GARDP

Global Antibiotic Research & Development Partnership

GLOBAL CHALLENGES

SEXUALLY TRANSMITTED INFECTIONS

CHALLENGES OF TREATING DRUG-RESISTANT STIs

A little over a century ago when syphilis became the very first disease to be treatable with antibiotics, it triggered a new golden era in modern medicine and a significant decline in sexually transmitted infections (STIs). However, today STIs are at record high levels, with more than one million potentially curable sexually transmitted infections acquired every day. A major contributing factor to this trend is the rise and spread of antimicrobial resistance (AMR), because drug-resistant infections are making it increasingly difficult to treat some bacterial STIs.

With the decline of antibiotic research and development (R&D) in recent decades, treatments that have been lost to resistance have not been replaced with new antibiotics that are effective against multidrug-resistant infections. As a result, treatment options for once-curable STIs, like gonorrhoea, are now running out. Without the development of, and access to, new and effective antibiotic treatments, gonorrhoea is now in danger of becoming one of the first once-curable diseases to be no longer treatable.

NEGLECTED DISEASES

STIs can affect the sexual and reproductive health of both men and women in a wide range of ways, with serious and potentially permanent impacts on fertility, ectopic pregnancy, pelvic inflammatory disease and more. If not effectively treated they can also affect the nervous system, cause cardiovascular disease and increase the risk of HIV transmission. Babies born while a mother is infected with gonorrhoea are at risk of severe eye infections that can result in blindness. All this not only affects the lives of patients, their families and communities, but it also comes with broader economic impacts.

In the US alone, which has been experiencing what the US Centers for Diseases Control & Prevention (CDC) has described as an epidemic, with more than 2.4 million reported STI cases in 2023, the annual cost of treating STIs exceeds $16 billion. In low- and middle-income countries (LMICs), where the burden of disease is greatest, the situation is even more profound. According to the World Bank, the economic burden of STIs in LMICs is so high that the treatment of curable STIs is considered one of the most cost-effective ways to improve health worldwide.

Despite this, R&D into new STI treatments remains neglected and underfunded. For example, even though there are now more than 82 million new cases of gonorrhoea each year, it has been more than four decades since ceftriaxone, the last new treatment was introduced. In the face of rising resistance to other antibiotics, ceftriaxone has become the last available recommended treatment for gonorrhoea globally, and now cases are emerging that are also resistant to this.

GARDP'S APPROACH

Bacterial STIs rarely kill people, but the potential public health benefits of treating them, and the corresponding contribution this has towards addressing AMR, are significant. For this reason, a core part of GARDP's work is focused on the evaluation and development of new and effective antibiotic treatments that target multidrug-resistant STIs, and on ensuring that people in need get access to them.

GARDP aims to do this by identifying potential drug candidates and use its unique antibiotic R&D and access model to complete their development, and bring them to market, ensuring that high-risk populations have access to them. This model includes a partnership approach to integrate key access requirements in the pharmaceutical development of affordable products

GONORRHOEA – Towards an untreatable disease?

Over the past 80 years, the *Neisseria gonorrhoeae* bacterium has developed defenses against all classes of antibiotic medicines.

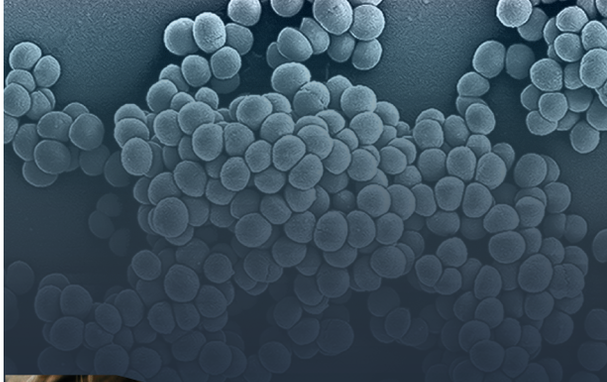
YEAR OF REPORTED RESISTANCE	
1944	SULPHONAMIDES
1946	PENICILLIN
1967	SPECTINOMYCIN
1986	TETRACYCLINE
1990	CIPROFLAXIN
1997	AZITHROMYCIN
2002	CEFIXIME
2011	CEFTRIAXONE

Ceftriaxone (sometimes in combination with azithromycin) is the only highly effective treatment left. But now several countries—including Australia, Cambodia, Canada and the United Kingdom—are increasingly reporting cases of drug resistance to ceftriaxone.

and in the clinical and non-clinical research needed to develop optimal and appropriate treatments for all impacted populations. Accessibility of new treatments is through the use of innovative licensing agreements to manufacture and commercialize affordable treatments once approved.

Since access is a key part of GARDP's mission, we also carry out surveillance and prevalence studies in high-risk populations in LMICs, and work with local partners to develop introduction strategies aimed at using the treatments optimally to both improve outcomes and slow the rate at which resistance develops against new treatments. We also carry out work to develop novel access pathways with partners at the national level to ensure treatments are affordable, quality-assured and meet the public health need.

With an initial focus on *Neisseria gonorrhoeae*, one of the World Health Organization (WHO) priority pathogens, GARDP supports the WHO goal of reducing the global incidence of *N. gonorrhoeae* by 90% by 2030, through the development of innovative antibiotic treatments for gonorrhoea infections, such as zoliflodacin (see box). GARDP's long-term goal extends beyond gonorrhoea and aims to contribute to the overall reduction of incidence of STIs caused by other key bacterial pathogens of interest as determined by the WHO, including *Treponema pallidum* (syphilis), *Mycoplasma genitalium* and *Chlamydia trachomatis*.



ZOLIFLODACIN

Through its public-private partnership with Innoviva Specialty Therapeutics (IST), GARDP is co-developing zoliflodacin, a new first-in-class, single-dose, oral antibiotic treatment for uncomplicated gonorrhoea. If approved, zoliflodacin could be the first new antibiotic treatment developed solely for gonorrhoea in decades.

In 2023, a pivotal phase 3 clinical trial, sponsored and funded by GARDP, was completed producing positive results. This trial was carried out across 16 sites in regions with a high prevalence of gonorrhoea across five countries, including Belgium, The Netherlands, South Africa, Thailand, and the U.S. With a total of 930 patients enrolled with uncomplicated gonorrhoea, including women, adolescents and patients with HIV, this was the largest clinical trial ever conducted for a new treatment against gonorrhoea infection.

Following the positive results of this trial, a new drug application (NDA) will be submitted, by IST, to the US Food and Drug Administration (FDA) in Q2 of 2025. If approved, GARDP has the right to register and commercialize zoliflodacin in more than three-quarters of the world's countries, including all low-income countries, most middle-income countries and several high-income countries.

To make this possible, GARDP will initiate registration activities in selected priority countries to optimize the introduction of zoliflodacin in GARDP's territories. For instance, GARDP plans to submit the registration dossier in Thailand and South Africa shortly after FDA submission or in parallel. Once approval is obtained in these two countries, we will expand access to zoliflodacin through a process of collaborative approvals within a number of countries.

As part of its long-term strategy, GARDP is also looking to have additional options once resistance emerges. So, in addition to its work on zoliflodacin, GARDP is looking at options for gonorrhoea in the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) portfolio, and assessing the need to secure better optimal treatments for syphilis. To this end, we recently signed a memorandum of understanding with Swiss-based global pharmaceutical company, Debiopharm, to explore the possible development of Debio 1453, a novel compound representing a new antibiotic class that targets *N. gonorrhoeae*.