BENCHMARK PERFORMANCE

Johnson & Johnson performs well in its evaluated Research Areas, and is one of the leaders when compared to other large R&D-based pharmaceutical companies in scope.

R&D: Middle-performing. Pipeline consists of 11 projects for medicines and vaccines for priority pathogens. Reports the second largest investment in relevant R&D in 2017 and 2018 and is active in intellectual capital sharing.

Responsible Manufacturing: Performs strongly. Reports comprehensive environmental risk-management strategy for own sites and suppliers; risk assessments based on discharge limits have been completed at own sites and are ongoing at suppliers’ sites.

Appropriate Access: Performs well. Files its relevant on- and off-patent products for registration in access countries. Employs strategies including forecasting and capacity building to ensure continuous supply.

Stewardship: Performs well. It has educational programmes with broad conflict of interest (COI) mitigation. It does not deploy sales agents to promote bedaquiline (Sirturo®). It is active in surveillance and adapts brochures and packaging to facilitate appropriate use.

SALES AND OPERATIONS

Therapeutic areas: Cardiovascular diseases; Diabetes; Immunology; Infectious diseases; Neurology; Oncology; Pulmonology

Business segments: Consumer Healthcare; Medical Devices; Pharmaceuticals

Product categories: Consumer health; Medical devices; Innovative medicines; Vaccines

Manufacturing & supply: Johnson & Johnson reports selling its antibacterial and antifungal medicines across 136 countries, 66 of which are low- and middle-income countries.

M&A since 2018: None in the antibacterial and/or antifungal sectors

Pipeline: 11 projects for priority pathogens* (9 antibacterial medicines; 2 antibacterial vaccines)

Development stages: 3 clinical projects, including a Phase I clinical vaccine candidate for the prevention of infections caused by extraintestinal pathogenic E. coli (ExPEC), and seven projects for which the stage of development was provided on the basis of confidentiality.

Novelty: No novel clinical-stage medicine projects

Regulatory approvals: 0 approvals for priority pathogens

Access plans: 2 of 2 late-stage R&D projects with project-specific access plans

Stewardship plans: 1 of 2 late-stage R&D medicine projects with project-specific stewardship plans.

PORTFOLIO

Comparatively small portfolio: At least 25 products (8 unique INNs): 7 antibacterial medicines; 16 antifungal medicines; 2 antibacterial and antifungal medicine combinations

Essential medicines: 28% (7) of products are on the 2019 WHO EML

AWaRe medicines**: None

Anti-TB medicines**: 2 products

The number of products is based on data from public sources, IQVIA, and data submitted by the company. It may not account for Johnson & Johnson’s entire portfolio.

* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.

** Listed on the 2019 WHO EML (Section 6). Levofloxacin (Levaquin®) is not approved for the treatment of TB but is listed on WHO EML 2019 as an anti-TB medicine (Section 6.2.5).
OPPORTUNITIES FOR JOHNSON & JOHNSON

Target critical/urgent priority pathogens. Johnson & Johnson has one of the largest R&D pipelines targeting antibacterial infections but only very few projects that target critical/urgent priorities. It should ensure that future projects target such pathogens.

Follow up to public commitments and increase public disclosure on environmental risk management. Following up on its commitments as a signatory to the Industry Roadmap for Progress on Combating AMR, Johnson & Johnson can work with stakeholders to develop a practical mechanism to publicly disclose (1) a list of its suppliers and waste-treatment plants and (2) the results of environmental audits and the levels of antibacterial discharge from its own sites and the sites of its suppliers.

Ensure affordability of bedaquiline as part of regimens for treatment of multidrug-resistant tuberculosis (MDR-TB). Bedaquiline (Sirturo®) is recommended as part of MDR-TB regimens by international and national treatment guidelines. Johnson & Johnson can continue ensuring the affordability of its tiered pricing strategy for bedaquiline, when used in combination with other tuberculosis (TB) medicines.

