

Thalidomide

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Article Discussion Edit this page History

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This article is about the drug. For the musical about a person with Thalidomide disability, see [Thalidomide!! A Musical](#)

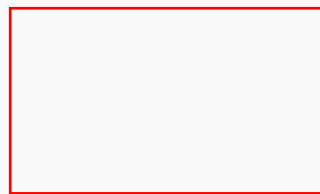
Thalidomide (pronounced /θəˈlɪdəmaɪd/) is a [sedative-hypnotic](#) and [multiple myeloma medication](#). The drug is a potent [teratogen](#) in rabbits and [primates](#) including humans: severe birth defects may result if the drug is taken during pregnancy.^[2]

Thalidomide was sold in a number of countries across the world from 1957 until 1961 when it was withdrawn from the market after being found to be cause birth defects in what has been called "the biggest medical tragedy of modern times".^[3] It is not known exactly how many worldwide victims of the drug there have been, although estimates range from 10,000 to 20,000.^[4]

Since then thalidomide has been found to be a valuable treatment for a number of medical conditions and it is being prescribed again in a number of countries, although its use remains controversial.^{[5][6]} The thalidomide tragedy led to much stricter testing being required for drugs and pesticides before they can be licensed.^[7]

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Thalidomide

Systematic (IUPAC) name

2-(2,6-dioxopiperidin-3-yl)-1*H*-isoindole-1,3(2*H*)-dione

Identifiers

CAS number	50-35-1
ATC code	L04AX02
PubChem	5426
DrugBank	APRD01251
ChemSpider	5233

Chemical data

Formula	C ₁₃ H ₁₀ N ₂ O ₄
Mol. mass	258.23 g/mol
SMILES	eMolecules & PubChem

Pharmacokinetic data

Bioavailability	?
Protein binding	55% and 66% for the (+)- <i>R</i> and (−)- <i>S</i> enantiomers, respectively
Metabolism	Hepatic (CYP2C19) ^[1]

- 6 Notable children affected
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History

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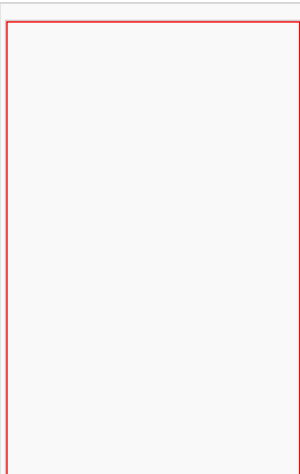
Development

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Thalidomide was said to have been developed by German pharmaceutical company Grünenthal in Stolberg (Rhineland) near Aachen, although this claim has recently been challenged. A report published by Dr Martin W Johnson, director of the Thalidomide Trust in the UK, detailed evidence that suggested the drug had been developed under the direction of a Nazi scientist in 1944, as an antidote to nerve gases such as sarin, ten years before Grünenthal secured a patent in 1954.^[8] Thalidomide was found to act as an effective tranquilliser and painkiller and was proclaimed as a "wonder drug" for insomnia, coughs, colds and headaches. It was also found to be an effective antiemetic which had an inhibitory effect on morning sickness, and so thousands of pregnant women took the drug to relieve their symptoms.^[4] At the time of the drug's development it was not thought likely that any drug could pass from the mother across the placental barrier and harm the developing foetus.^[7]

Birth defects

[edit]



1962 photo of baby born with an extra appendage connected to the foot caused by the pregnant mother

In the late 50s and early 60s, more than 10,000 children in 46 countries were born with deformities such as phocomelia, as a consequence of thalidomide use.^[9] The Australian obstetrician William McBride and the German pediatrician Widukind Lenz suspected a link between birth defects and the drug, and this was proved by Lenz in 1961.^{[10][11]} McBride was later awarded a number of honours including a medal and prize money by the prestigious L'Institut de la Vie in Paris.^[12] In the United Kingdom the drug was licensed in 1958 and, of the babies born with defects, 456 survived. The drug was withdrawn in 1961 but it wasn't until 1968, after a long campaign by The Sunday Times newspaper, that a compensation settlement for the UK victims was reached with Distillers Company Limited.^{[13][14]} In Germany approximately 2,500

