



The untold story of dolutegravir:

When climate impact goes hand-in-hand
with access to better treatments

Foreword from the Green Climate Fund

What harms our environment also harms our health. By this measure, the global health sector must be a leading champion of climate adaptation and mitigation. However, it is ironically a significant contributor to climate change, causing harm to our health and that of our planet.

At the Green Climate Fund, we recognize the threat that climate change poses to human health and wellbeing. At 1-1.5°C of warming above preindustrial levels, rising temperatures increase the frequency and intensity of heat waves and extreme weather events, exacerbate malnutrition, vector-borne, food-borne, and water-borne infections, zoonotic diseases, as well as occupational and mental health issues.

We recognize the need to use innovation to drive transformative solutions that tackle climate change, enhance resilience, and ensure sustainable development across all sectors. Unitaid's report "The untold story of dolutegravir: When climate impact goes hand-in-hand with access to better treatments" showcases how the introduction and scale-up of a single, widely used medicine has the potential of reducing carbon emissions. While it demonstrates the potential for health interventions

to contribute to our climate goals, it also highlights a missed opportunity: had climate considerations been mainstreamed into design of these efforts, its carbon footprint could have been reduced much further. Achieving a net-zero world demands integrating climate considerations into all aspects of human endeavor from the beginning. The scientific evidence in this report underscores the urgent need for decarbonization through integrating climate objectives into health product design, manufacturing, and distribution. By leveraging market-shaping interventions, fostering innovation, and forging strong partnerships, Unitaid demonstrates that we can create a net-zero, resilient health sector while delivering equitable access to life-saving health products.

Recent milestones, such as the Health Declaration at COP28, the Alliance for Transformative Action on Climate and Health, and the resolution on climate and health at the most recent World Health Assembly, underscore the growing recognition of the critical link between climate and health. They provide a strong foundation for integrating climate resilience into health systems globally.

This report is a call to action.

Sincerely,



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Director of External Affairs
Green Climate Fund

Acknowledgements

This report was developed by Unitaid. It builds on our previous report “From milligrams to megatons: a climate and nature assessment of ten key health products”, extending the analysis using the same methodology with fact-based analytical support from McKinsey & Company. The findings and recommendations in this report belong to Unitaid only.

Background: the success story of HIV treatment

When the HIV epidemic started in the 1980s, being diagnosed with HIV was in most cases a death sentence, as no efficacious treatment was available. However, the advancement of combination antiretroviral therapies in the following decades brought extraordinary progress. New generations of treatment became available, resulting in massive improvements in efficacy, safety and affordability, making it possible for people in low and middle-income countries (LMICs) to access lifesaving treatment. Today, a person living with HIV in LMICs can be treated for less than US\$45 per year, be virally suppressed, and enjoy a normal life with no (or limited) side effects.

The current standard of care for HIV treatment, also known as “dolutegravir-based regimen” (DTG, for short), is the latest major development in this exceptional story. It was approved in the United States and Europe in 2013-2014 and became available in record time – just three years later in LMICs – thanks to a massive effort from countries, civil society, communities living with HIV and industry, with support from global health and research funders including National Agency for Research on AIDS and Viral Hepatitis (ANRS), the Medicines Patent Pool (MPP), the National Institutes of Health (NIH), the President’s Emergency Plan for AIDS Relief (PEPFAR), the Global Fund, the World Health Organization (WHO), Unitaid, the United States Agency for International Development (USAID) and other international partners. The impact of the switch from the previous standard of care (“efavirenz-based regimen,” EFV for short) to DTG is unequivocal: DTG enables faster viral suppression, has fewer side effects, and is significantly more affordable.



Unitaid played a key role in leading the introduction and scale-up of DTG. By investing over US\$100 million through nine implementing partners,¹ Unitaid set out to provide robust clinical evidence on the safety and efficacy of DTG in previously overlooked vulnerable populations in LMICs, reduce treatment costs, secure the sustainable supply of formulations for adults and children, and accelerate their introduction.

The evidence generated was critical for shaping global and national policy. Today, over 110 LMICs have now adopted DTG as the preferred treatment option. The work also enabled the rapid voluntary licensing of the medicine, including its pediatric version, to over a dozen generic manufacturers, significantly driving down prices. Moreover, early introduction efforts in over a dozen countries enabled rapid access, allowed countries to test DTG's use in routine treatment programs for the

first time, drove demand, and set the foundation for countries to expand DTG's use to all people who could benefit.² As a result of these efforts, over 24 million people living with HIV were using DTG by 2023. It is estimated that the introduction of DTG will have saved 1.1 million additional lives by 2027 and that the use of DTG will generate financial savings of US\$8 billion by 2028 for HIV programs in LMICs, relative to what would have been achieved with EFV.

