MINISTRY OF HEALTH

2349

Pursuant to Article 62, paragraph 8 of the Medicinal Products Act (Official Gazette 76/13 and 90/14), the Minister of Health hereby issues this

ORDINANCE

ON THE SUSPENSION OF THE PLACEMENT ON AND WITHDRAWAL OF MEDICINAL PRODUCTS FROM THE MARKET

Article 1

This Ordinance stipulates the conditions and manner of the suspension of the placement on and withdrawal of medicinal products from the market, and the deadlines and manner of notification on the suspension of the placement on and withdrawal of medicinal markets from the market.

Article 2

1) Health care professionals coming into contact with medicinal products, or patients/users of medicinal products and legal and natural persons producing or performing the trade of medicinal products are obliged, in the cases that could be the reason for the suspension of the placement on and withdrawal of medicinal products from the market from Article 62 of the Medicinal Products Act (hereinafter: the Act), are obliged to notify the Agency for Medicinal Products and Medical Devices (hereinafter: the Agency) thereof in writing.

2) The patient/user of the medicinal product may report a suspicion of an irregularity in the quality of the medicinal product, or suspicion of a counterfeit medicinal product, to the Agency.

3) In addition to persons from paragraphs 1 and 2 of this Article, the Agency may receive a report or statement of suspicion of a counterfeit medicinal product from the personnel of the Custom's Administration and the Ministry of the Interior.

Article 3

1) Prior to administering the medicinal product to the patient/user, or at the warning of the patient/user of the case from Article 2 of this Ordinance, the health care professional is obliged to notify the Agency in writing on the reporting form printed in the Appendix to this Ordinance, and which forms its integral part.

2) In the reporting form from paragraph 1 of this Article, the health care professional shall list:

1. the name of the medicinal product, number of the marketing authorisation, INN or generic name of the medicinal product, pharmaceutical form and strength of the medicinal product,

2. manufacturer/ marketing authorisation holder for the medicinal product/ holder of the authorisation for parallel import of the medicinal product/ medicinal product importer/ wholesaler,

3. lot number of the medicinal product,

4. type and size of packaging of the medicinal product,

5. expiry date and production date of the medicinal product,

6. description of the irregularity/ reason for suspension of placement on or withdrawal from the market,

7. name and surname, title, telephone number and work address of the person filing the report,

8. assessed class of irregularity of the medicinal product, or suspicion of a counterfeit medicinal product.

3) The health care professional is obliged to submit the filled out reporting form from paragraph 2 of this Article to the Agency by post, fax or as an attachment to an electronic mail within 24 hours of the observed case.

Article 4

In the case from Article 3, paragraph 1 of this Ordinance, the health care professional will not administer the medicinal product to the patient/user, and instead will save a sample of the medicinal product for the purposes of the pharmaceutical inspection of the ministry responsible for health (hereinafter: ministry).

Article 5

1) The health care professional who has observed or has suspicions of the existence of a reason to suspend the placement on or withdrawal of a medicinal product from the market from Article 2 of this Ordinance during the period of administration of the medicinal product in patients in a health care institution is obliged to inform the Agency in writing thereof.

2) In the reporting form from Article 3, paragraph 1 of this Article, the health care professional shall list:

1. the name of the medicinal product, number of the marketing authorisation for the medicinal product, INN or generic name of the medicinal product, pharmaceutical form and strength,

2. manufacturer/ marketing authorisation holder for the medicinal product/ holder of the authorisation for parallel import of the medicinal product/ medicinal product importer/ wholesaler,

3. lot number of the medicinal product,

4. type and size of packaging of the medicinal product,

5. initials of the patient,

6. expiry date and production date of the medicinal product,

7. description of the irregularity/ reason for suspension of placement on or withdrawal from the market,

8. name and surname, title, telephone number and work address of the person filing the report,

9. assessed class of irregularity of the medicinal product, or suspicion of a counterfeit medicinal product.

3) The health care professional from paragraph 1 of this Article shall ensure that the medicinal product from paragraph 1 of this Article (medicinal product from the same individual packaging, in the case of a suspicion of an entire lot of the medicinal product, medicinal products form the same lot number) is no longer used, and is obliged to keep it for the purposes of the pharmaceutical inspection.

