USAID MEDICINES, TECHNOLOGIES, AND PHARMACEUTICAL SERVICES (MTaPS) PROGRAM

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Exploring Antimicrobial Stewardship Policies, Activities, Regulatory Framework, and Supply Chain Management in Uganda: Findings of a Multisectoral Assessment

BACKGROUND

Antimicrobial resistance (AMR) is a major global public health challenge, with over 4.9 million associated deaths reported in 2019 (https://doi.org/10.1016/S0140-6736(21)02724-0). Uganda is currently implementing its National Action Plan on AMR 2018, which is based on the Global Action Plan for AMR containment. Other global frameworks, such as the World Health Organization's (WHO) International Health Regulations (IHRs) and Joint External Evaluation (JEE)-2 tools are also being applied to guide activity implementation. The goal of the JEE-2 tool is to guide countries in building systematic capacity for the IHRs. The USAID Medicines, Technologies, and Pharmaceutical Services (MTaPS) program is supporting the Government of Uganda in systematically building capacity over various JEE-2 activities related to WHO IHR benchmark 3.4 (Optimize use of antimicrobial medicines in human, animal health, and agriculture), which has 14 actions. Countries are required to complete an action under capacity level 2 under benchmark 3.4 to assess stewardship policies and activities, including regulatory framework and supply chain management of antimicrobials, by using a multisectoral approach.

The purpose of the activity was to identify existing policies, legislation, and regulations on antimicrobial use; identify gaps; and make recommendations to improve the use of antibiotics in humans, crops, fish, and animals with the overall goal of reducing the further emergence and spread of AMR. The findings also informed other JEE-2 activities, for example, developing a national antimicrobial stewardship (AMS) strategy under capacity level 2; under capacity level 3, developing or reviewing the national regulatory framework for appropriate use of antimicrobials in humans and approving and enacting legislation and regulations on import, marketing authorization, production, and use of antimicrobials. Findings also informed policy review, reform of national legislation and regulations on use, availability, and quality of antimicrobials—another 3.4 capacity level 2 action of the WHO benchmarks for IHR.

METHODOLOGY

The activity was conducted by technical experts from the Ministry of Health and Ministry of Agriculture, Animal Industry, and Fisheries (MAAIF), with collaborative support from the USAID MTaPS program between February 2021 and December 2021. A three-phased approach was used to implement activities, including a desk review of the literature, key informant interviews for verification of information gathered, and stakeholder validation of findings. An assessment tool developed by USAID MTaPS validated and used in eight other low- and middle-income countries was used for data collection. Areas of data collection included regulatory processes for marketing authorization, licensing of establishments, and regulatory inspections; post-marketing surveillance and pharmacovigilance (PV); supply management policies and guidelines; and prescribing, dispensing, and use of antimicrobials.

KEY FINDINGS

A total of 11 acts of parliament, 13 statutory instruments/regulations, 13 guidelines and circulars, and 5 professional body acts were found and used to inform this assessment. The laws, guidelines, and regulations in place were found adequate, addressed the four thematic areas of the assessment, and, to some extent, accounted for AMS. However, enforcement was found to be inadequate.

MARKETING AUTHORIZATION, LICENSING OF ESTABLISHMENTS, AND REGULATORY INSPECTIONS

Uganda has a National Medicines Policy (2002) that guides the regulatory framework for antimicrobials. The National Drug Authority (NDA) is designated with responsibility to regulate importation and in-country manufacture of antimicrobials as well as registering all antimicrobial products in Uganda. The National Drug Policy and Authority Act (NDPA) 1993 clearly stipulates regulation of pharmaceutical premises, distributor outlets, and pharmacies, including which medical professionals are authorized to prescribe, dispense, and distribute drugs, and designates the NDA as the enforcing body. Drugs are also categorized by class (A, B, C) with restrictions on access, prescribing, and sale of specific categories, including antibiotics, however, this is not strictly adhered to or enforced. NDA regulates all pharmaceutical manufacturing and sale premises in Uganda and enforces this through annual licensure and routine inspection against a checklist of expected standards, such as storage, prescription of restricted categories, and authorized personnel handling medicines. NDA regulates imports of all pharmaceuticals and raw materials in the country and tests them to confirm the quantity, quality, and activity of active ingredients. However, there is no national system for monitoring antimicrobial sales and use.

SUPPLY MANAGEMENT POLICIES AND GUIDELINES

The NDA has QC/QA checks in place to monitor the quality of antimicrobials imported (through prequalification and registration of suppliers) and laboratory analysis of samples (e.g., for specific reports, such as bioavailability, quantity of active ingredient), compliance of manufacturers importing products into the country (through inspection of manufacturing plants to certify good manufacturing practice),

and inspections of pharmacies for human and animal antimicrobials to enforce national guidelines on distribution and use of antimicrobials.

There is an Essential Medicines and Health Supplies List for Uganda (EMHSLU) that includes antimicrobials. The EMHSLU is revised every five, years, however the current version is outdated. According to WHO, the EMHSLU has 363 medicines, of which 247 are on the WHO Model Essential Medicines List (EML). Medicines are listed by pharmacological group, and not by level of care. The EMHSLU classifies antimicrobials only according to VEN (vital, essential, necessary) and has not been updated to include the WHO access, watch and reserve (AWaRe) classification.

Health workers are routinely trained on the concept of an EML and standard treatment guidelines (STGs), however, there is no publicly available data on the extent of availability of EMLsn in health facilities.

The National Medical Stores (NMS) Act of 1993 mandates that NMS procure, store, and distribute medicines, including antibiotics, equipment, and health supplies, to all public health facilities and that they advise NDA, the Ministry of Health, Ministry of Finance, and Ministry of Local Government (MLG) on issues of medicine quantification, procurement, and distribution.