Half life	mean ranges from approximately 5 to 7 hours following a single dose; not altered with multiple doses
Excretion	?
Therapeutic considerations	
Pregnancy cat.	X(AU) X(US)
Legal status	• Prescription only
Routes	oral

taking thalidomide

thalidomide babies were born.^[11]

The impact in the United States was minimized when the [pharmacologist Frances Oldham Kelsey](#) refused [Food and Drug Administration \(FDA\)](#) approval for an application from [Richardson Merrell](#) to market thalidomide, saying more study was needed. Richardson Merrell gave the tablets to doctors on the understanding that the drug was still under investigation. Seventeen children in the U.S. were born with the defects.^[9]

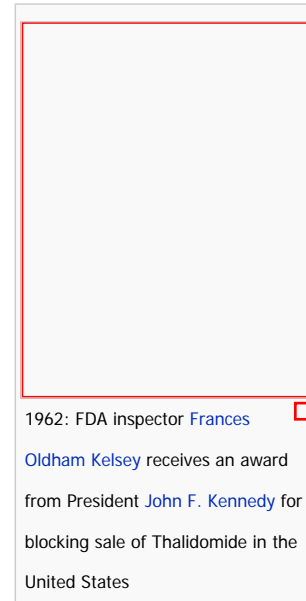
In 1962, the [United States Congress](#) enacted laws requiring tests for safety during pregnancy before a drug can receive approval for sale in the U.S.^[15] Other countries enacted similar legislation, and thalidomide was not prescribed or sold for decades.

However, it was soon found that it was only one particular [optical isomer](#) of thalidomide which caused the teratogenicity. The pair of [enantiomers](#), although mirror images of each other, cause different effects^[16] although it is now known that the "safe" isomer can be converted to the teratogenic one in the human body.^{[11][17]} (see *[Teratogenic mechanism](#)*).

Revived interest

In 1964 [Prof. Jacob Sheskin](#), Professor at the [Hebrew University of Jerusalem](#) at Hadassah University Hospital (he was also the chief staff and manager of Hansen Leper Hospital in Jerusalem), administered thalidomide to a critically ill patient with [erythema nodosum leprosum \(ENL\)](#), a painful complication of [leprosy](#), in an attempt to relieve his pain in spite of the ban. The patient slept for hours, and was able to get out of bed without aid upon awakening. The result was followed by more favorable experiences and then by a clinical trial.^[18]

He found that patients with [erythema nodosum leprosum](#), a painful skin condition, experienced relief of their pain by taking thalidomide. Further work conducted in 1991 by Dr. Gilla Kaplan at Rockefeller University in New York City showed that thalidomide worked in leprosy by inhibiting tumor necrosis factor alpha. Kaplan partnered with Celgene Corporation to further develop the potential for thalidomide. Subsequent research has shown that thalidomide is effective in the treatment of [multiple myeloma](#), and it was approved for use in the United States by the FDA for use in this [malignancy](#). The FDA has also since approved the drug's use in the treatment of [erythema nodosum leprosum](#). There are studies underway to determine the drug's effects on [arachnoiditis](#) and several types of [cancers](#). However, [physicians](#) and patients alike must go through a special process to prescribe and receive thalidomide (S.T.E.P.S) to ensure no more children are born with birth defects traceable to the medication. Celgene Corporation has also developed analogues to thalidomide, such as [lenalidomide](#), that are substantially more powerful and have fewer side effects - except for greater [myelosuppression](#).^[19]



1962: FDA inspector [Frances](#)

[Oldham Kelsey](#) receives an award from President [John F. Kennedy](#) for blocking sale of Thalidomide in the United States

[edit]

United States

On July 16, 1998, the FDA approved the use of thalidomide for the treatment of lesions associated with Erythema Nodosum Leprosum (ENL). Because of thalidomide's potential for causing birth defects, the distribution of the drug was permitted only under tightly controlled conditions. The FDA required that [Celgene Corporation](#), which planned to market thalidomide under the brand name *Thalomid*, establish a System for Thalidomide Education and Prescribing Safety (S.T.E.P.S) oversight program. The conditions required under the program include: limiting prescription and dispensing rights only to authorized prescribers and pharmacies, keeping a registry of all patients prescribed thalidomide, providing extensive patient education about the risks associated with the drug and providing periodic pregnancy tests for women who are prescribed it.^[20]

