

Prošireni apstrakt

DOI: 10.5937/SVS26016A

ALIMS I VETERINARSKI ANTIMIKROBNI LEKOVI

Jelena Anđelković^{1*}

¹Agencija za lekove i medicinska sredstva Srbije, Beograd, Republika Srbija

*e-mail kontakt osobe: jelena.andjelkovic@alims.gov.rs

Kratak sadržaj

Antimikrobna rezistencija predstavlja jedan od najznačajnijih globalnih izazova za javno zdravlje, veterinarsku medicinu i bezbednost hrane. Zbog mogućnosti prenosa rezistentnih mikroorganizama i gena rezistencije između životinja, ljudi i životne sredine, kontrola primene antimikrobnih lekova u veterinarskoj medicini postala je jedan od ključnih segmenata koncepta „Jedno zdravlje“ (engl. „One Health“). U tom procesu, regulatorni organi imaju značajnu ulogu kroz procenu odnosa koristi i rizika veterinarskih lekova, uspostavljanje odgovarajućih uslova njihove primene i praćenje obrazaca korišćenja antimikrobnih supstanci na nacionalnom nivou.

Agencija za lekove i medicinska sredstva Srbije (ALIMS) nadležna je za izdavanje dozvola za stavljanje u promet veterinarskih lekova u skladu sa Zakonom o lekovima i medicinskim sredstvima Republike Srbije („Službeni glasnik RS“ br. 30/2010, 107/2012, 105/2017 – dr. zakon i 113/2017 – dr. zakon) i odgovarajućim podzakonskim aktima. Postupak izdavanja dozvole za lek podrazumeva detaljnu procenu dokumentacije koja se odnosi na kvalitet, bezbednost i efikasnost predloženog leka. Tokom procene uzimaju se u obzir ne samo zahtevi nacionalnog zakonodavstva, već i relevantni propisi Evropske unije, smernice Evropske agencije za lekove (EMA), kao i smernice Međunarodne saradnje za harmonizaciju tehničkih zahteva za registraciju veterinarskih lekova (VICH). Na osnovu sprovedene stručne procene izdaju se dozvole samo za one lekove kod kojih je potvrđeno da njihov odnos koristi i rizika odgovara uslovima predviđenim za ciljnu vrstu životinja i predložene indikacije. Podaci o svim registrovanim lekovima sa ažuriranim Sažecima karakteristika leka i Uputstvima za lek dostupni su na internet stranici Agencije: www.alims.gov.rs.

Kada su u pitanju lekovi namenjeni životinjama čiji se proizvodi koriste u ishrani ljudi, dozvola za lek može biti izdata samo ukoliko sadrži farmakološki aktivne supstance za koje je utvrđen maksimalni nivo rezidua u hrani životinjskog porekla. Istovremeno, regulativa zabranjuje primenu određenih grupa supstanci, uključujući hormone sa anaboličkim dejstvom, stilbene i njihove derivate, beta-agoniste, kao i antimikrobne supstance koje su rezervisane isključivo za humanu medicinu. Na taj način, obezbeđuje se zaštita zdravlja potrošača, očuvanje efikasnosti značajnih antimikrobnih lekova i usklađenost nacionalnog regulatornog sistema sa međunarodnim standardima.

Posebno značajan deo regulatorne procene odnosi se na veterinarske antimikrobne lekove. Tokom postupka registracije procenjuju se podaci o farmakološkim i toksikološkim osobinama, reziduama u hrani životinjskog porekla, mogućem uticaju na životnu sredinu i potencijalnom doprinosu razvoju antimikrobne rezistencije. Takođe se definišu indikacije, doziranje, dužina terapije, karenca, kontraindikacije, interakcije, upozorenja i mere opreza koje omogućavaju racionalnu i odgovornu upotrebu leka. Nakon izdavanja dozvole za lek, ALIMS kontinuirano prati kvalitet, bezbednost i efikasnost tokom celog životnog ciklusa proizvoda. Nova saznanja o bezbednosti, efikasnosti ili rezistenciji mogu dovesti do izmena odobrene dokumentacije kroz odgovarajuće regulatorne procedure, čime se obezbeđuje da informacije o leku budu stalno usklađene sa najnovijim naučnim dokazima.

