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Why Did The European Commission Decide All Antimicrobials Should Be Rx-Only?

by David Ridley

The European Commission responds to questions from HBW Insight regarding its decision to include OTC antivirals and antifungals, including commonly used products like thrush and cold sore creams, in the expanded prescription-only requirements for antimicrobials, as part of proposed measures to combat antimicrobial resistance.

As part of the European Union's pharmaceutical legislation update, the European Commission has proposed making all antimicrobials, including OTC antifungals and antivirals, prescription-only.

Designed to combat anti-microbial resistance (AMR) – responsible for more than 35,000 deaths every year in the EU, according to the EC– the measures in the draft revised directive could see commonly used topical brands like Bayer's Canesten thrush creams (fluconazole, clotrimazole) and Haleon's Zovirax cold sore treatments (acyclovir) removed from non-prescription sale in pharmacy and grocery outlets.

Although published on 26 April, the full implications of this proposal didn't hit many in the OTC market until a month later at the 59th Annual Meeting of the Association of the European Self-Care Industry (AESGP), when the EC's Olga Solomon outlined it explicitly to a somewhat stunned audience. (Also see "*AESGP Annual Meeting: OTC Antifungals, Antivirals Could Become Rx In EU*" - HBW Insight, 24 May, 2023.)

Since then, the proposal has come under fire from numerous sources, not just industry associations across the EU but also the German medicines regulator, BfArM, and the Dutch central government, De Rijksoverheid. (Also see "*German Regulator, Dutch Government Criticize EU's OTC Antimicrobial Reverse-Switch Plans*" - HBW Insight, 28 Jun, 2023.)

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Criticism from national regulators and governments is particularly welcome, from industry's point of view, as member states, under the provisions of the proposed directive, specifically Article 51(5), will have the ability to adapt the proposal based on national needs by waiving the requirement for prescription.

"They can also adapt requirements on the dosage, strength/form/packaging or other circumstances linked to the use of the antimicrobial," an EC representative told HBW Insight.

The directive also needs to go through the EU Parliament and the European Council. Already the EU rapporteur, Parnelle Weiss, has suggested restricting the Rx requirement to systemic antimicrobials, which would ensure topical antifungals and antivirals remain available as OTC medicines. (Also see "*Systemic, Not Topical Antimicrobials Should Be Prescription-Only, Says EU Rapporteur*" - HBW Insight, 7 Nov, 2023.)

"Totally Unacceptable" – Industry, Experts React To EU OTC Antimicrobial Reverse-Switch Proposal

By David Ridley

26 Jun 2023
HBW Insight asked European consumer healthcare trade associations and experts for reactions to the news that OTC antifungals, like treatments for athlete's foot, and OTC antivirals, like cold sore creams, could soon become prescription-only within the European Union.

Read the full article here

Whatever happens, it won't be resolved anytime soon, notes legal expert Els Janssens: "The sensitivity of the measures contained in the proposals and the divergence in views that we are already seeing around them show that this will be a very complex legislative process."

"The parliamentary elections in June 2024 will only bring added pressure to the timings and negotiations," added Janssens, who is counsel in commercial law, litigation and healthcare regulatory issues at law firm Baker McKenzie.

Why OTC Antimicrobials?

To better understand where the proposal came from, what the evidence is for AMR relating to antifungals and antivirals, and whether the impact has been assessed of requiring consumers to visit a doctor for self-treatable conditions such as thrush and cold sores, HBW Insight has directly questioned the EC.

Asked why the EC decided to include OTC antimicrobials, a spokesperson said it "chose to opt for the stricter approach with a full harmonization across the EU (i.e., placing all antimicrobials under prescription by a healthcare professional) to preserve the effectiveness of existing antimicrobials and reduce the need of new antimicrobials."

"As a matter of fact, all antimicrobials (antibiotics, antivirals, antifungals and antiprotozoals) are concerned by AMR," the spokesperson continued. "Currently, the resistance is mostly observed against antibiotics however resistances have been described against all antimicrobials and the concern is growing together with the capacity to detect drug resistances in all settings and countries."

The EC representative noted that "prescription practices can vary across member states, meaning that a product considered OTC in one member state may be a prescribed medicine in another."

Antibiotics, antivirals, antifungals and antiprotozoals, whether they are OTC or not, are "in principle" also concerned by AMR considerations "both in terms of resistance of the pathogens in patients as well as resistance cause by their environmental fate."

It is this principle, alongside "consultations and desk research" carried out by the EC, that informed its decision to include these products within the broader definition of antimicrobials, included in the prescription requirements of the new directive, the representative explained.

What's The Evidence?

Of all the documents published in support of this legislative process since the publication of the first "roadmap" in 2020, HBW identified one report detailing support for removing OTC access to antimicrobials.

In an *outcome assessment* of the 2017 EU AMR Action Plan, published by ICF International and RAND Europe – commissioned by the EC to undertake the assessment with the help of the Romanian Health Observatory and a panel of individual experts working in the field of AMR – workshop participants and interviewees suggested preventing OTC sales of antimicrobials as a way to strengthen the EU response to AMR through regulation.

Regarding the issue of OTC antimicrobials contributing to AMR, HBW Insight found one explicit mention in the scientific evidence published by the EC during its legislative process.

Researchers from the Netherlands Institute for Health Services Research and the University of Antwerp, *in a paper* describing the results of the "antimicrobial resistance and the causes of non-prudent use of antibiotics" (ARNA) project, commissioned by the EC, pointed out that "resistance to antifungals is increasing."

In the same sentence, however, the researchers also note that the "number of infections with drug-resistant fungi is far smaller than those caused by antimicrobial-resistant bacteria."