However, despite Unitaid's intense involvement in the transition to DTG-based treatment for nearly a decade, there is a question we never asked ourselves: how does the DTG regimen compare to the previous EFV-based treatments in terms of carbon emissions? This paper attempts to answer this question for the first time and explores the implications for the future management of HIV treatment and health interventions.

1 Partners included: Institut Bouisson Bertrand, WITS RHI, University of Stellenbosch, University of New South Wales, University of Liverpool, The Medicines Patent Pool, CHAI, EGPAF, WHO.

2 <https://unitaid.org/assets/Antiretroviral-Therapy-ART-Optimization-End-of-Grant-Evaluation-Final-Report.pdf>

DTG vs. EFV – unveiling the carbon-side of the story

Unitaid’s 2023 study “From milligrams to megatons: a carbon and nature assessment of ten key health products,” was the first to examine the carbon emissions of 10 essential products in global health.³ DTG was one of the products under review (see Figure 1) and was found to be associated with significant emissions, primarily due to the successful scale-up of the treatment reaching millions of

people. It was found that DTG will emit 2.6 million tons of CO₂e per year by 2030, the equivalent of the annual emissions of the city of Geneva, Switzerland. The contrast between the large weight of these emissions – several megatons – and the small weight of the active ingredient contained in a daily treatment – 650 milligrams – inspired the name of the report.

Figure 1: The DTG emissions as estimated in the 2023 Unitaid report “From milligrams to megatons”

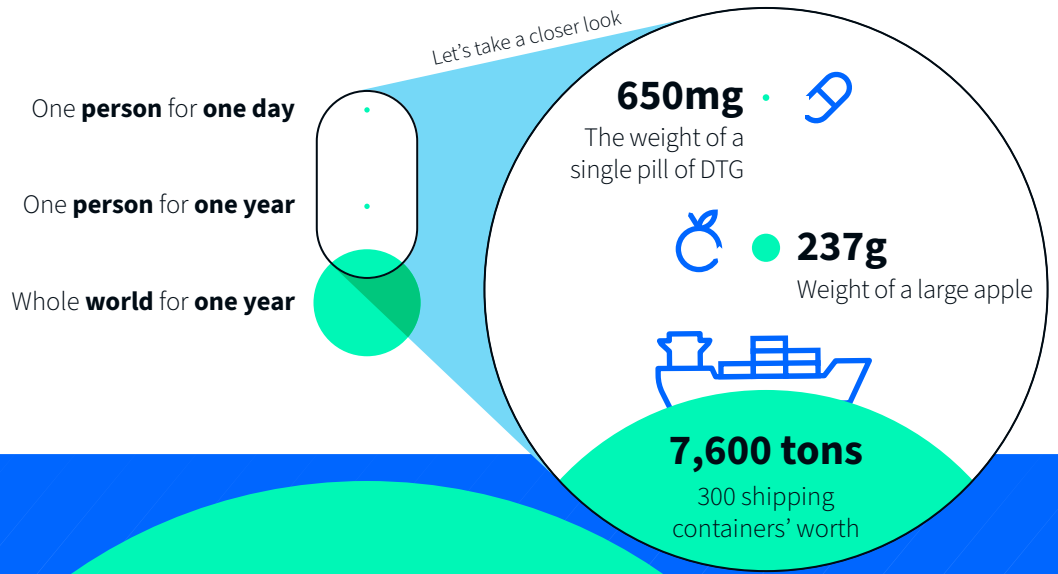
The carbon footprint of health sector represents 5% of global greenhouse gas emissions, with 50 to 70% of these emissions coming from supply chains. Data on the carbon emissions of individual medicines or health products remains scarce in the public domain. To fill this gap, Unitaid conducted a study in 2023 which assessed 10 key health products from a climate and nature standpoint, including carbon emissions. As per the standard Life Cycle Assessment (LCA) methodology, this study assessed carbon emissions along the entire supply chain of these products, from the acquisition of raw materials to manufacturing, distribution, use and disposal/waste management. The analyses revealed that close to 90% of the emissions of DTG come from the manufacturing of the Active Pharmaceutical Ingredient (API), as happens with most medications. The large DTG footprint is attributed to the large quantity of API required for the global market each year, as it is taken daily by millions of people around the world to suppress the HIV virus. Also, the multi-step manufacturing process involved in this production utilizes very large quantities of raw materials, solvents (themselves derived from fossil fuel and with significant carbon content) and energy. The table below summarizes the key figures associated with DTG, as projected in 2030.