Pored aktivnosti vezanih za izdavanje i održavanje dozvola za lekove, ALIMS je nadležan i za prikupljanje, obradu i analizu podataka o prometu veterinarskih lekova u Republici Srbiji. Metodologija prikupljanja i obrade podataka usklađena je sa metodologijom koja se primenjuje u Evropskoj uniji, dok se podaci o prometu antimikrobnih lekova analiziraju u skladu sa preporukama i metodologijom Svetske organizacije za zdravlje životinja (WOAH). Ovi podaci predstavljaju važan indikator trendova u primeni antimikrobnih supstanci i osnovu za planiranje nacionalnih aktivnosti usmerenih ka očuvanju njihove efikasnosti.

Analiza podataka o prometu antimikrobnih lekova u Republici Srbiji za period od 2014. do 2024. godine pokazuje da se godišnji promet kretao između 56 i 76 tona aktivnih antimikrobnih supstanci. Najveći deo ovih supstanci korišćen je kod životinja namenjenih proizvodnji hrane za ljude, što dodatno naglašava značaj kontinuiranog praćenja njihove primene. U posmatranom periodu, među najzastupljenijim grupama antimikrobnih lekova bili su penicilini, tetraciklini i aminoglikozidi. Sa aspekta upravljanja rizikom od razvoja rezistencije, posebno je značajno da penicilini i tetraciklini prema AMEG (Antimicrobial Advice ad hoc Expert Group) kategorizaciji Evropske unije pripadaju grupi D („Odgovorna primena“), odnosno grupi koja nosi najniži rizik za javno zdravlje i čija se primena smatra prihvatljivom kada je medicinski opravdana, dok su aminoglikozidi svrstani u grupu C („Primena sa oprezom“).

Istovremeno, u poređenju sa 2014. godinom uočen je porast prometa polimiksina, makrolida i amfenikola. Ovaj podatak zaslužuje posebnu pažnju jer polimiksini pripadaju grupi B („Ograničena primena“), koja obuhvata antimikrobne supstance čiju upotrebu treba ograničiti radi očuvanja njihove efikasnosti u humanoj medicini. Makrolidi i amfenikoli svrstani su u grupu C („Primena sa oprezom“), što ukazuje na potrebu za razboritom primenom uz procenu raspoloživih terapijskih alternativa. Praćenje kretanja prometa ovih grupa antibiotika predstavlja važan element nacionalnih strategija za kontrolu antimikrobne rezistencije i identifikaciju oblasti u kojima su potrebne dodatne edukativne, regulatorne ili stručne aktivnosti.

Kontinuirano unapređenje regulatornog sistema, praćenje tržišta veterinarskih lekova i analiza obrazaca primene antimikrobnih supstanci predstavljaju ključne instrumente za odgovornu upotrebu antibiotika u veterinarskoj medicini. Podaci prikupljeni kroz regulatorne i nadzorne aktivnosti ALIMS omogućavaju pravovremeno prepoznavanje trendova u korišćenju antimikrobnih lekova i pružaju stručnu osnovu za donošenje mera usmerenih ka očuvanju njihove efikasnosti. Na taj

način, regulatorni sistem Republike Srbije daje značajan doprinos nacionalnim i međunarodnim aktivnostima u borbi protiv antimikrobne rezistencije i zaštiti zdravlja ljudi, životinja i životne sredine u skladu sa principima koncepta „Jedno zdravlje“.

Ključne reči: AMEG kategorizacija, antimikrobna rezistencija, veterinarski lekovi, dozvola za lek, One Health, promet lekova, regulatorna procena

ALIMS AND VETERINARY ANTIMICROBIALS

Jelena Anđelković^{1*}

¹Medicines and Medical Devices Agency of Serbia, Belgrade, Serbia

*Corresponding author's e-mail: jelena.andjelkovic@alims.gov.rs

Summary

Antimicrobial resistance (AMR) represents one of the most significant global challenges to public health, veterinary medicine, and food safety. Due to the possibility of transmission of resistant microorganisms and resistance genes among animals, humans, and the environment, the control of antimicrobial use in veterinary medicine has become a key component of the One Health concept. In this context, regulatory authorities play an important role through the assessment of the benefit-risk balance of veterinary medicinal products, the establishment of appropriate conditions for their use, and the monitoring of antimicrobial use patterns at the national level.