Publicly share raw data from surveillance programme. Johnson & Johnson reports that, because the study is an FDA postmarketing requirement, access to the DREAM database was restricted. Now that data collection has been completed, Johnson & Johnson can share publicly (e.g., with the AMR Register) the raw data collected for this long-term, multinational surveillance programme.

PERFORMANCE BY RESEARCH AREA

A RESEARCH & DEVELOPMENT Evaluated: medicine & vaccine pipelines for priority* bacteria & fungi

A.1 Second largest investment in relevant R&D
Johnson & Johnson reports to the Benchmark how much it invested in R&D for antibacterial medicines and vaccines in 2017 and 2018. Johnson & Johnson reports the second largest investment in such R&D in 2017 and 2018. As a proportion of its revenues from pharmaceuticals and vaccines, the size of these investments is average compared to investments in such R&D made by other large research-based pharmaceutical companies evaluated in the Benchmark. The Benchmark is not able to publish further information, as the details were provided on the basis of confidentiality.

Pipeline targeting priority pathogens: 11*** As at 16 October 2019

<table>
<thead>
<tr>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
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<tbody>
<tr>
<td>+ S. aureus</td>
<td>+ ExPECColV - Active immunization for the prevention of invasive ExPEC Disease caused by O-serotypes 1A, 2, 4, 6A, 8, 15, 16, 18A, 25B, 75 in adults 60 years of age and older (Phase I/IIa)</td>
<td>Bedaquiline (Sirturo®) - Drug-susceptible M. tuberculosis - Adaptation (additional indication) - In partnership with the TB Alliance</td>
<td>Bedaquiline (Sirturo®)† - Multidrug-resistant M. tuberculosis - Adaptation (pediatric formulation and additional target populations: pediatric and adolescent patients)</td>
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* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.

CHANGES SINCE 2018

- Announced its ten-year initiative in September 2018 to help eliminate TB by 2030, and committed in October 2019 more than USD 500 million over the next four years to R&D and access programmes for TB (and HIV).
- Received FDA approval in 2019 for bedaquiline (Sirturo®) tablets for MDR-TB in paediatric patients over the age of 12 years and weighing at least 30 kilograms.
- Expanded the availability of bedaquiline to 130+ countries from 103 in 2018, including all 30 countries with high MDR-TB burden.
- Reduced the price for bedaquiline to USD 400 per six-month course in South Africa and any country purchasing through the GDF; original tiered prices for LMICs range from USD 900 - 3000.
- Joined Gavi’s STEP programme in 2018, which aims to solve gaps in supply chain management.

*** Includes 7 confidential projects not shown in the figure.
* Johnson & Johnson received an approval for bedaquiline from the FDA in August 2019, outside the period of analysis, for an adolescent indication. Phase I studies are ongoing for paediatric patients, with a new paediatric formulation in development.
A.2.3 Active in vaccine R&D
Johnson & Johnson has two new vaccine projects, one in clinical development for the prevention of infections due to extra-intestinal pathogenic E. coli and one in discovery stage to help prevent S. aureus infections.

A.2.4 One candidate targeting critical and/or urgent priorities
Johnson & Johnson has one candidate targeting pathogens considered critical and/or urgent R&D priorities for limiting AMR, as identified by WHO and/or the US Centers for Disease Control and Prevention (CDC). This is its ExPEC vaccine for the prevention of infections due to extra-intestinal pathogenic E. coli. Further details were provided on the basis of confidentiality.

A.3 Four intellectual capital sharing initiatives
Its four relevant initiatives include its collaboration with WIPO Research consortium, sharing a library of molecules that might help develop new treatments for TB. In addition, the company reports its collaboration with the Indian Council of Medical Research (ICMR) and its India TB research consortium, providing support to researchers. Further, it is part of the TB Drug Accelerator Programme, a consortium of research institutions and pharmaceutical companies that is developing new treatments for TB.