POST-MARKETING SURVEILLANCE AND PV

The country has a PV monitoring unit under NDA. Within the STGs, health workers are provided clear instructions on how to manage and report adverse drug reactions.

NDA also conducts market surveillance for substandard and falsified products and issues alerts to health workers and the public to recall or stop the use of any identified products in this category. However, a national report highlighting how many substandard or falsified products have been identified in the last two years is not available.

PRESCRIBING, DISPENSING, AND USE OF ANTIMICROBIALS

The country's STGs are used for managing infectious diseases and guiding rational prescription and appropriate use of antimicrobials. The Uganda clinical guidelines are aligned with the EMHSLU and are categorized by condition, not level of care. The STGs are revised every five years; however, since the current version has not been updated, it does not include AWaRe categorization of antibiotics to guide prescribing.

Over the past two years, there have been various infection prevention and control (IPC), antimicrobial use, and antimicrobial resistance awareness sessions conducted for targeted groups (health workers, medical students, professional body members) and the public through the annual World Antimicrobial Awareness week sessions. However, data on the impact of these trainings and campaigns is not yet available.

GAPS

Overall, many of the guidelines and policies have not been revised and updated within the last five years and, as such, do not incorporate most of the pertinent recommendations on containing AMR by optimizing use of antimicrobials.

Information on the quantity of antimicrobials imported into the country, and the proportion of antimicrobials consumed in Uganda, disaggregated by public and private sector contributions, is also not currently available, which makes it difficult for policy makers and implementers to design targeted interventions for improving antimicrobial use. Additionally, there is currently no system for monitoring antimicrobial sales and use throughout the country as total national consumption and expenditure on antimicrobials by pharmacologic class, AWaRe category, or condition.

Data on the extent to which standard guidelines and policies are enforced and adhered to is not being routinely tracked at both national and user levels (public and private).

Despite having laws and guidelines that gazette antimicrobials as prescription-only medicines, this is not adhered to or enforced, especially in the private sector.

Specific to AMS and optimal use of antimicrobials in animals, crops, and fish, specific deficiencies in the current guidelines and policies include but are not limited to:

- Lack of AMS-specific policies to guide AMS strategy
- Lack of a department responsible for veterinary drug regulation, in line with World Organization for Animal Health (OIE) terrestrial code and African Union Inter-African Bureau for Animal Resources (AU-IBAR)–East African Community (EAC) recommendations
- Merger of human and veterinary antimicrobial schedules in NDPA, which affects restrictions and enforcement of these restrictions
- Conflict of the mandates between MAAIF and NDA over development of a veterinary EML and formulary for animals, fish, and crops
- No listing of fish drugs in the NDA drug register, even though the drugs themselves are registered with NDA; no specific guidelines for licensing antimicrobials used in fish and crop protection
- Low post-marketing surveillance for veterinary antimicrobials and circulation of unlicensed antimicrobials at border districts, because of weak enforcement
- Low antimicrobial post-market quality assurance
- Weak PV system for animal antimicrobials due to low level of veterinary staff at NDA; widespread intermittent community outreach and laxity in adverse drug event reporting by veterinarians and farmers
- Irregular antimicrobial supply practices that affect AMS, including lack of guidelines for antimicrobial donations to farmers, poor antimicrobial dispensing practices, and lack of antimicrobial consumption data

RECOMMENDATIONS

First, it is imperative that ministries impress the urgency of AMR on government with specific emphasis on how antimicrobial use can be optimized to reduce costs to government and patients' out-of-pocket expenditure as well as minimize misuse due to wastage. As such, all government commitments should be backed with the financial obligations to tackle AMR by improving stewardship, surveillance, and IPC in both human and animal health in the public and private sectors.

Second, ministries should spearhead amendment of outdated acts/regulations and guidelines to meet current challenges in AMS and reflect current global guidelines on AMS and AMR, such as AWaRe classification.

Training institutions for health care workers and veterinarians should emphasize AMR and AMS during training and postgraduate on-the-job training to better equip the health work force.

Research should be supported in AMS for both human and animal & agricultural sectors, such that data is available on the impact of regulations and guidelines and the extent of their enforcement. This information will inform policy reforms and guideline updates and subsequently optimize the distribution, prescription, and use of antimicrobials in Uganda.

Health care institutions and farms under MAAIF should be supported with the infrastructure and capacity to handle antimicrobial waste, for example, construction of pits, dumping sites, and incinerators to avoid leakage of antimicrobial waste into the environment.

Because enforcement is the major issue with currently existing laws and guidelines, ministries and regulatory bodies should support enforcement and routinely measure compliance to laws, treatment guidelines, and other guidelines for prescription and use of antimicrobials in both humans and animals in the public and private sectors. Additionally, NDA should amend drug schedules to recognize new prescribers that have been designated at the lowest levels of care (nurses and clinical officers) who are not recognized as authorized prescribers in the current law.

To strengthen AMS in the animal, fish, and crop sectors, it is recommended that MAAIF:

- Develop AMS-specific policies
- Incorporate AMS into the laws for regulating animal health workers and disease control in animals, fish, and crops
- Strengthen structures for regulating antimicrobials, in line with OIE and AU-IBAR-EAC recommendations
- Invest in laboratory diagnostic infrastructure to enhance good clinical practices
- Promote rational prescription and use of antimicrobials and strengthen post-marketing surveillance
- In collaboration with MLG, incorporate the AMR NAP into their routine or annual activity plans and allocate financial resources for implementation, monitoring, evaluation, and reporting

Because there is no law or legal provisions to specifically regulate management of health care waste (including antimicrobial waste) in both humans and animals, and neither is it provided for in the National Environment Act, special consideration should be made to have it one in place.