

Developed by









Bedaquiline long-acting

Supported by



Johnson &Johnson Johnson & Johnson Originator <u>https://innovativemedicine.jnj.com/</u>

United States

Drug structure



Bedaquiline structure

pubchem

Drug information

Associated long-acting platforms

unknown, unknown

Administration route

Subcutaneous, Intramuscular

Therapeutic area(s)

ТΒ

Use case(s)

Pre-Exposure Prophylaxis (PrEP) Post-Exposure Prophylaxis (PEP) Treatment Prevention

Use of drug

Ease of administration

To be determined

User acceptance

Dosage

Available dose and strength

investigational

Frequency of administration

unknown

Maximum dose

Not provided

Recommended dosing regimen

Not provided

Additional comments

Not provided

Dosage link(s)

Drug information

Drug's link(s)

https://go.drugbank.com/drugs/DB08903

Generic name

long-acting bedaquiline

Brand name

Sirturo (long-acting version)

Compound type

Small molecule

Summary

Long-Acting Bedaquiline is in development as an injectable formulation (intramuscular or subcutaneous). Various technologies like nanoemulsions, lipid nanoparticles, and insitu forming polymer gels have been explored to enable slow drug release and less frequent administrations while keeping an optimal concentration of the medicine in the body.

Approval status

investigational

Regulatory authorities

investigational

Delivery device(s)

Scale-up and manufacturing prospects

Scale-up prospects

Not provided

Tentative equipment list for manufacturing

Not provided

Manufacturing

Not provided

Specific analytical instrument required for characterization of formulation

Clinical trials

A Single Ascending Dose, Single-Centre Study, to Assess Pharmacokinetics, Safety and Tolerability of a Single Intramuscular Dose of Bedaquiline Long-Acting Injection Formulation in Healthy Participants

Identifier

EUCT 2023-508810-41-00

Link

https://euclinicaltrials.eu/ctis-public/view/2023-508810-41-00?lang=en

Phase

Phase I

Status

Recruiting

Sponsor

Janssen Cilag International

More details

Not provided

Purpose

Safety and Tolerability of a Single Intramuscular Dose of Bedaquiline Long-Acting Injection Formulation

Interventions

Intervention 1

Single Intramuscular Dose of Bedaquiline Long-Acting Injection Formulation

Countries

Austria

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

2024-06-03 00:00:00

Actual Start Date

2024-07-02 00:00:00

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date 2026-02-17 00:00:00

Actual Primary Completion Date

Not provided

Actual Completion Date Not provided

Studied populations

Age Cohort

Adults

Genders

• All

Accepts pregnant individuals Unspecified

Accepts lactating individuals

Unspecified

Accepts healthy individuals

Yes

Comments about the studied populations

study protocol code: TMC207TBC1006

Health status

Negative to : TB

Study type

Interventional (clinical trial)

Enrollment

Not provided

Allocation

Non-randomized

Intervention model

Not provided

Intervention model description

Not provided

Masking

Open label

Masking description

Not provided

Frequency of administration

Other : "unknown "

Studied LA-formulation(s)

Injectable

Studied route(s) of administration

To be determined

Use case

Treatment

Key results

Excipients

Proprietary excipients used

Not provided

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

Not provided

Residual solvents used

Patent info

Compound patent families

Patent informations

	Representative			Licence with	Patent
Patent description	patent	Categories	Patent holder	MPP	source
Bedaquiline Long-acting	WO2019012100	Composition	Janssen Pharmaceutica	No	
formulations (suspension of micro-			Nv		
or nanoparticles)					
Expiry date: 2038-07-13					
This invention concerns					
pharmaceutical compositions for					
administration via intramuscular or					
subcutaneous injection, comprising					
micro- or nanoparticles of the anti-					
TB compound bedaquiline,					
suspended in an aqueous					
pharmaceutically acceptable					
carrier, and the use of such					
pharmaceutical compositions in the					
treatment and prophylaxis of a					
pathogenic mycobacterial infection.					