3 https://unitaid.org/assets/Report_From-milligrams-to-megatons_A-climate-and-nature-assessment-of-ten-key-health-products.pdf

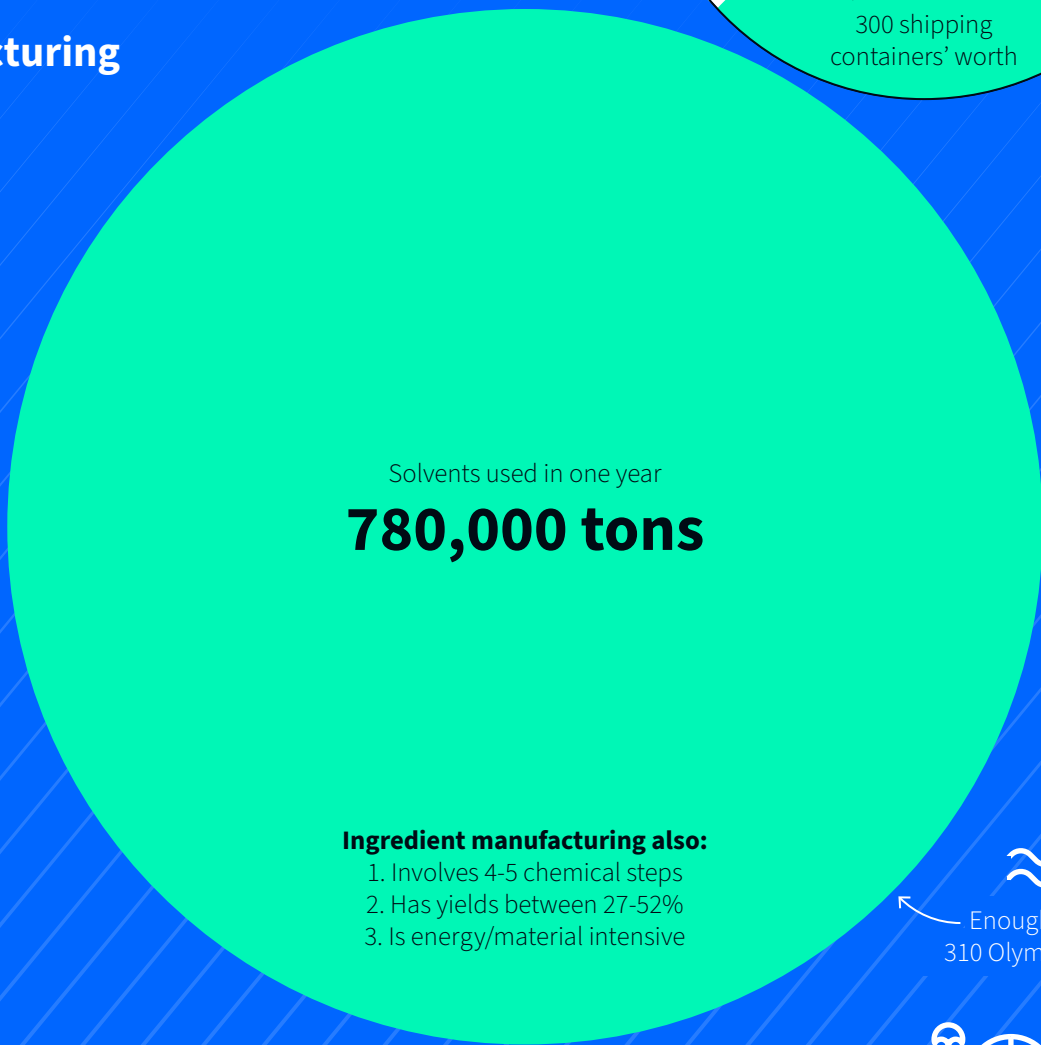
Milligrams to megatons

How the active pharmaceutical ingredients in the Tenofovir-Lamivudine-Dolutegravir (DTG) HIV treatment leave a large climate impact.

