Tritone, 181 - 00187 - Roma
Tel. +39 06 5978401
www.aifa.gov.it

ISTITUTO POLIGRAFICO
E ZECCA DELLO STATO S.p.A.
Via Salaria, 691 - 00138 - Roma
Tel. +39 06 85081 - bollini@ipzs.it
www.ipzs.it