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	China, Kazakhstan, Morocco, Tunisia,	Australia, Russian Federation,
	Albania, Serbia, Bosnia and	Liechtenstein, Italy, Norway, Malta,
	Herzegovina, Cambodia, Montenegro,	Denmark, Belgium, United Kingdom,
	Türkiye, Moldova, Republic of, North	Greece, Netherlands, Hungary, Croatia,
	Macedonia, Jordan, Peru, Ukraine, South	Switzerland, Spain, San Marino,
	Africa, Sierra Leone, Eswatini, Liberia,	Slovenia, Austria, Romania, Iceland,
	Namibia, Sao Tome and Principe,	Cyprus, Finland, France, Bulgaria,
	Mozambique, Uganda, Zambia,	Slovakia, Poland, Latvia, Ireland,
	Zimbabwe, Tanzania, United Republic	Estonia, Germany, Luxembourg,
	of, Malawi, Ghana, Sudan, Botswana,	Portugal, Czechia, Lithuania, Monaco,
	Lesotho, Kenya, Gambia (the),	Sweden, Japan, Korea, Republic of,
	Indonesia, Mexico, Nigeria, Congo,	Saudi Arabia, United States of America,
	Mauritania, Guinea-Bissau, Niger,	Hong Kong
	Senegal, Cameroon, Mali, Togo, Burkina	
	Faso, Benin, Côte d'Ivoire, Central	
	African Republic, Comoros, Guinea,	
	Gabon, Equatorial Guinea, Chad, Viet	
	Nam	

Patent statu	is/countries
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Low, Low- middle and upper-middle High income

Filed	Brazil, China, Albania, Serbia, Türkiye, North Macedonia, Philippines, Papua New Guinea, Thailand, Uzbekistan	Canada, Liechtenstein, Italy, Norway, Malta, Denmark, Belgium, United Kingdom, Greece, Netherlands, Hungary, Croatia, Switzerland, Spain, San Marino, Slovenia, Austria, Romania, Iceland, Cyprus, Finland, France, Bulgaria, Slovakia, Poland, Latvia, Ireland, Estonia, Germany, Luxembourg, Portugal, Czechia, Lithuania, Monaco, Sweden, Kuwait, Qatar
Not in force	World Intellectual Property Organization (WIPO), Colombia, Tajikistan, Belarus, Azerbaijan, Turkmenistan, Armenia, Kyrgyzstan, Morocco, Tunisia, Bosnia and Herzegovina, Cambodia, Montenegro, Moldova, Republic of, India, Rwanda	World Intellectual Property Organization (WIPO), Korea, Republic of

Patent informations

				Licence	
	Representative			with	Patent
Patent description	patent	Categories	Patent holder	МРР	source
Bedaquiline fumarate salt and solid	WO2008068231	Salt	Aelterman, Wim,	No	
compositions			Albert, Alex, Faure,		
Expiry date: 2027-12-03			Anne, Hegyi, Jean		
Bedaquiline fumarate salt,			Francois, Alexandre,		
pharmaceutical compositions			Lucas, Janssen		
comprising as active ingredient said			Pharmaceutica N.V,		
salt and to processes for their			Lang, Yolande, Lydia,		
preparation.			Leys, Carina,		
			Stokbroekx, Sigrid,		
			Carl, Maria, Van		
			Remoortere, Peter,		
			Jozef, Maria		

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Türkiye, Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Sudan, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Mexico, Peru, South Africa, Lebanon, Indonesia, Jordan, Montenegro, Philippines, Viet Nam, Kosovo, Sri Lanka, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Serbia, North Macedonia, Bosnia and Herzegovina, Albania	United States of America, Australia, Canada, Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Slovenia, Hungary, Romania, Poland, Iceland, Lithuania, Latvia, Malta, Hong Kong, Japan, Korea, Republic of, Norway, New Zealand, Taiwan, Province of China, Chile, Russian Federation, Uruguay, Bahrain, Kuwait, Qatar, Saudi Arabia, Oman, United Arab Emirates, Israel, Brunei Darussalam, Panama, Singapore, Croatia
Filed	Venezuela (Bolivarian Republic of), Pakistan	