4) The health care professional is obliged to submit the filled out reporting form from paragraph 2 of this Article to the Agency by post, fax or as an attachment to an electronic mail within 12 hours of the observed case.

Article 6

1) The holder of the marketing authorisation for the medicinal product, holder of the authorisation for the parallel import of the medicinal product, manufacturer of the medicinal product, importers and wholesalers included in manufacturing or in performing wholesale trade of medicinal products are obliged to inform the Agency in writing of each observed case from Article 2 of this Ordinance which could result in the suspension of the placement on or withdrawal of the medicinal product from the market, or limitations to the use of the medicinal product that are not listed in the approved summary of product characteristics and the approved package leaflet.

2) In the case of a suspicion of an irregularity in the quality of a medicinal product, the natural and legal persons from paragraph 1 of this Article are obliged to inform the Agency in writing within:

– 12 hours of determining the irregularity, if the irregularity corresponds to a Class I irregularity from Article 12 of this Ordinance,

– 24 hours of determining the irregularity, if the irregularity corresponds to a Class II irregularity from Article 12 of this Ordinance, or for a suspicion of a counterfeit medicinal product,

– 7 days of determining the irregularity, if the irregularity corresponds to a Class III irregularity from Article 12 of this Ordinance.

3) Natural and legal persons from paragraph 1 of this Article are obliged to implement all remaining measures which pertain to the suspension of the placement on or withdrawal of a medicinal product from the market that are prescribed by the valid ordinances on good

manufacturer's practice and good practice in the wholesale trade of medicinal products, and their standard operating procedures.

4) Natural and legal persons from paragraph 1 of this Article are obliged to submit the written report on implemented measures in the cases from paragraphs 1, 2 and 3 of this Article to the Agency within 14 days of the date of taking the measures.

Article 7

Upon receipt of the report and/or report of the manufacturer, marketing authorisation holder for the medicinal product, holder of the authorisation for parallel import, importer or wholesalers on the plan and measures taken in the cases from Article 1 of this Ordinance, the Agency may take the following actions:

a) agree with the proposed measures and inform the Ministry thereof with a notification on its website, or

b) if it deems that the proposed measures are insufficient to protect the health and safety of users:

– to request additional data from the manufacturer, or the marketing authorisation holder for the medicinal product, holder of the authorisation for parallel import of the medicinal product, user or other competent body,

– give recommendations and advice to the manufacturer, holder of the marketing authorisation for the medicinal product or holder of the authorisation for parallel import of the medicinal product,

– request changes be introduced to the manner and course of the implementation of the proposed measures.

Article 8

1) The Agency shall process every received report from Articles 3, 5 and 6 of this Ordinance immediately upon receipt.

2) The Agency shall determine the responsible person for cases that may be reason for the suspension of placement on or withdrawal of a medicinal product from the market and who will be available 24 hours a day.

3) The responsible person from paragraph 2 of this Article is obliged to forward the filled out reporting form from Articles 3 and 5 of this Ordinance to the manufacturer/ wholesaler/ importer/ marketing authorisation holder/ holder of the authorisation for parallel import.

Article 9

1) If in the cases prescribed under Article 62 of the Act, the Agency suspends the placement of the medicinal product on the market, the medicinal product or lot of the medicinal product shall be kept at the place it was found regardless of whether this is the warehouse of the manufacturer, importer, wholesaler or end user.

2) The suspension of placement of a medicinal product on the market shall remain in effect until the completion of the testing of the quality of the medicinal product, or until the completion of the risk to benefit analysis for the users of the medicinal product, and may end with the return of the medicinal product to the market or its withdrawal from the market.

3) The Agency shall publish information on its website regarding the suspension of placement of a medicinal product on the market, the return of the medicinal product on the market or withdrawal of the medicinal product from the market.

Article 10

The Agency may suspend the placement of a medicinal product on the market and/or request the withdrawal of a medicinal product or a lot number of a medicinal product pursuant to the decision of the European Medicines Agency or European Commission.

