World Health Organization

Utilizing data on antimicrobial use and knowledge to inform regulatory changes to antibiotic packaging and support antimicrobial stewardship efforts in Bangladesh

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Background

Antimicrobial stewardship efforts undertaken to date include the development of national treatment guidelines and the piloting of selected interventions in a small number of hospitals. The Directorate General of Drug Administration (DGDA), operating under the Ministry of Health & Family Welfare, serves as the national regulatory authority tasked with ensuring the quality, safety, and efficacy of pharmaceutical products through the enforcement of relevant legislation. Enforcing the regulations to prohibit over-the-counter sale of prescription-only medicines, including antibiotics, has been challenging due to the 86 local manufacturers producing 98% of medicines for the pharmaceutical market and the vast number of pharmacies in the country (approximately 202,500 in 2022), leading to a large proportion of antibiotics being obtained over the counter and self-medication with antibiotics. Compounding this issue is a lack of understanding about antibiotics and AMR among the general population. This lack of awareness further perpetuates inappropriate antibiotic usage in Bangladesh.

To address these challenges effectively, concerted efforts are needed to strengthen regulatory enforcement, enhance public awareness campaigns, and promote antimicrobial stewardship practices across all sectors of society. Collaboration between governmental bodies, healthcare

professionals, pharmaceutical manufacturers, and community stakeholders is crucial in mitigating the threat of AMR and safeguarding the effectiveness of antimicrobial treatments in Bangladesh.

In addition, significant increases observed in the use of antibiotics in Bangladesh prompted investigation and intervention. Total antibiotic use more than doubled from 19.8 defined daily doses per 1,000 inhabitants per day (DID) in 2018 to 55.5 DID in 2021 and 48.9 DID in 2022 (compared with the median of 16.6 DID in 26 countries contributing data to the Global Antimicrobial Resistance and Use Surveillance System [GLASS] in 2020). In 2022, Access group antibiotics made up 29% of overall national use, falling well below the 60% target and indicating widespread overuse and misuse of broad-spectrum Watch antibiotics. Major increases of three- to four-fold were seen in the use of third-generation cephalosporins (e.g., ceftriaxone), sulfamethoxazole/trimethoprim, fluoroquinolones (e.g., moxifloxacin) and nitroimidazoles (e.g., metronidazole). Third- generation cephalosporins, largely cefixime and ceftriaxone, made up 33.3% of total national antibiotic use. This is concerning given their use is associated with an increased risk of infection and colonization with extended-spectrum beta-lactamases (ESBLs).

With technical support from the World Health Organization (WHO) Country Office in Bangladesh and Staten's Serum Institute in Denmark, alongside financial backing from the Fleming Fund, the DGDA investigated the escalating antibiotic use in the country. This collaborative effort aimed to identify the underlying causes and devise interventions to tackle the issue effectively. Subsequently, an initiative was launched to overhaul antibiotic packaging for all antibiotics manufactured and sold within Bangladesh. This initiative was a proactive measure to address inappropriate antibiotic use and combat AMR in the country.

Antibiotic packaging initiative

A baseline survey was conducted in November and December 2021 by Assistant Director of DGDA, Ms. S.M. Sabrina Yesmin, which has provided valuable insights into the knowledge levels of pharmacy retailers regarding antibiotics and AMR in Bangladesh. The survey encompassed 427 pharmacy retailers across 8 divisions of the country and utilized a mixed-method approach to gather data. Approximately one-third of retailers were not suitably qualified as pharmacists and over two-thirds could not readily identify examples of antibiotics. To complement the survey, key informant interviews were conducted between December 2021 and January 2022 with a range of policymakers, healthcare professionals, manufacturers, pharmacy retailers, graduate pharmacists, development partners, and researchers. Interviewees were asked a series of questions about the adequacy of existing labeling of antibiotics and to provide feedback on different proposed designs of antibiotic packaging and the feasibility of their implementation. The consensus among stakeholders was that existing primary packaging (which comes into direct contact with the antibiotic e.g. blister pack for tablets) and secondary packaging (outer packaging to protect storage and transportation e.g. cardboard box) of antibiotics did not distinguish it from other medicines, making it difficult for both retailers and consumers to distinguish antibiotics from other medicines.