Not in force

Low, Low- middle and upper-middle High income

Argentina, Brazil, China, Malaysia, India, World Intellectual Property Organization (WIPO), Ukraine, Thailand, Egypt Japan, World Intellectual Property Organization (WIPO)

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Bedaquiline to treat latent TB Expiry date: 2025-12-08 Use of bedaquiline for the manufacture of a medicament for the treatment of latent tuberculosis	WO2006067048	Use	Janssen Pharmaceutica N.V	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Sudan, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Brazil, China, Jordan, Ukraine, South Africa, Montenegro, Indonesia, Sri Lanka, Mexico, Benin, Cameroon, Burkina Faso, Chad, Guinea- Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Pakistan, Albania, Bosnia and Herzegovina, North Macedonia	Canada, Australia, Bulgaria, Cyprus, Germany, Denmark, Belgium, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Monaco, Portugal, Ireland, Finland, Czechia, Estonia, Slovakia, Slovenia, Hungary, Romania, Poland, Iceland, Lithuania, Latvia, Hong Kong, Croatia, Israel, Japan, Korea, Republic of, Norway, New Zealand, Taiwan, Province of China, Panama, Bahrain, Kuwait, Qatar, Saudi Arabia, Oman, United Arab Emirates, Macao, Malta, Singapore, Trinidad and Tobago
Filed	Nicaragua, Kosovo, Lebanon, Thailand, Venezuela (Bolivarian Republic of)	Cyprus, Germany, Denmark, Spain, Portugal, Slovenia, Poland, Japan
Not in force	Türkiye, Argentina, China, Costa Rica, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Malaysia, Serbia, India, World Intellectual Property Organization (WIPO), Ecuador, Egypt, Philippines, Viet Nam	Bulgaria, Estonia, Latvia, Japan, Korea, Republic of, United States of America, Russian Federation, World Intellectual Property Organization (WIPO)

Patent informations

				Licence	
	Representative			with	Patent
Patent description	patent	Categories	Patent holder	MPP	source
Bedaguiline to treat MDR TB and/or	WO2005117875	Use	Janssen Pharmaceutica	No	
combinations with other			N.V		
antimycobacterial agents					
Expiry date: 2025-05-24					
The invention relates to the use of a					
substituted guinoline derivative for					
the preparation of a medicament					
for the treatment of an infection					
with a drug resistant					
Mycobacterium strain wherein the					
substituted quinoline derivative is a					
compound according to Formula (Ia)					
or Formula (lb) the					
pharmaceutically acceptable acid or					
base addition salts thereof, the					
stereochemically isomeric forms					
thereof, the tautomeric forms					
thereof and the N-oxide forms					
thereof. Also claimed is a					
composition comprising a					
pharmaceutically acceptable carrier					
and, as active ingredient, a					
therapeutically effective amount of					
the above compounds and one or					
more other antimycobacterial					
agents.					

Patent status

Patent status/countries

Low, Low- middle and upper-middle High income

Türkiye, Brazil, China, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, Mexico, Malaysia, Serbia, South Africa, Indonesia, Kosovo, Lebanon, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Philippines, Venezuela (Bolivarian Republic of), Viet Nam, Montenegro, Jordan, Albania, North Macedonia Canada, Australia, Germany, Belgium, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Czechia, Estonia, Slovakia, Slovenia, Hungary, Romania, Poland, Iceland, Lithuania, Hong Kong, Israel, Japan, Korea, Republic of, Norway, New Zealand, Taiwan, Province of China, Russian Federation, Panama, Bahrain, Kuwait, Qatar, Saudi Arabia, Oman, United Arab Emirates, Croatia, Latvia, Macao

Pakistan, Thailand, Egypt

World Intellectual Property Organization (WIPO), Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sierra Leone, Sudan, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Argentina, China, Ukraine, India, Sri Lanka, Bosnia and Herzegovina Bulgaria, Korea, Republic of, United States of America, World Intellectual Property Organization (WIPO), Chile