Global demand

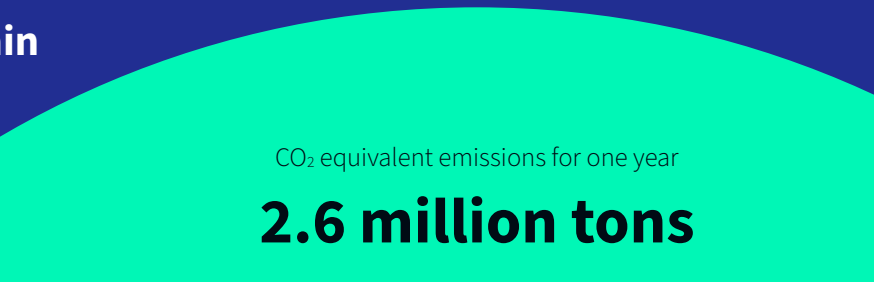


Manufacturing process



Enough solvents to fill 310 Olympic-sized pools

Supply chain emissions



The same annual emissions as the city of Geneva

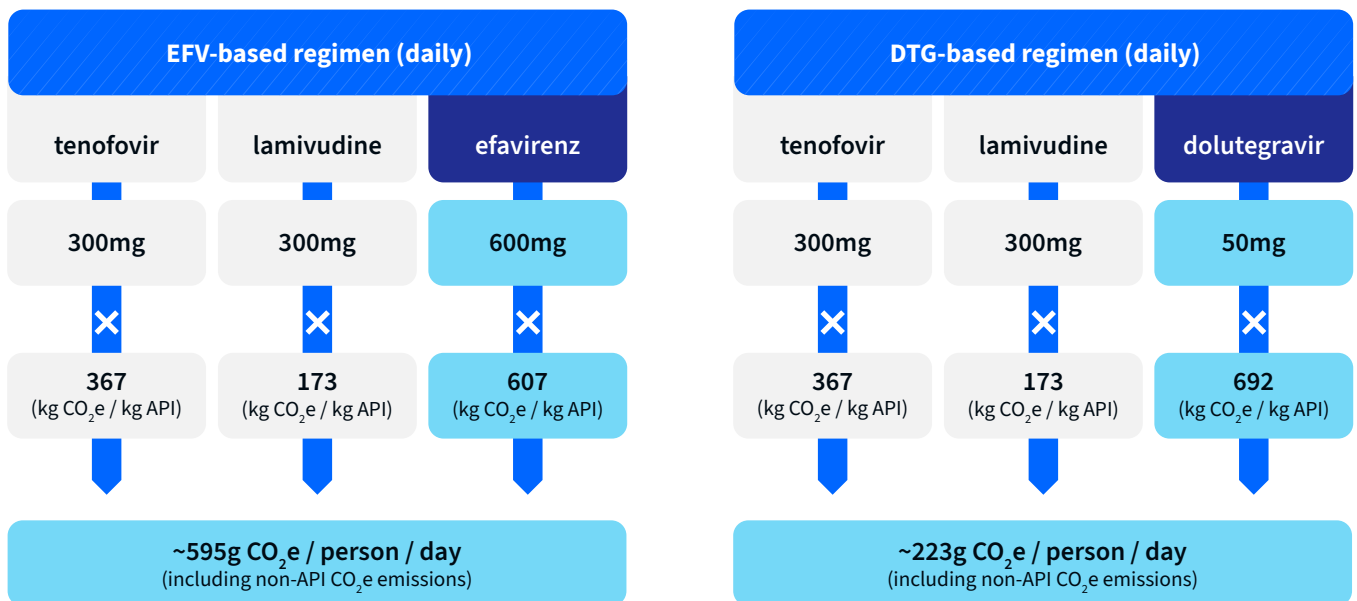
Source: Unitaid.

Note: 650mg has been set to a minimum size for legibility and scaled using square root.

However, the report did not allow for a comparison of DTG’s emissions relative to EFV, the treatment that it replaced. In other words, the counterfactual scenario – what the emissions would have been if EFV had remained as the standard of care – was not known. To address this gap, an additional analysis using the same methodology was conducted. The result for a one-day pill of EFV versus DTG is shown in Figure 2. The analysis revealed that EFV

is significantly more emissive than DTG by a factor of 2.6. This is primarily driven by the larger amount of Active Pharmaceutical Ingredient (API) in EFV (1200mg across all three chemicals) compared to DTG (650mg across all three chemicals). While the API emission factor of efavirenz is estimated to be slightly under that of dolutegravir, this does not offset the large difference in API weight.