Article 11

1) Following the processing of the received written report and/or reports by natural or legal persons on the cases prescribed by Article 62 of the Act, the Agency may, depending on the risk assessment or possible consequences for patients/users, perform and/or order the following actions:

– request sampling of the medicinal product from the market by the pharmaceutical inspection and conduct special quality control on the results upon which the further actions of the Agency depend,

– request the manufacturer, marketing authorisation holder for the medicinal product, holder of the authorisation for parallel important of the medicinal product, importer or wholesaler to suspend the placement of the medicinal product on the market or to withdraw the medicinal product or lot of the medicinal product from the market,

– initiate the procedure to suspend or withdraw the medicinal product or lot of the medicinal product from the market if there is no possibility for the manufacturer, holder of the authorisation for parallel important of the medicinal product, importer or wholesaler to do so.

2) In the cases from paragraph 1, subparagraph 3 of this Article, the Agency shall notify users of the medicinal product via the Notification Centre of the Republic of Croatia, while the actual withdrawal procedure for the medicinal product is carried out by the manufacturer, importer or wholesaler supplying the user with that medicinal product.

3) In the cases from paragraph 1, subparagraphs 2 and 3 of this Article, the Agency shall immediately inform the pharmaceutical inspection.

4) If in the case of paragraph 1, subparagraphs 2 and 3 of this Article, the Agency assesses that it is necessary to inform the population for the purpose of public health protection, prior to issuing such notice to the population, it shall inform the Ministry thereof.

Article 12

Reports on irregularities or suspicions on the quality of a medicinal product are classified based on their level of urgency, as follows:

1. Class I reports are reports on irregularities that are a threat to life or with serious consequences for health, such as:

– wrong medicinal product (labelling and composition/ingredients of the medicinal product do not relate to the same medicinal product),

– wrong strength of the medicinal product, which could cause serious medical consequences, microbiological impurities in 'sterile' injections/infusions or preparations for eyes,

– chemical impurities that could cause serious medical consequences,

– wrong active compound in a medicinal product with multiple ingredients with serious medical consequences;

2. Class II reports are reports on irregularities that could cause illness or incorrect treatment, but do not fall within Class I, for example:

– wrong labelling (incorrect or missing text or data),

– no package leaflet or insertion of the wrong package leaflet,

– microbiological impurities in sterile medicinal products that are not for use as injection/infusion or preparations for eyes with possible medical consequences, chemical or physical impurities (larger quantity of impurities, contamination with other medicinal products),

– submixture of products in containers, inadequate quality of the medicinal product (content, stability or filling/mass of the container for one-time dosage do not correspond to the requirements),

– uncertain closure of the medicinal product with serious medical consequences (cytotoxic medicinal products, medicinal products with a safety seal, long life medicinal products);

3. Class III reports are reports on irregularities that cannot cause serious consequences to health, but which could suspend the placement on or withdrawal of the medicinal product from the market due to other reasons (for example: lack or incorrect listing of the lot/control number, or expiry period, improper closure, microbiological or mechanical contamination).

Article 13

1) In the case of a received report of a suspicion of a counterfeit medicinal product, the Agency shall request the pharmaceutical inspection conduct sampling of the medicinal product in order to perform special quality tests and if necessary to implement the procedure prescribed by Article 11, paragraph 1, subparagraph 2 and 3 of this Ordinance.

2) If the suspicion of counterfeiting is confirmed, the Agency shall, via the Notification Centre of the Republic of Croatia, inform the users of the withdrawal of the medicinal product

from the market, while if the legal participant in the marketing of the medicinal product is not determined, the withdrawal procedure shall be carried out by the pharmaceutical inspection.

Article 14

In the case of Class I and Class II irregularities, and suspicions of counterfeiting of a medicinal product that could seriously threaten human health, the Agency shall inform other European Union Member States pursuant to the Compilation of Community Procedures on Inspections and Exchange of Information.