The results of the survey and interviews, as well as proposed changes to antibiotic packaging, were presented by DGDA to the Bangladesh Association of Pharmaceutical Industries for discussion in January 2022. The association initially raised concerns that regulations could limit market access for existing antibiotics, reducing profitability and disincentivizing manufacturers from producing antibiotics. They also highlighted that adhering to new regulations would necessitate significant

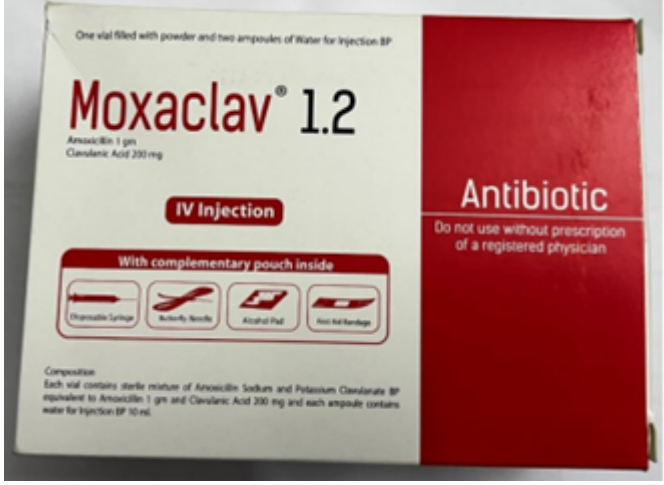
investment in updating packaging processes and ensuring compliance, leading to increased operational costs. However, evidence generated from the survey and meetings held to sensitize manufacturers on the impact of AMR helped to alleviate these concerns.

Based on engagement with key stakeholders, DGDA proposed regulatory changes to the packaging of all antibiotics for human and veterinary use marketed in Bangladesh. This involved the inclusion of red markings and the text “antibiotic” on the primary and secondary packaging, as well as the phrase “Do not take antibiotics without the prescription of a registered physician” (Figure 1). This decision aimed to enhance public, retailer and health worker awareness and ability to identify antibiotics from other medicines and modify their behaviors to reduce self-medication. The decision was endorsed by the Ministry of Health & Family Welfare’s Drug Control Committee in March 2022. An official letter was circulated to all pharmaceutical companies in the country, detailing requirements for samples of the new packaging for antibiotic products to be submitted to the DGDA by November 2022 and enforcement of the required changes from December 2022. The delayed enforcement was to allow for the stocks of products with older packaging to be depleted, but new batches of antibiotics would be required to adhere to the red label packaging immediately. The antibiotic packaging initiative in Bangladesh was officially launched and publicly promoted during World Antimicrobial Awareness Week in November 2022. . It was further supported by the inclusion of relevant regulations in Section 40(d) of the Drug and Cosmetics Act 2023, which implemented strict measures, including fines of up to 20,000 Bangladeshi taka (BDT) (equivalent to USD 182) for the sale of antibiotics or any other prescription-only medicine without a prescription from a registered doctor. DGDA conducts regular inspections of retail pharmacies to monitor compliance and issue penalties for infringements. As of January 2024, approximately 80% of pharmaceutical companies had implemented changes to their antibiotic packaging in accordance with the regulatory requirements. This indicates significant progress in the adoption of the new packaging standards and reflects the commitment of both regulatory authorities and pharmaceutical companies to combat AMR and promote responsible antibiotic use in Bangladesh. The impact of the initiative will be measured through ongoing national antimicrobial use surveillance and a post survey of relevant stakeholders. Any unintended consequences, such as reduced access of lifesaving treatments for marginalized or vulnerable populations, will also be evaluated.

Conclusion

While regulatory decisions and interventions may be time- and resource-intensive to implement, these are indispensable in promoting the appropriate use of antimicrobials and enabling antimicrobial stewardship efforts to be effective and sustainable. There must be robust mechanisms to ensure they are enforced, with processes in place to objectively measure their impact, as well as monitor any unintended consequences.

Figure 1. Example of red marking initiative on antibiotic packaging in Bangladesh


One vial filled with powder and two ampoules of Water for Injection BP
Moxaclav® 1.2
Amoxicillin 1 gm
Clavulanic Acid 200 mg
IV Injection
With complementary pouch inside
Antibiotic
Do not use without prescription of a registered physician
Composition
Each vial contains sterile mixture of Amoxicillin Sodium and Potassium Clavulanate BP equivalent to Amoxicillin 1 gm and Clavulanic Acid 200 mg and each ampoule contains water for Injection BP 10 mL


Moxaclav® 1.2
Antibiotic