LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

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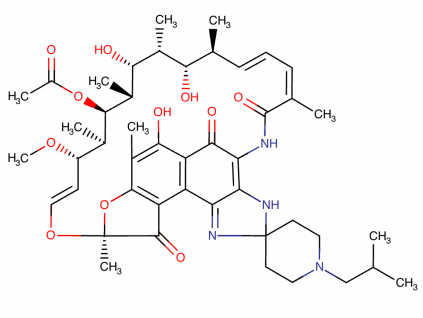


Rifabutin

Developer(s)

Pfizer

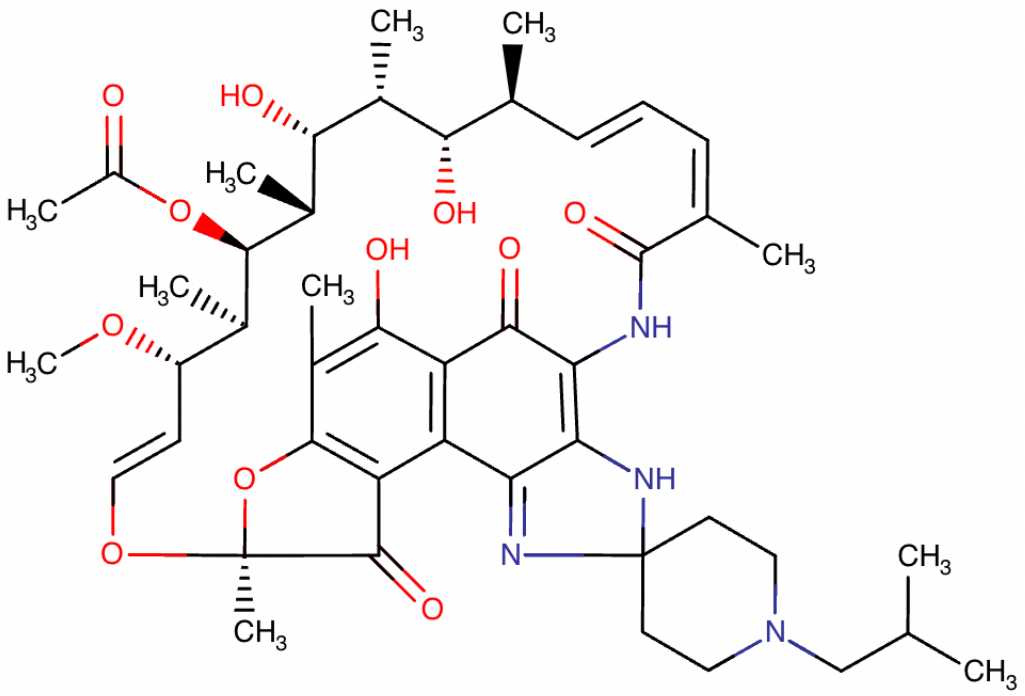
Originator

https://www.pfizer.com/

United States

Pfizer is a multinational pharmaceutical company headquartered in Manhattan, New York, USA. Pfizer develops vaccines and medicines for therapeutic areas including neurology, immunology, Covid-19, endocrinology, cardiology and oncology. Rifabutin was originally discovered by the Italian pharma company Archifar in 1975, who were subsequently acquired by Pharmacia in 1980 and later by Pfizer in 2003.

Drug structure



Structure of Rifabutin

Sourced from Drugbank

Drug information

Associated long-acting platforms

In-situ forming gel/implant

Administration route

Oral, Subcutaneous

Therapeutic area(s)

TB

Use case(s)

Pre-Exposure Prophylaxis (PrEP)
Treatment

Use of drug

Ease of administration

Administered by a nurse
Administered by a specialty health worker

User acceptance

Not provided

Dosage

Available dose and strength

Not provided

Frequency of administration

Not provided

Maximum dose

Not provided

Recommended dosing regimen

Not provided

Additional comments

Not provided

Dosage link(s)

Not provided

Drug information

Drug's link(s)

https://go.drugbank.com/drugs/DB00615

Generic name

Rifabutin

Brand name

Mycobutin

Compound type

Small molecule

Summary

Rifabutin is a broad-spectrum antibiotic used for the treatment of tuberculosis (TB) and has applications as mycobacterium avium complex prophylaxis in HIV-positive individuals. Rifabutin displays a wide range of bactericidal activity and functions through the inhibition of the bacterial DNA-dependent RNA polymerase. Given concerns regarding potential antibiotic resistance, the prescribing of Rifabutin is often restricted to the treatment mycobacterium infection and other limited applications. Rifabutin is well tolerated when administered orally, and is readily distributed throughout the body including the cerebrospinal fluid. Long-acting injectable versions of Rifabutin are currently in development and could potentially transform TB prevention and treatment.