On May 26, 2006, the U.S. Food and Drug Administration granted accelerated approval for thalidomide (Thalomid, Celgene Corporation) in combination with dexamethasone for the treatment of newly diagnosed [multiple myeloma](#) (MM) patients.^[21] The FDA approval came seven years after the first reports of efficacy in the medical literature^[22] and Celgene took advantage of "off-label" marketing opportunities to promote the drug in advance of its FDA approval for the myeloma indication. Thalomid, as the drug is commercially known, sold over \$300 million per year, while only approved for leprosy.^[23]

United Kingdom

Thalidomide is available to only a small number of patients in the UK, generally in specialist cancer treatment centres where research trials are taking place and specialist doctors have experience in its use.^[24]

Brazil

Brazil has the highest prevalence rate of [leprosy](#) in the world and thalidomide has been used by Brazilian physicians as the drug of choice for the treatment of severe ENL since 1965. A study published in 1994 found 61 people born after 1965 whose limb defects and exposure history were compatible with thalidomide embryopathy. In 63.6% of these cases, thalidomide had been prescribed without the physician informing the patient about the drug's teratogenicity. Since then production, dispensing and prescription of thalidomide have been strictly controlled and no cases of thalidomide embryopathy are thought to have occurred since 1997.^[25]

Possible indications

Research on thalidomide slowed in the 1960s, but never stopped. At least one university in the United States pursues thalidomide research, even though performed by only one tenured professor. The medication is an example of how potentially dangerous compounds can be used therapeutically with appropriate precautions and procedures.

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Serious infections including [sepsis](#) and [tuberculosis](#) cause the level of [Tumor necrosis factor-alpha](#) (TNFα) to rise. TNFα is a chemical mediator in the body, and it may enhance the wasting process in cancer patients as well. Thalidomide may reduce the levels of TNFα, and it is possible that the drug's effect on ENL is caused by this mechanism.^[15]

Thalidomide also has potent anti-inflammatory effects that may help ENL patients. In July 1998, the FDA approved the application of [Celgene](#) to distribute thalidomide under the brand name Thalomid for treatment of ENL. Pharmion Corporation, who licensed the rights to market Thalidomide in Europe, Australia and various other territories from Celgene, received approval for its use against [multiple myeloma](#) in Australia and New Zealand in 2003.^[26] Thalomid, in conjunction with [dexamethasone](#), is now standard therapy for multiple myeloma.

Thalidomide is also prescribed for its anti-inflammatory effects in [actinic prurigo](#), an autoimmune skin disease.

Thalidomide also inhibits the growth of new blood vessels ([angiogenesis](#)), which may be useful in treating [macular degeneration](#) and other diseases. This effect helps [AIDS](#) patients with [Kaposi's sarcoma](#), although there are better and cheaper drugs to treat the condition. Thalidomide may be able to fight painful, debilitating [aphthous](#) lesions in the mouth and esophagus of AIDS patients which prevent them from eating. The FDA formed a Thalidomide Working Group in 1994 to provide consistency between its divisions, with particular emphasis on safety monitoring. The agency also imposed severe restrictions on the distribution of Thalomid through the System for Thalidomide Education and Prescribing Safety (STEPS) program.^[15]

Thalidomide is also being investigated for treating symptoms of [prostate cancer](#), [glioblastoma](#), [lymphoma](#), [arachnoiditis](#), [Behçet's disease](#), and [Crohn's disease](#). In a small trial, Australian researchers found thalidomide sparked a doubling of the number of [T cells](#) in patients, allowing the patients' own [immune system](#) to attack cancer cells.

Full list of indications currently being investigated in clinical trials:^[27]

- Amyotrophic lateral sclerosis
- Aphthous ulcer
- Behcet's syndrome
- Brain cancer
- Breast cancer
- Cachexia
- Colorectal cancer
- Congestive heart failure

- Crohn's disease
- Diarrhoea
- Fibrodysplasia ossificans progressiva
- Graft-versus-host disease
- Haematological malignancies
- HIV infections
- Hodgkin's disease
- Kaposi's sarcoma
- Leukaemia
- Macular degeneration
- Malignant melanoma
- Mycobacterium avium complex infections
- Myelodysplastic syndromes
- Myelofibrosis
- Myeloid leukaemia
- Non-Hodgkin's lymphoma
- Non-small cell lung cancer
- Ovarian cancer
- Pain
- Prostate cancer
- Prurigo nodularis
- Renal cancer
- Rheumatoid arthritis
- Small cell lung cancer
- Systemic lupus erythematosus
- Thyroid cancer
- Tuberculosis