Not in force

Filed

Patent informations

Patent description	Representative patent	Categories	Patent holder	Licence with MPP	Patent source
Bedaquiline compounds Expiry date: 2023-07-18 Novel compounds, in particular substituted quinoline derivatives, having the property of inhibiting growth of mycobacteria and therefore useful for the treatment of mycobacterial diseases, particularly those diseases caused by pathogenic mycobacteria such as Mycobacterium tuberculosis, M. bovis, M. avium and M. marinum.	WO2004011436	Compound	Janssen Pharmaceutica N.V	No	

Patent status

Patent status/countries	Low, Low- middle and upper-middle	High income
Granted	Montenegro, Sri Lanka	United States of America, Belgium,
		Germany, France, Luxembourg,
		Netherlands, United Kingdom, Sweden,
		Italy, Austria, Greece, Denmark, Finland,
		Cyprus, Bulgaria, Estonia, Slovakia,
		Hungary, Romania, Russian Federation,
		Israel, Iceland, Japan, Korea, Republic
		of, Norway, Poland, Taiwan, Province of
		China, Chile, Latvia, Lithuania, Malta,
		Singapore
Filed		Cyprus

Not in force

Türkiye, Argentina, Brazil, China, Turkmenistan, Belarus, Tajikistan, Kazakhstan, Azerbaijan, Kyrgyzstan, Armenia, Moldova, Republic of, World Intellectual Property Organization (WIPO), Mexico, Malaysia, Yugoslavia/Serbia and Montenegro, Ukraine, South Africa, India, Bosnia and Herzegovina, Egypt, Indonesia, Kosovo, Benin, Cameroon, Burkina Faso, Chad, Guinea-Bissau, Mali, Senegal, Congo, Guinea, Gabon, Niger, Equatorial Guinea, Mauritania, Togo, Côte d'Ivoire, Central African Republic, Pakistan, Philippines, Thailand, Viet Nam, Botswana, Gambia (the), Ghana, Kenya, Lesotho, Malawi, Mozambique, Sierra Leone, Sudan, Eswatini, Tanzania, United Republic of, Uganda, Zambia, Zimbabwe, Albania, North Macedonia

Australia, Canada, Belgium, Germany, France, Luxembourg, Netherlands, Switzerland, United Kingdom, Sweden, Italy, Austria, Liechtenstein, Greece, Spain, Denmark, Monaco, Portugal, Ireland, Finland, Cyprus, Bulgaria, Czechia, Estonia, Slovakia, Slovenia, Hungary, Romania, Hong Kong, Croatia, New Zealand, World Intellectual Property Organization (WIPO), Bahrain, Kuwait, Qatar, Saudi Arabia, Oman, United Arab Emirates, Latvia, Lithuania

Supporting material

Publications

Bedaquiline: what might the future hold? Shaw, Emily S et al., The Lancet Microbe, Volume 5, Issue 12, 100909

Tuberculosis drug development has stagnated for decades, so the recent availability of bedaquiline is welcome. Bedaquiline-containing regimens, now the first-line therapy recommended by WHO, have transformed the treatment of drug-resistant tuberculosis, offering safer and more effective oral treatment options. However, key obstacles need to be overcome to ensure global access and prevent the rapid development of resistance against this promising class of drugs. In this Personal View, building on an international workshop held in 2023, we evaluate the current evidence and suggest possible ways forward, recognising the tension between increasing use and slowing the rise of resistance. We also discuss problems in accessing bedaquiline-containing regimens, the potential widening of their use beyond drug-resistant tuberculosis, and lessons for utilising new drugs as they are developed.