For this reason, the ARNA project, which ran from 2014 to 2016, collected data on non-

prescription antibiotic use, drawing on a wide range of sources, including Eurobarometer surveys, literature reviews, and interviews with healthcare professionals and experts from across the EU.

In its conclusions, the report notes that "throughout the whole EU, antibiotics for human use are legally available only with a prescription issued by a healthcare professional (Directive 2001/83/EC). OTC selling still exists in some Member States. Other forms of non-prescription use are the use of leftover antibiotics or buying through the internet."

As far as the EC's published evidence shows, then, AMR is related to the mis-and over-prescription of antibiotics where they are not effective, rather than with the mis- and over-use of OTC antimicrobials.

Responding to this point, the EC spokesperson stressed that the proposed directive "gives flexibility to Member States, which may choose to adapt the measures at national level" and that the proposal may be subject to amendment by co-legislators of the European Parliament and Council.

Impact Assessments

Were physician consultations and prescriptions required to deal with those minor ailments currently treated by OTC antimicrobials there would be significant increases in healthcare costs.

Research by the AESGP found that in the case of nail, vaginal or oral fungal infections, just under 50m packs of topical antifungals were sold in Germany, Austria and the Netherlands combined in 2022. This total represents the potential number of additional medical consultations needed if these medicines were subject to a medical prescription. (Also see "*AESGP: Rx Status For Antifungals And Antivirals Risks Health System Overload*" - HBW Insight, 22 Aug, 2023.)

HBW Insight asked the EC whether the cost of pushing people back to the doctors, in some cases perhaps also to hospitals, had been taken into account within its impact assessments related to the proposed directive.

The spokesperson said that the "proposal of putting all antimicrobials under prescription was supported by *policy element B.2.5* ('Tighten prescription requirements for antimicrobials') which was considered in the *Impact Assessment* (cf Annex 11 page 46) and which gives a positive outcome in the assessment against all factors (cf. pg. 48)."

In the section referred to above, the EC claims that "indirectly, health systems may see savings because of better prescription practices and reduced consumption, albeit this may be offset by increased costs associated with diagnostic tests and a switch to more costly antimicrobials. If successful, this policy element should reduce consumption and that in turn should reduce the

potential for negative environmental impacts."

However, there is no specific mention of reverse switching antimicrobials, nor is there a consideration of the increased costs associated with additional doctor and hospital visits or the increased human capital costs of people having to wait longer for treatment and perhaps minor conditions worsening as a result.

Big Tickets

HBW Insight pressed the EC on this issue, pointing out that neither this document, nor any other that we had found, took into account the specific costs of making all antimicrobials prescription-only.

"Regarding your follow up question," the spokesperson responded, "please note that the impact assessment had to cover over 76 policy elements in at least three combinations. According to the Commission's *better regulation rules* the impact to various stakeholders (including to health systems) needs to be calculated on the basis of each option which in this case inevitably included a mix of policy elements that addressed the problems identified."

"This has been conducted both in a quantitative and qualitative way in the impact assessment and the analysis was mostly influenced by the big tickets. It would not be opportune to conduct the analysis in the granularity you are looking for."

The big-ticket policies that the EC mentions here, in relation to AMR, are the incentives to promote the development of novel antimicrobials, such as transferable exclusivity vouchers for antimicrobial products.

"A transferable regulatory protection voucher (transferable exclusivity voucher) allows the developer of a novel antimicrobial that reduces AMR to benefit from an additional year of RP on another product in their portfolio or sell the voucher to another company," the EC explained in *this impact assessment.*

"This is a measure supported mostly by industry as a way to underpin the substantial R&D costs of bringing new classes of antimicrobials to the market."

However, given that only medicines that are "game changing" antimicrobials for reducing AMR can receive "novel antimicrobial" status, which is to say they either represent a new class of antimicrobials or have a new mechanism of action that is distinctly different from the mode of action of any authorized antimicrobial, this is unlikely to appease OTC manufacturers that could potentially lose entire categories of OTC medicines to the policy.

Again, the EC reiterated in its response to HBW Insight the fact that member states "may choose

to adapt the measure at national level" and concluded therefore that the "final burden on health systems being a factor of too many variables not in the scope of the reform cannot be readily quantified."

Why Bother?

All of this then begs the question of why introduce such a controversial measure in the first place, especially as the evidence for AMR suggests mis- or over-prescription of antibiotics, rather than misuse of OTC antimicrobials.

This question seems even more pertinent given that the Council of the EU has adopted the *Commission's recommendations* for reducing antimicrobial consumption and the spread of AMR, which include proposals to enforce the prudent use of antimicrobials across EU member states.

The Council notes the fact that "almost one in 10 EU citizens are taking antibiotics without prescription," as shown by the *2022 Special Eurobarometer on AMR*. "Those results demonstrate the need to increase and improve communication and awareness-raising activities on AMR and prudent use of antimicrobials at all levels as means to promote knowledge and behavioral change."

The Council recommends that member states should collect data on antimicrobial consumption "to allow the monitoring of antimicrobial prescribing and to provide timely feedback on prescription trends and patterns involving, among others, prescribers, pharmacists and other parties collecting such data, and where possible and appropriate using EU level digital infrastructure."

The Council also notes that the recommendation complements the 2017 *EU Guidelines on the prudent use of antimicrobials in human health*, which already state that:

- National, regional and local governments should "ensure compliance with the regulations with regards to the dispensing of antimicrobials by pharmacies without prescription."
- Pharmacists should "only dispense antimicrobials with prescription, unless specific provisions allow for regulated dispensation in specific circumstances."
- Public/patients should "use antimicrobials only when prescribed."

So, the question remains: If member states are not managing to enforce existing prescribing rules for antibiotics, what makes the Commission think that placing more antimicrobials behind the counter will help?