Thalidomide and multiple myeloma

[\[edit\]](#)

Thalidomide was first tested as a single agent for the treatment of [multiple myeloma](#) in 1999 due to its antiangiogenesis activity.^[28] Since then many studies have shown that thalidomide in combination

with **dexamethasone** has increased the survival of multiple myeloma patients. The combination of thalidomide and dexamethasone, often in combination with **melfalan**, is now one of the most common regimens for patients with newly diagnosed multiple myeloma, with an improved response rate of up to 60-70%.^{[29][30]} However, thalidomide may also cause side effects such as **polyneuropathy**, fatigue, skin rash, and **venous thromboembolism (VTE)**, or blood clots, which could lead to **stroke** or **myocardial infarction**.^[31] Bennett et al. have conducted a systematic review of VTE associated with thalidomide in multiple myeloma patients.^[32] They have found that when Thalidomide was administered without **prophylaxis**, VTE rates reached as high as 26%. Due to the high rates of VTE associated with thalidomide in combination with dexamethasone or **doxorubicin**, a **black box warning** was added in 2006 to the package insert for thalidomide, indicating that patients with multiple myeloma who receive thalidomide-dexamethasone may benefit from concurrent thromboembolism prophylaxis or **aspirin**. In addition, due to these side effects, newer drugs, such as a thalidomide derivative **lenalidomide** (marketed as Revlimid) and **bortezomib** (marketed as Velcade) have increased in popularity.^{[[]*citation needed*[]]}

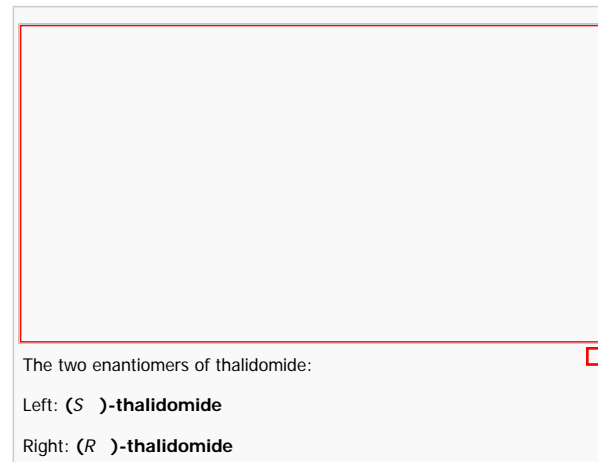
Teratogenic mechanism

[[edit](#)]

Thalidomide is **racemic** – it contains both left- and right-handed **isomers** in equal amounts. The (*R*) **enantiomer** is effective against morning sickness but the (*S*) is **teratogenic** and causes birth defects.

The enantiomers can interconvert *in vivo*^[33] – that is, if a human is given pure (*R*)-thalidomide or (*S*)-thalidomide, both isomers can be found in the **serum** – therefore, administering only one enantiomer will not prevent the teratogenic effect.

The mechanism of thalidomide's teratogenic action has led to over 2000 research papers and the proposal of fifteen or sixteen plausible mechanisms.^[34] A theoretical synthesis in 2000^[34] suggested the following mechanism: Thalidomide **intercalates** (inserts itself) into **DNA** in G-C (**guanine-cytosine**) rich regions.^{[35][36]} Due to its glutarimide part, (S) thalidomide fits neatly into the major groove of DNA at purine sites.^[34] Such intercalation impacts upon the promoter regions of the genes controlling the development of limbs, ears, and eyes such as **IGF-1** and **FGF-2**. These normally activate the production of the cell surface attachment **integrin** αvβ3 with the resulting alphavbeta3 integrin dimer stimulating **angiogenesis** in developing limb buds. This then promotes the outgrowth of the bud (IGF-1 and FGF-2 are also both known to stimulate angiogenesis). Therefore, by inhibiting the chain of events, thalidomide causes the truncation of limb development. In 2009 this theory^[34] received strong support, with research showing "conclusively that loss of newly formed blood vessels is the primary cause of thalidomide teratogenesis, and developing limbs are



[37]

particularly susceptible because of their relatively immature, highly angiogenic vessel network.