Kaushik A, Ammerman NC, Tasneen R, Lachau-Durand S, Andries K, Nuermberger E. Efficacy of Long-Acting Bedaquiline Regimens in a Mouse Model of Tuberculosis Preventive Therapy. *Am J Respir Crit Care Med*. 2022;205(5):570-579. doi:10.1164/rccm.202012-45410C

Rationale: Completion of preventive therapy is a major bottleneck in global tuberculosis control. Long-acting injectable drug formulations would shorten therapy administration and may thereby improve completion rates. Recently, a long-acting formulation of bedaquiline demonstrated antituberculosis activity for up to 12 weeks after injection in a validated mouse model of preventive therapy. **Objectives:** The objectives of this study were to 1) determine the total duration of activity after an

injection of long-acting bedaquiline and 2) evaluate the activity of regimens comprised of long-acting bedaquiline plus short (2-4 wk) oral companion courses of bedaquiline, with or without rifapentine, using the validated mouse model of tuberculosis preventive therapy. **Methods:** After the establishment of a stable *Mycobacterium* tuberculosis lung infection in bacillus Calmette-Guérin (BCG)-immunized BALB/c mice, treatment was initiated with 1 of 12 randomly assigned regimens. In addition to positive and negative controls, six regimens included one or two injections of longacting bedaquiline (alone or with oral bedaquiline with or without rifapentine), and four comparator regimens consisted of oral agents only. Lung bacterial burden was measured monthly for up to 28 weeks. Measurements and Main Results: One injection of long-acting bedaquiline at 160 mg/kg exerted antituberculosis activity for 12 weeks. Compared with the positive control (daily isoniazid-rifapentine for 4 wk), six regimens had equivalent bactericidal activity (including two all-oral comparator regimens), and two regimens had superior sterilizing activity: one injection with 2 weeks of oral bedaquiline and high-dose rifapentine; and two injections with 4 weeks of oral bedaquiline. **Conclusions:** Long-acting injectable bedaquiline has significant potential for shortening tuberculosis preventive therapy.

Ammerman NC, Nuermberger EL, Owen A, Rannard SP, Meyers CF, Swindells S. Potential Impact of Long-Acting Products on the Control of Tuberculosis: Preclinical Advancements and Translational Tools in Preventive Treatment. Clin Infect Dis. 2022 Nov 21;75(Suppl 4):S510-S516. doi: 10.1093/cid/ciac672. PMID: 36410384; PMCID: PMC10200320.

A key component of global tuberculosis (TB) control is the treatment of latent TB infection. The use of long-acting technologies to administer TB preventive treatment has the potential to significantly improve the delivery and impact of this important public health intervention. For example, an ideal long-acting treatment could consist of a single dose that could be administered in the clinic (ie, a "1-shot cure" for latent TB). Interest in long-acting formulations for TB preventive therapy has gained considerable traction in recent years. This article presents an overview of the specific considerations and current preclinical advancements relevant for the development of long-acting technologies of TB drugs for treatment of latent infection, including attributes of target product profiles, suitability of drugs for long-acting formulations, ongoing research efforts, and translation to clinical studies.

Kaushik A, Ammerman NC, Tyagi S, Saini V, Vervoort I, Lachau-Durand S, Nuermberger E, Andries K. Activity of a Long-Acting Injectable Bedaquiline Formulation in a Paucibacillary Mouse Model of Latent Tuberculosis Infection. Antimicrob Agents Chemother. 2019 Mar 27;63(4):e00007-19. doi: 10.1128/AAC.00007-19. PMID: 30745396; PMCID: PMC6437534.

The potent antituberculosis activity and long half-life of bedaquiline make it an attractive candidate for use in long-acting/extended-release formulations for the treatment of latent tuberculosis infection (LTBI). Our objective was to evaluate a longacting injectable (LAI) bedaquiline formulation in a validated paucibacillary mouse model of LTBI.

Additional documents

 <u>RespiriTB announces the start of a Phase 1 clinical trial with bedaquiline long- acting</u> <u>injectable</u>

Useful links

- Excitement builds for long-acting TB treatments, but research still at early stage
- Are long-acting injectables the future of TB treatment?
- A Single Ascending Dose, Single-Centre Study, to Assess Pharmacokinetics, Safety and Tolerability of a Single Intramuscular Dose of Bedaquiline Long-Acting Injection Formulation in Healthy Participant

Access principles

Collaborate for development



Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided Share technical information for match-making assessment



Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided Work with MPP to expand access in LMICs



In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Comment & Information