A.4 Specific access and/or stewardship plans for late-stage projects
Johnson & Johnson has project-specific access plans for its two late-stage antibacterial projects targeting TB, bedaquiline (Sirturo®). In general, once a product is initially approved, Johnson & Johnson commits to submit applications for product registration in countries where the clinical trials for the product have taken place. For its late-stage bedaquiline paediatric project, it conducts clinical trials in access countries where it commits to file for registration (in the Johnson & Johnson territories) upon initial approval. Existing stewardship initiatives and activities for adult use of bedaquiline will be expanded to broaden the audience to those who treat young children. For the use of bedaquiline in DS-TB (TB Alliance), information on access planning was provided on the basis of confidentiality.

B RESPONSIBLE MANUFACTURING
Evaluated: antibacterials manufacturing (APIs and drug products)

B.1 Comprehensive environmental risk-management for own sites and suppliers
Johnson & Johnson reports a comprehensive strategy to minimise the environmental impact of wastewaters and solid waste from antibacterial manufacturing at its sites, with an aim to limit AMR. This includes audits every three years. The company reports setting discharge limits for all antibacterials manufactured at its sites, based on PNECs to limit AMR (or more stringent PNECs), as published by the AMR Industry Alliance. It uses these PNECs to conduct risk assessments applying a mass-balance approach, complemented by direct sampling and analytical testing, where needed.

Johnson & Johnson expects third-party suppliers of antibacterial APIs and drug products to follow the same standards, including meeting environmental PNECs. It reports that suppliers are audited typically every three years and are requested to complete a risk assessment as described above for the company’s own sites. Johnson & Johnson expects external private waste-treatment plants to comply with its environmental standards and reports auditing them on the basis of risk, typically between one and three years. All wastewater sent to these plants is set to be incinerated. Johnson & Johnson does not audit publicly-owned wastewater treatment plants (not in scope of the Benchmark).

B.2 Publicly discloses some information on environmental risk management
Johnson & Johnson publishes some components of its environmental risk-management strategy. Further, it is a member of the AMR Industry Alliance, which publishes a list of recommended antibacterial discharge targets. The underlying methodology was summarised in an open-access journal article co-authored by Alliance members including Johnson & Johnson. Johnson & Johnson does not publish: (1) the results of environmental audits, whether conducted at its own sites, the sites of suppliers or external private waste-treatment plants; (2) a list of these suppliers and waste-treatment plants; or (3) the levels of antibacterial discharge from its own sites.

B.3 Has system to maintain production quality for own and suppliers’ sites; no requests for official corrective action
Johnson & Johnson reports having a system to maintain high-quality antibacterial production, consistent with international GMP standards. This includes risk-based internal audits and tracking of corrective and preventive actions. The company reports requiring suppliers to abide by regulatory and company quality standards. This includes submitting suppliers to a qualification process, after which a quality agreement is established. It reports auditing its suppliers as its sites and having the same expectations in terms of corrective action implementation. The Benchmark found no requests for official corrective action from the FDA or EMA related to non-conformities with cGMP at Johnson & Johnson’s own sites or any subsidiaries.

C APPROPRIATE ACCESS & STEWARDSHIP – ACCESS
Evaluated: access activities relating to antibacterial & antifungal medicines & vaccines in 102 access countries

C.1.1 Filed to register one of its two relevant on-patent products in 10+ access countries
Johnson & Johnson is one of the leaders with regard to filing patented products for registration. It has filed its antibacterial bedaquiline (Sirturo®), for TB, for registration in 28 access countries and has plans to file bedaquiline for registration in Namibia, Zambia, and Zimbabwe.

C.1.2 Filed to register its relevant off-patent products in 22.5% access countries on average
Johnson & Johnson is one of the leaders when it comes to filing relevant off-patent products for registration. It has filed all of its relevant products for registration in access countries. It has filed the antifungal itraconazole (Sporanox®) for registration in 33 countries and its antibacterial levofloxacin (Levaquin®) for registration in eight access countries.