The Medicines and Medical Devices Agency of Serbia (ALIMS) is responsible for granting marketing authorisations for veterinary medicinal products in accordance with the Law on Medicines and Medical Devices of the Republic of Serbia („Official Gazette of the Republic of Serbia“, No. 30/2010, 107/2012, 105/2017 - other law and 113/2017 - other law) and the associated secondary legislation. The marketing authorisation procedure includes a comprehensive assessment of documentation related to the quality, safety, and efficacy of the proposed medicinal product. During the evaluation process, not only national legislative requirements are considered, but also relevant European Union legislation, guidelines of the European Medicines Agency (EMA), and the guidelines issued by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). Marketing authorisations are granted only to medicinal products for which the benefit-risk balance has been demonstrated to be favourable for the target animal species and proposed indications. Information on all authorised veterinary medicinal products, including up-to-date Summaries of Product Characteristics (SPCs) and Package Leaflets, is publicly available on the Agency's website (www.alims.gov.rs).

For medicinal products intended for food-producing animals, a marketing authorisation may only be granted if they contain pharmacologically active substances for which maximum residue limits (MRLs) have been established in food of animal origin. Furthermore, the legislation prohibits the use of certain categories of substances, including hormones with anabolic effects, stilbenes and their

derivatives, beta-agonists, as well as antimicrobial substances reserved exclusively for human medicine. These measures contribute to consumer protection, preservation of the effectiveness of important antimicrobial agents, and harmonization of the national regulatory framework with international standards.

A particularly important aspect of regulatory assessment concerns veterinary antimicrobial medicinal products. During the authorisation procedure, data on pharmacological and toxicological properties, residues in food of animal origin, potential environmental impact, and the possible contribution to the development of antimicrobial resistance are thoroughly evaluated. In addition, indications, dosage regimens, treatment duration, withdrawal periods, contraindications, interactions, warnings, and precautions are defined to ensure the prudent and responsible use of the product. Following the granting of a marketing authorisation, ALIMs continuously monitors the quality, safety, and efficacy of veterinary medicinal products throughout their entire life cycle. New information regarding safety, efficacy, or antimicrobial resistance may lead to modifications of the approved documentation through appropriate regulatory procedures, ensuring that product information remains aligned with the latest scientific evidence.

In addition to activities related to granting and maintaining marketing authorisations, ALIMs is also responsible for collecting, processing, and analysing data on the sales of veterinary medicinal products in the Republic of Serbia. The methodology used for data collection and analysis is harmonized with that applied within the European Union, while antimicrobial sales data are processed in accordance with the recommendations and methodology of the World Organisation for Animal Health (WOAH). These data represent an important indicator of trends in antimicrobial use and provide a basis for planning national activities aimed at preserving their effectiveness.

Analysis of antimicrobial sales data in the Republic of Serbia for the period 2014–2024 showed that annual sales ranged from 56 to 76 tonnes of active antimicrobial substances. The majority of these substances were used in food-producing animals, further emphasizing the importance of continuous monitoring of their use. During the observed period, the most represented antimicrobial classes were penicillins, tetracyclines, and aminoglycosides. From the perspective of antimicrobial resistance risk management, it is particularly important that penicillins and tetracyclines belong to Category D (“Prudent Use”) of the European Union AMEG (Antimicrobial Advice ad hoc Expert Group) classification system, representing the category associated with the lowest risk to public health and considered acceptable when their use is medically justified. Aminoglycosides are classified within Category C (“Caution”).

At the same time, compared with 2014, an increase in the sales of polymyxins, macrolides, and amphenicols was observed. This finding deserves particular attention because polymyxins belong to Category B (“Restrict”), which includes antimicrobial substances whose use should be limited in order to preserve their effectiveness in human medicine. Macrolides and amphenicols are classified within Category C (“Caution”), indicating the need for prudent use following careful assessment of available therapeutic alternatives. Monitoring trends in the sales of these antimicrobial classes represents an important element of national strategies

aimed at controlling antimicrobial resistance and identifying areas where additional educational, regulatory, or professional measures may be required.

Continuous improvement of the regulatory system, monitoring of the veterinary medicinal products market, and analysis of antimicrobial use patterns represent key tools for promoting the responsible use of antibiotics in veterinary medicine. Data generated through the regulatory and surveillance activities of ALIMs enable timely identification of trends in antimicrobial use and provide a scientific basis for the implementation of measures aimed at preserving antimicrobial effectiveness. In this way, the regulatory system of the Republic of Serbia makes a significant contribution to national and international efforts to combat antimicrobial resistance and to protect human, animal, and environmental health in accordance with the principles of the One Health approach.

Keywords: AMEG classification; antimicrobial resistance; veterinary medicinal products; marketing authorisation; One Health; sales of veterinary medicinal products; regulatory assessment