Other side effects

[[edit](#)]

Apart from its infamous tendency to induce birth defects and [peripheral neuropathy](#), the main side effects of thalidomide include fatigue and [constipation](#).^[*citation needed*] It is also associated with an increased risk of [deep vein thrombosis](#) especially when combined with [dexamethasone](#), as it is for treatment of multiple myeloma.^[*citation needed*] High doses can lead to [pulmonary oedema](#), [atelectasis](#), [aspiration pneumonia](#) and refractory [hypotension](#).^[*citation needed*] In multiple myeloma patients, concomitant use with zoledronic acid may lead to increased incidence of renal dysfunction.^[*citation needed*]

Thalidomide analogs

[[edit](#)]

The exploration of the [antiangiogenic](#) and immunomodulatory activities of thalidomide has led to the study and creation of thalidomide [analogs](#). In 2005, Celgene received FDA approval for [lenalidomide](#) (Revlimid) as the first commercially useful derivative. Revlimid is only available in a restricted distribution setting to avoid its use during pregnancy. Further studies are conducted to find safer compounds with useful qualities. Another analog, [Actimid \(CC-4047\)](#), is in the clinical trial phase.^[*38*] These thalidomide analogs can be used to treat different diseases, or used in a regimen to fight two conditions.

Notable children affected

[[edit](#)]

- [Mat Fraser](#), a comedian, actor, co-presenter of the BBC's [Ouch Podcast](#).
- [Alison Lapper](#) is an English artist who was the subject of Marc Quinn's sculpture *Alison Lapper Pregnant*, which was on display in Trafalgar Square in London from 2005 until late 2007.
- [Alvin Law](#), a motivational speaker and former radio broadcaster.
- [Tony Meléndez](#) is a guitarist who was born without arms. He plays only with his feet.
- [Terry Wiles](#) internationally known through *On Giants' Shoulders*, a book and film about his life.
- [Brett Nielsen](#), a musician, was the first Australian thalidomide child.
- [Louise Medus Mansell](#), daughter of David Mason, campaigner for increased compensation for Thalidomide children, born with no arms or legs.^[*39*]
- [Thomas Quasthoff](#) is an internationally acclaimed bass-baritone who describes himself: "1.34 meters tall, short

arms, seven fingers - four right, three left - large, relatively well formed head, brown eyes, distinctive lips;

profession: singer."^[40]

- **Matthias Berg** is a lawyer, renowned **hornist** and multiple **Paralympics** gold medalist.
- **Melody Potter** Native Alabamian disability activist, severe deformities, no arms or legs.
- **Giancarlo Cosio**, Italian Waterski World disabled Champion.
- **David Lega**, Swedish swimmer. Paralympian and current holder of 5 world records.^[41]
- **Gary Skyner**, a comedian and motivational speaker.
- **Frankie Shum**, an actor, starred in Kung fu films **Crippled Masters** and **Crippled Heroes**.

References

[[edit](#)]

- ↑ Ando Y, Fuse E, Figg WD (01 June 2002). "Thalidomide metabolism by the CYP2C subfamily". *Clinical Cancer Research : an Official Journal of the American Association for Cancer Research* **8** (6): 1964–73. PMID 12060642. http://clincancerres.aacrjournals.org/cgi/pmidlookup?view=long&pmid=12060642. Retrieved 2009-06-18.
- ↑ Thalidomide: Drug safety during pregnancy and breastfeeding / DRUGSAFETYSITE.COM
- ↑ Anon. "Thalidomide - A Second Chance? - programme summary". BBC. http://www.bbc.co.uk/science/horizon/2004/thalidomide.shtml. Retrieved 2009-05-01.
- ↑ ^a ^b Anon. "Born Freak". *Happy Birthday Thalidomide*. Channel 4. http://www.channel4.com/life/microsites/B/bornfreak/birthday.html. Retrieved 2009-05-01.
- ↑ Anon (March 10, 2006). "Thalidomide:controversial treatment for multiple myeloma". *Health news*. http://www.healthyforms.com/health-news/2006/03/thalidomide-controversial-treatment.php. Retrieved 2009-05-01.
- ↑ Bowditch, Gillian (March 26, 2006). "Can thalidomide ever be trusted?". *The Sunday Times* (News International Limited). http://www.timesonline.co.uk/tol/news/uk/scotland/article695193.ece?token=null&offset=0&page=1. Retrieved 2009-05-01.
- ↑ ^a ^b Heaton, C. A. (1994). *The Chemical Industry*. Springer. pp. 40. ISBN 0751400181.
- ↑ Foggo, Daniel (2009-02-08). "Thalidomide 'was created by the Nazis'". London: The Times. http://www.timesonline.co.uk/tol/life_and_style/health/article5683577.ece. Retrieved 2009-06-18.
- ↑ ^a ^b Bren, Linda (2001-02-28). "Frances Oldham Kelsey: FDA Medical Reviewer Leaves Her Mark on History". *FDA Consumer* (US Food and Drug Administration). http://www.fda.gov/fdac/