C.2.1 Takes socioeconomic factors into account when setting prices for on-patent products
For its two relevant on-patent products bedaquiline (Sirturo®) and itraconazole (Sporanox®), Johnson & Johnson reports considering socioeconomic factors when setting prices. Factors include countries’ levels of income and economic development, ability to pay and disease burden, as well as the value the product brings to patients and health system. Johnson & Johnson offers bedaquiline to more than 130 low- and middle-income countries, via the Stop TB Partnership’s Global Drug Facility, at the price of USD 400 per six-month course, a reduction from the original tiered prices ranging from USD 900 – USD 3000. Further, the company has committed to donate 105,000 courses of bedaquiline to eligible low- and middle-income countries through a four-year donation agreement.
C APPROPRIATE ACCESS & STEWARDSHIP – STEWARDSHIP

C.4 Broad strategy to mitigate COI for all educational programmes

The Benchmark analysed five AMR-related educational programmes for healthcare professionals (HCPs) from Johnson & Johnson. Johnson & Johnson reports broad COI mitigation for all five programmes. To mitigate COI for four programmes, it provides financial resources to independent third parties to carry out the entire programme. For the remaining programme, Johnson & Johnson includes two of three COI mitigation strategies looked for by the Benchmark: (1) content is developed independently from its marketing department; (2) a policy on not using branded materials. However, for this programme, it is unclear whether financial or material incentives are provided to participants. The company may pay for travel, hotel, meals and registration fees to attend third party or company organised events, congresses or symposia for professional or medical education.

C.5 Adapts sales practices to address appropriate use

Johnson & Johnson engages in practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines via its sales practices. Johnson & Johnson does not disclose marketing practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines. It is, however, one of the three companies evaluated to report that it does not deploy any sales agents to promote a subset of its antibacterial and/or antifungal medicines, namely bedaquiline (Sirturo®). This is not the case for any of its other products.

C.6 Makes several adaptations to brochures and/or packaging to facilitate appropriate use

Johnson & Johnson adapts brochures and packaging to facilitate the appropriate use by patients of relevant products: namely its antibacterial bedaquiline (Sirturo®). These adaptations take account of language and adherence to treatment for bedaquiline. It produces a package insert with information in four languages. Further, it produces a 6-month treatment regimen packaged in a single bottle to improve adherence to treatment.

C.7 Active in one AMR surveillance programme focused on TB

Johnson & Johnson runs one long-term AMR surveillance programme. The Drug Resistance Emergence Assessment in MDR-TB (DREAM) focuses on resistance of bedaquiline (Sirturo®) in 11 countries and has been repeated every year since 2015. The number of antibacterials tested in this programme is 12. Methodological aspects were shared in a peer-reviewed journal article. Data collection is now complete and Johnson & Johnson commits to also sharing raw data via the Yale University Open Data Access (YODA) platform where researchers can request access to raw data from its clinical trials. Johnson & Johnson currently makes some consumption data available about bedaquiline (e.g., from its donation programme) with the Stop TB Partnership.

DIAGNOSTICS, ANIMAL HEALTH & AGRICULTURE

Activities in this area are not scored by the Benchmark. This information is provided given the importance of diagnostics, animal health and agriculture on the topic of AMR.

Johnson & Johnson is supporting development of bedaquiline sensitivity diagnostic tests and panels that are to be deployed on the Becton Dickinson and Thermo Fisher Scientific Inc. lab infrastructure. Next steps are to establish supply agreements to align supply of the tests to the needs of the market. It has also entered into several collaborations including: (1) collaboration with a diagnostic manufacturer to support MDR-TB patient finding in poverty-stricken regions in China through molecular diagnostic testing; and (2) IMI project consisting of an academic and private consortium to identify diagnostic technologies suitable for use in primary care settings. Johnson & Johnson also provides bedaquiline powder for susceptibility testing.