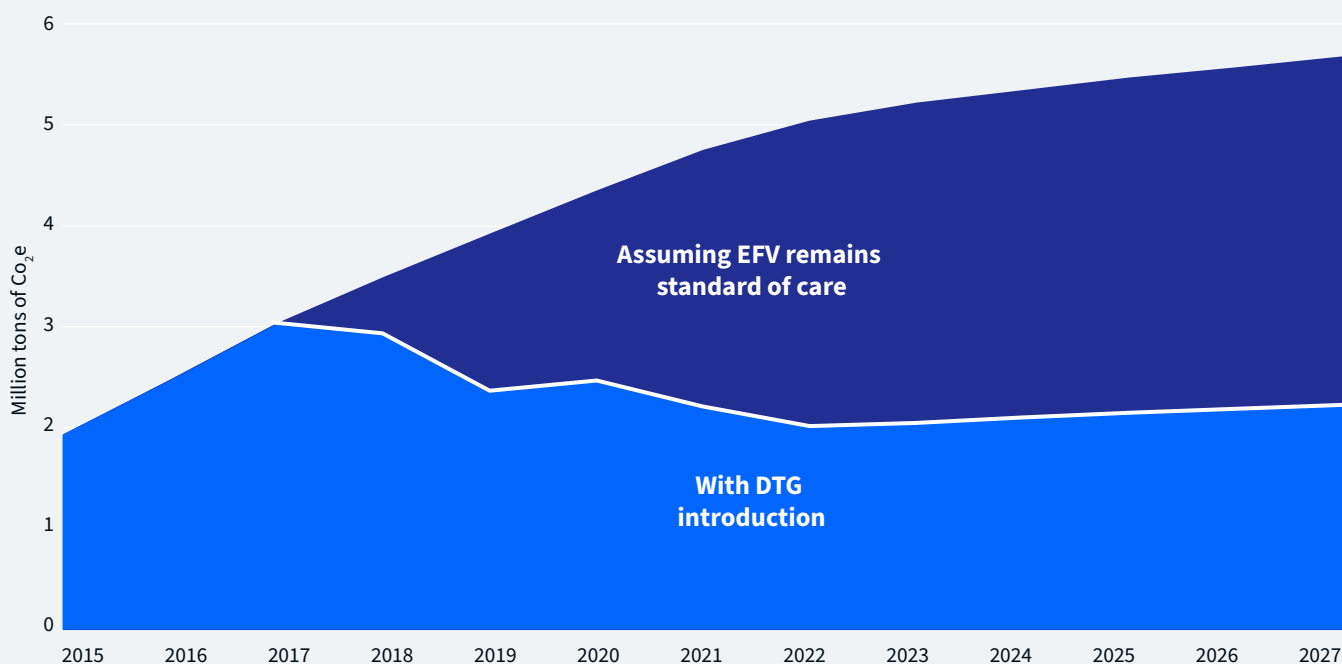
Figure 2: Comparison of the emissions of a daily efavirenz-based regimen (EFV) and dolutegravir-based regimen (DTG); the weights in mg refer to the quantity of API in a daily treatment; the emissions per day indicated for each regimen, while mostly driven by API (which represents close to 90% of overall emissions), also include other emissions along the life cycle of the product.



When evaluating the impact on worldwide emissions, the shift in treatment turns out to have made a drastic difference, as shown in Figure 3. It is estimated that the transition from EFV to DTG resulted in a decrease of annual emissions from HIV treatment by 3.4 million tons of CO₂e by 2027, with a cumulative difference of 26 million tons over the decade 2017-2027. This is equivalent to having removed the full CO₂e emissions of the

city of Geneva over the same 10-year period. It is also useful to compare this to the health care sector’s overall footprint, which was estimated to be roughly 1 billion tons of CO₂e in 2019 for LMICs.⁴ The transition to DTG – a single key medicine – was enough to reduce this global footprint by roughly 0.3-0.4%. This magnitude of carbon footprint reduction surpasses many hard-won achievements of climate mitigation in health and other sectors.

Figure 3: Estimated CO₂e emissions from HIV 1st line treatment (DTG and EFV only) under the current scenario of DTG introduction, and under a counterfactual assuming DTG was not introduced; the upward overall trend reflects the continued uptake of HIV treatment worldwide (from 14.4 million people in 2016 to 27.2 million in 2027 on first-line treatments). This graphic focuses only on DTG and EFV products, which represented more than 80% of first-line treatment volumes in 2016-2017, and over 93% in 2018 and later years. The difference between EFV 400 and EFV 600 was accounted for in emission calculations. All HIV market numbers (actuals up to 2022 and forecast for 2023+) are derived from the CHAI HIV market reports funded by Unitaid.



⁴ Estimated from on the 2019 report of Health Care without Harm (https://noharm-global.org/sites/default/files/documents-files/5961/HealthCaresClimateFootprint_092319.pdf), based on the overall estimates and excluding US, EU, Japan, South Korea, Australia and Canada.

Discussion: what the DTG climate story tells us about how we manage health products

While these climate outcomes are incredibly positive in retrospect, it is equally puzzling to realize that this has happened by mere chance, as the unintended consequence of an otherwise very impactful public health initiative. In fact, the exact opposite outcome could have happened, with the world adopting a new medicine that later proved to be substantially harmful to the climate. It is therefore worth examining several fundamental implications of this analysis.