Approval status

Unknown

Regulatory authorities

Unknown

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

Formulations for long-acting Rifabutin are currently in the pre-clinical development stage, and therefore detailed scale-up information is not currently available. One promising formulation termed RFB14KH developed at the University of North Carolina, Chapel Hill contains several FDA-approved components utilised in existing in-situ forming implants, including Kolliphor®HS 15 (Macrogol (15)-hydroxystearate), DMSO and PLGA (poly(lactic-co-glycolic acid)).

Tentative equipment list for manufacturing

Information regarding industrial processes and/or manufacturing equipment is currently not available as long-acting Rifabutin formulations have been only been produced at small-scale for research use.

Manufacturing

The previously mentioned RFB14KH formulation developed by researchers at the University of North Carolina, Chapel Hill was stored at room temperature in the absence of light and maintained stability for 18 months.

Specific analytical instrument required for characterization of formulation

HPLC and UV-Vis absorbance spectrometer for the evaluation of drug degradation and drug concentration. Zeiss Supra 25 field emission scanning electron microscope for characterisation of in-vitro implant formation.

Clinical trials

Not provided

Excipients

Proprietary excipients used

No proprietary excipient used

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

Not provided

Residual solvents used

Dimethyl sulfoxide (DMSO) which is a ICH Q3C class 3 solvent.

Patent info

Description

Rifamicyn compounds

Brief description

Rifabutin compound

Representative patent

US4219478

Category

Compound

Patent holder

Archifar Lab Chim Farm

Exclusivity

Not provided

Expiration date

June 2, 1996

Status

expired

Supporting material

Publications

Kim, M., Johnson, C.E., Schmalstig, A.A. *et al.* A long-acting formulation of rifabutin is effective for prevention and treatment of *Mycobacterium tuberculosis*. *Nat Commun* **13**, 4455 (2022). DOI: https://doi.org/10.1038/s41467-022-32043-3

Tuberculosis (TB) is a communicable disease caused by *Mycobacterium tuberculosis* (*Mtb*) and is a major cause of morbidity and mortality. Successful treatment requires strict adherence to drug regimens for prolonged periods of time. Long-acting (LA) delivery systems have the potential to improve adherence. Here, we show the development of LA injectable drug formulations of the anti-TB drug rifabutin made of biodegradable polymers and biocompatible solvents that solidifies after subcutaneous injection. Addition of amphiphilic compounds increases drug solubility, allowing to significantly increase formulation drug load. Solidified implants have organized microstructures that change with formulation composition. Higher drug load results in smaller pore size that alters implant erosion and allows sustained drug release. The translational relevance of these observations in BALB/c mice is demonstrated by (1) delivering high plasma drug concentrations for 16 weeks, (2) preventing acquisition of Mtb infection, and (3) clearing acute Mtb infection from the lung and other tissues.

Chang YS, Li SY, Pertinez H, Betoudji F, Lee J, Rannard SP, Owen A, Nuermberger EL, Ammerman NC. Using dynamic oral dosing of rifapentine and rifabutin to simulate exposure profiles of long-acting formulations in a mouse model of tuberculosis preventive therapy. bioRxiv [Preprint]. 2023 Apr 12:2023.04.12.536604. doi: 10.1101/2023.04.12.536604. PMID: 37090528; PMCID: PMC10120629.

Administration of tuberculosis preventive therapy (TPT) to individuals with latent tuberculosis infection is an important facet of global tuberculosis control. The use of long-acting injectable (LAI) drug formulations may simplify and shorten regimens for this indication. Rifapentine and rifabutin have anti-tuberculosis activity and physiochemical properties suitable for LAI formulation, but there are limited data available for determining the target exposure profiles required for efficacy in TPT

regimens. The objective of this study was to determine exposure-activity profiles of rifapentine and rifabutin to inform development of LAI formulations for TPT. We utilized a validated paucibacillary mouse model of TPT in combination with dynamic oral dosing of both drugs to simulate and understand exposure-activity relationships to inform posology for future LAI formulations. This work identified several LAI-like exposure profiles of rifapentine and rifabutin that, if achieved by LAI formulations, could be efficacious as TPT regimens and thus can serve as experimentally-determined targets for novel LAI formulations of these drugs. We present novel methodology to understand the exposure-response relationship and inform the value proposition for investment in development of LAI formulations that has utility beyond latent tuberculosis infection.

Additional documents

No documents were uploaded

Useful links

There are no additional links

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

Not provided

Comment & Information

Not provided