Article 15

The Agency carries out the notification from Article 14 of this Ordinance using the form for the *Rapid Alert Notification of a Quality Defect/Recall* which is found in Appendix II of the Compilation of Community Procedures on Inspections and Exchange of Information. The results of testing and all data pertaining to less serious cases of irregularities are forwarded to other European Union Member States using the form *Follow-up and Non-urgent Information for Quality Defects* which is Appendix III of the Compilation of Community Procedures on Inspections and Exchange of Information.

Article 16

As of the date of entry of this Ordinance into force, the Ordinance on the manner of monitoring irregularities in the quality of medicinal products (Official Gazette 36/05) shall cease to have effect.

Article 17

This Ordinance shall enter into force on the eighth day from the date of its publication in the Official Gazette.

Class: 011-02/14-02/56

Reg no: 534-10-1-2-2/4-14-1

Zagreb, 1 October 2014

Minister

Primarius Siniša Varga, DDM, m. p.

PRILOG

OBRAZAC

Prijave neispravnosti u kakvoći lijeka

Polja označena zvjezdicom (*)moraju se obvezno popuniti

1. Podaci o prijavitelju

1. Ime i prezime*	
2. Naziv i adresa zdravstvene ustanove*	
3. Broj telefona za kontakt*	
4. Broj faxa	
5. E-adresa	
6. Inicijali bolesnika	
7. Datum i vrijeme prijave	

2. Podaci o lijeku

upisati podatke navedene na vanjskom pakiranju lijeka na kojeg se prijava neispravnosti odnosi

1. Naziv lijeka	
2. Djelatna tvar	
3. Serija/e lijeka*	
4. Rok valjanosti*	
5. Broj odobrenja za stavljanje lijeka u promet*	
6. Farmaceutski oblik lijeka*	
7. Jačina lijeka*	
8. Vrsta i veličina pakiranja	
9. Proizvođač lijeka	
10. Nositelj odobrenja za stavljanje lijeka u promet/nositelj odobrenja za paralelni uvoz lijeka*	

3. Podaci o uočenoj neispravnosti

1. Detaljan opis neispravnosti*	
2. Ostali podaci koje podnositelj prijave smatra značajnim	

3. Procjena klase neispravnosti lijeka	Klasa I ☐ Klasa II ☐ Klasa III ☐

Klasa I: neispravnosti opasne po život ili s ozbiljnim posljedicama za zdravlje (krivi lijek (označavanje i sastav/sastojci lijeka ne odnose se na isti lijek), kriva jačina lijeka koja može izazvati ozbiljne medicinske posljedice, mikrobiološko onečišćenje u »sterilnim« injekcijama/infuzijama ili pripravcima za oči, kemijska onečišćenja koja mogu izazvati ozbiljne medicinske posljedice, kriva djelatna tvar u lijeku s više sastojaka sa ozbiljnim medicinskim posljedicama,

Klasa II: neispravnosti koje mogu uzrokovati oboljenja ili pogrešno liječenje, a ne pripadaju klasi I. (krivo označavanje (krivi ili izostavljeni tekst ili podatak), nedostatak upute o lijeku ili prilaganje krive upute o lijeku, mikrobiološko onečišćenje u sterilnim lijekovima koji nisu za primjenu kao injekcije/infuzije ili pripravci za oči s mogućim medicinskim posljedicama, kemijska ili fizička onečišćenja (veća količina onečišćenja, onečišćenja drugim lijekovima), podmješavanje proizvoda u spremnicima, neodgovarajuća kakvoća lijeka (sadržaj, stabilnost ili punjenje/masa kod spremnika za jednokratno doziranje ne odgovaraju zahtjevu), nesigurno zatvaranje lijeka s ozbiljnim medicinskim posljedicama (citotoksični lijekovi, lijekovi sa sigurnosnim zatvaračima, lijekovi jakog djelovanja),

Klasa III.: neispravnosti koje ne mogu izazvati ozbiljne posljedice po zdravlje, ali se može obustaviti stavljanje lijeka u promet ili povući iz prometa zbog drugih razloga (primjerice: nedostatak ili krivo navođenje serijskog/kontrolnog broja ili roka valjanosti, manjkavo zatvaranje, mikrobiološka ili mehanička onečišćenja).