First, it demonstrates **the importance of understanding the environmental impacts of health supply chains**. Health products are key contributors to climate and environmental footprints, all along their supply chain. While some methodological questions remain to be solved, such as defining specific LCA standards for health products and establishing common methods for procurers and buyers, existing approaches such as the ones used for the “From Milligrams to Megatons” report should be enough to provide a first-level understanding of the carbon or environmental footprint of a given product or product class. This understanding can inform policy decisions. In the case of DTG, knowing its carbon footprint at the time of the switch would have only reinforced the decision. One could even argue that this extra powerful argument in favor of DTG could have further amplified and accelerated the transition effort, mobilizing additional advocates and funders around a clear win-win for health and climate, and unlocking DTG’s health, economic and climate benefits earlier and faster.



Second, it highlights a **critical gap in health policy making**. Consider the following question: what if a new medicine or health product became available, which was proven to be better for patients than existing alternatives, but worse for the climate or the environment? Until recently and despite a few notable exceptions, decarbonization was not a major priority in the health sector; as a result, the health-climate trade-offs were rarely identified or known to health policy makers.⁵ Back in 2017, the carbon footprint of the health sector had not yet been estimated and health was a marginal topic in climate discussions such as COP.

Fortunately, the present-day situation is drastically different. The COP28 in the UAE in 2023 held the first-ever dedicated “health day” where 150 countries signed a declaration calling for low carbon and resilient health systems⁶; the WHO now leads the Alliance for Transformative Action in Climate and Health⁷ (ATACH), launched at COP26 in Glasgow in 2021; and private sector initiatives such as the Sustainable Markets Initiative⁸ (SMI) are emerging, bringing together several major pharmaceutical companies to accelerate their efforts towards net zero. This momentum is promising.

However, much of the work remains ahead of us. To-date, very few health systems or policy makers are equipped to assess tradeoffs between health and environmental benefits. Similar tradeoffs are already being made across multiple dimensions such as economic, health and equity as part of Health Technology Assessments (HTA). Inclusion of carbon emissions and other environmental factors as part of HTA appears to be an essential addition moving forward and can build on recent examples.⁹ Finally, it should be noted that climate benefits are also health benefits. Indeed, every ton of CO₂e that is not emitted into the atmosphere will contribute to better health for current and future generations.¹⁰

Third, this story serves as a stark reminder that “what does not get measured does not get done.” DTG’s carbon footprint, while significantly lower than its predecessor, remains very high. It is also addressable. Up to 40% of these emissions could be abated with cost-saving measures such as through process optimization which would improve energy and material efficiency. Additionally, another 50% of emissions could be abated with the adoption of green energy and materials (see Figure 3). However, because this carbon footprint was not publicly known and understood, little or no effort was made during DTG’s introduction to pursue a low carbon pathway.

5 <https://ssir.org/articles/entry/health-care-industry-climate-change>

6 <https://www.cop28.com/en/cop28-uae-declaration-on-climate-and-health>

7 <https://www.who.int/initiatives/alliance-for-transformative-action-on-climate-and-health>

8 <https://www.sustainable-markets.org/taskforces/health-systems-taskforce/>

9 <https://www.sciencedirect.com/science/article/pii/S1098301524000925>

10 This is illustrated by recent economic estimates of the Social Cost of CO₂ (i.e., the monetized value of damages to society caused by an incremental metric ton of CO₂ emissions), which concluded that about half of the negative externalities are related to increased mortality, the other half being mostly driven by the impact on agriculture (which itself will impact the health of populations). <https://www.nature.com/articles/s41586-022-05224-9>

This represents a missed opportunity, as DTG's introduction was largely driven by public actors, including Unitaid and its partners, through a comprehensive market shaping effort: the voluntary licensing mechanism from the originator to over a dozen generic manufacturers through the Medicines Patent Pool, the demand generation through communities, and the procurement pooling and coordination have collectively enabled a fast and largescale introduction in LMICs. These powerful measures could have been used to shape DTG's market not just for health, but also to respond to the climate crisis.

While decarbonizing this market remains feasible and critical, it may require more efforts now than it would have required from the onset. And every year lost to decarbonize DTG has resulted in unnecessary carbon emissions: several million tons of CO₂e emissions could already have been avoided since the introduction of DTG in 2017. Therefore, measuring product carbon emissions should not be seen as a constraint, but rather as a powerful catalyst for climate action in the health sector.

This isn't about choosing between saving lives and reducing CO₂e emissions. Rather, it highlights the importance of identifying and addressing the high-emission aspects of commonly used medicines. Understanding the carbon intensity of the production process allows us to implement measures to reduce emissions, sometimes at little to no additional cost. Medicines and health tools, like every other aspect of modern life, need to undergo decarbonization to align with the Paris Agreement targets.



Figure 4: Abatement potential of DTG

Cost of reducing CO₂ emissions for dolutegravir-based HIV treatment by 2040

Measures that can reduce CO₂ equivalent emissions by 2040.



Source: TLD regimen, Marginal Abatement Cost Curve, McKinsey Catalyst Zero

Fourth, the case of DTG points to **the importance of innovation in service of a joint health and climate agenda**. DTG is the successful outcome of years of medical innovation and clinical research. To fully decarbonize health supply chains the innovation frontier needs to be pushed further and harder. Some important steps have already been taken: for instance, Medicines for All is developing and publishing optimized chemical synthesis routes for key global health drugs¹¹; these optimized routes, if adopted widely by manufacturers, offer opportunities to improve yield, reduce cost and reduce carbon emissions.

Some of the abatement levers relate to technologies that are not yet mature (e.g., low carbon feedstock) and require further investment. Future product generations can also help reduce carbon footprints. For instance, long-acting HIV treatments are being developed to improve quality of life and adherence to treatment, with a long-acting treatment for pre-exposure Prophylaxis (PrEP) already available. Long-acting treatments often rely on smaller quantities of API than the oral version due to an improved

bioavailability. For instance, a single injection of long-acting cabotegravir (LA-CAB a medicine used for PrEP) provides two months of protection and contains only 600mg of API which is 50 times less API than what is required for a daily oral treatment taken over the same period. Because API drives a large part of the carbon emissions of medicines, this results in LA-CAB having a modest footprint over these two months (0.5kg CO₂e per person), at least a factor 15 smaller than oral PrEP.¹²

Beyond medicines, innovation is crucial for medical devices and other health tools. Product design (e.g., circularity) and material choices (e.g., compostable vector tools and recyclable or plant-based materials) can significantly impact carbon and environmental footprints. Incorporating climate and environmental objectives into health research and development priorities can greatly contribute to low carbon, climate-resilient and climate-responsive health products. For example, such requirements and aspirations could be included in target product profiles for medicines, diagnostics and other health tools.

11 <https://medicines4all.vcu.edu/our-portfolio/bmgf-projects/>

12 Our analysis compares the carbon footprint of Oral PrEP (300mg of tenofovir and 200mg of emtricitabine daily) to that of long-acting PrEP (a single injection of 600mg/3mL of cabotegravir) over a two-month period. According to the report "From milligrams to megatons," the carbon footprint of long-acting cabotegravir (LA CAB) API is 572kg CO₂ per kg, which equates to 0.34kg CO₂ per patient for a two-month dosage of 600mg of API (the API represents ~70% of the product emissions). For Oral PrEP, we calculated a lower bound estimation of the carbon footprint based on the API footprint of tenofovir (367kg CO₂ per kg), with a daily dosage of 300mg over two months. We assumed the footprint of emtricitabine (200mg per day) to be zero for a conservative estimate. The resulting carbon footprint is at least 6.6kg CO₂ per patient for the two-month period. Based on this assessment, LA CAB is calculated to be at least 10-15 times less carbon intensive than oral PrEP.

Conclusion and next steps

This report demonstrates how the introduction of a single medicine, DTG, has unintentionally led to a substantial reduction of CO₂e emissions of HIV treatment worldwide. This example illustrates the significant impact health products and related policies can have on the environment. It also points to a massive and largely untapped potential: by proactively managing the choice of health products, their design, and their manufacturing and distribution processes, we can contribute to a much greener and ultimately net-zero health sector. Moreover, the example of DTG shows that decarbonization of health supply chains and equitable access to health are not mutually exclusive – they can even reinforce each other.

DTG, like many of the 10 products studied in the “From Milligrams to Megatons” report will remain a staple in public health for many years due to its proven benefits. Therefore, decarbonizing these supply chains presents a clear and immediate opportunity for action, with potential to reduce global CO₂e emissions by several million tons and contribute to achieving a net-zero healthcare sector. Solutions must be tailored to each product and may involve a combination of market shaping interventions such as commercial incentives and other financing instruments, new procurement

approaches, support to create and upgrade local and regional manufacturing facilities, process innovation, technology transfers, pre-competitive collaboration, policy and regulatory adaptations and demand creation.

Strong partnerships will be required to align around a common vision and pathway for decarbonization. This includes collaboration with communities and countries who manufacture and use these products, as well as industry, regulators, financial and technical partners. Effective coordination among these actors will be essential to deliver rapid progress on decarbonization, while ensuring continued quality, supply security and affordability. It will also require new partners to join in and contribute new climate-smart technologies, carbon expertise (such as life-cycle assessment standards and methods), new forms of financing and climate advocacy.

This might be the first large-scale effort to decarbonize health products, presenting an exceptional opportunity for collective learning and ultimately, impact for people and the planet.

Priorities and opportunities for global health actors

This report shows that the introduction of DTG has significantly reduced CO₂e emissions from HIV treatment worldwide, illustrating the environmental impact of health products and policies, and highlighting the potential for a net-zero health sector where decarbonization and equitable health access can reinforce each other.

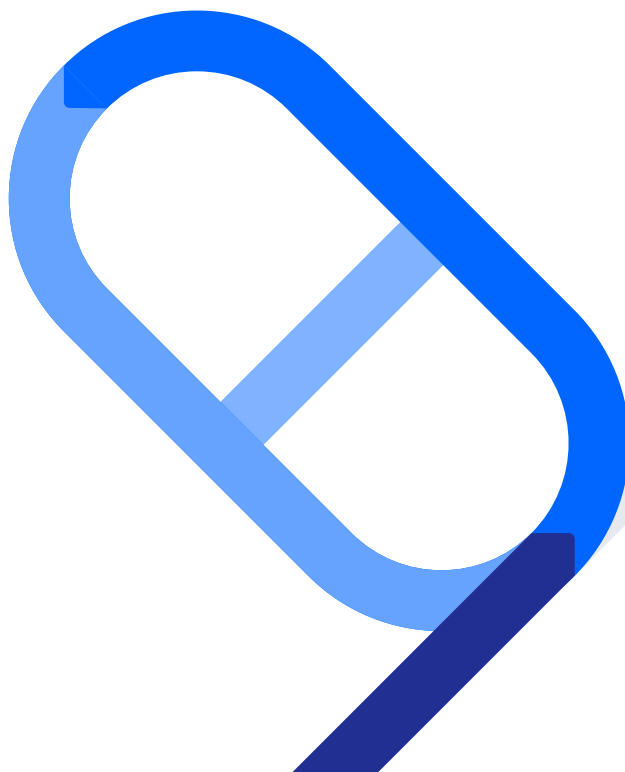
Several priorities emerge as clear opportunities for global health actors:

- 1. Embrace net zero objectives across the global health sector:** Building on COP28 declaration, and the new WHO resolution on Climate Change and Health adopted during the 77th World Health Assembly, commitments to a net zero global health sector and science-based targets must be integrated into the objectives of every stakeholder in global health (including public, private, non-governmental and multinational entities) at international, regional and national levels. These commitments need to cover all scopes of emissions (including the third scope, which is outside the direct control of an entity), be publicly disclosed and regularly reported on. New organizations such as the Climate Action Accelerator can support accelerating decarbonization efforts.
- 2. Decarbonize the supply chain of existing health products:** DTG, like many of the 10 products studied in the report “From milligrams to megatons,” will likely remain essential due to its public health value. Decarbonizing these supply chains presents an immediate opportunity to reduce global CO₂e emissions by several million tons. Solutions will need to be tailored to each product, and may entail a combination of market shaping interventions, commercial incentives, new financing instruments and procurement approaches, support for creating and upgrading manufacturing facilities (including at a regional level), process innovation and technology transfers, pre-competitive collaboration, policy and regulatory adaptations and demand creation.

3. Accelerate innovation to make health products climate-smart: Integrate climate and environmental objectives into health research and development priorities to develop low carbon, climate-resilient and climate-responsive health products. Include these goals in Target Product Profiles for medicines, diagnostics and other health tools. Enhance the broader innovation ecosystem with adequate incentives, financing and cross-sectoral collaboration.

4. Structure new partnerships around shared goals: Strong partnerships are required to create alignment around a common vision and pathway for supply chain decarbonization, at the sectoral level but also at lower levels where targeted and impactful initiatives can take place (e.g., for specific products or product classes). These partnerships should build on existing coalitions in global health, such as the multi-stakeholder partnership that supported the introduction of DTG to-date. They will need to include communities and countries who use these products, industry, civil society, regulators, financial and technical partners. New partners must join in and contribute carbon expertise (e.g., life-cycle assessment standards and methods), new forms of financing (e.g., development and climate finance, such as the Green Climate Fund) and climate advocacy. Coordination among these actors will be essential to deliver rapid progress on decarbonization, while ensuring continued quality, supply security and affordability.

What is at stake is the transformation of an entire sector. No single action will deliver that on its own. But there are plenty of opportunities to start or accelerate this journey, to learn collectively, and ultimately, deliver impact for people and the planet.





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