25. [^] Paumgartten, J.R.; Chahoud, Ibrahim (July 2006). "Thalidomide embryopathy cases in Brazil after 1965". *Reproductive Toxicology* (Elsevier) **22** (1): 1,2. doi:10.1016/j.reprotox.2005.11.007. http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TC0-4J2W0DX-1&_user=899537&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000047642&_version=1&_urlVersion=0&_userid=899537&md5=064ddf875924b5b116f6ed8d82049b07.
26. [^] Rouhi, Maureen. "Thalidomide". *Chemical & Engineering News*. American Chemical Society. http://pubs.acs.org/cen/coverstory/83/8325/8325thalidomide.html. Retrieved 2006-09-21.
27. [^]. ADIS R&D Insight. http://bi.adisinsight.com/rdi/viewdocument.aspx?render=view&mode=remote&adnm=800004827&PushValidation=121745. Retrieved 2009-08-21.
28. [^] Singhal S, Mehta J, Desikan R, *et al.* (November 1999). "Antitumor activity of thalidomide in refractory multiple myeloma". *The New England Journal of Medicine* **341** (21): 1565–71. doi:10.1056/NEJM199911183412102. PMID 10564685. http://content.nejm.org/cgi/pmidlookup?view=short&pmid=10564685&promo=ONFLNS19. Retrieved 2009-06-18.
29. [^] Gieseler F (June 2008). "Pathophysiological considerations to thrombophilia in the treatment of multiple myeloma with thalidomide and derivatives". *Thrombosis and Haemostasis* **99** (6): 1001–7. doi:10.1160/TH08-01-0009. PMID 18521500.
30. [^] Denz U, Haas PS, Wäsch R, Einsele H, Engelhardt M (July 2006). "State of the art therapy in multiple myeloma and future perspectives". *European Journal of Cancer (Oxford, England : 1990)* **42** (11): 1591–600. doi:10.1016/j.ejca.2005.11.040. PMID 16815703.
31. [^] Haas PS, Denz U, Ihorst G, Engelhardt M (April 2008). "Thalidomide in consecutive multiple myeloma patients: single-center analysis on practical aspects, efficacy, side effects and prognostic factors with lower thalidomide doses". *Eur. J. Haematol.* **80** (4): 303–9. doi:10.1111/j.1600-0609.2007.01022.x. PMID 18182082.
32. [^] Bennett CL, Angelotta C, Yarnold PR, *et al.* (December 2006). "Thalidomide- and lenalidomide-associated thromboembolism among patients with cancer". *JAMA : the Journal of the American Medical Association* **296** (21): 2558–60. doi:10.1001/jama.296.21.2558-c. PMID 17148721.
33. [^] Teo SK, Colburn WA, Tracewell WG, Kook KA, Stirling DI, Jaworsky MS, Scheffler MA, Thomas SD, Laskin OL (2004). "Clinical pharmacokinetics of thalidomide". *Clin Pharmacokinet.* **43** (5): 311–327. doi:10.2165/00003088-200443050-00004. PMID 15080764.
34. [^] ^a ^b ^c ^d Stephens TD, Bunde CJ, Fillmore BJ (June 2000). "Mechanism of action in thalidomide teratogenesis". *Biochemical Pharmacology* **59** (12): 1489–99. doi:10.1016/S0006-2952(99)00388-3. PMID 10799645.
35. [^] Koch HP, Czejka MJ. (1986). Evidence for the intercalation of thalidomide into DNA: clue to the molecular mechanism of thalidomide teratogenicity? *Z Naturforsch [C]*. 41(11-12):1057-61. PMID 2953123

36. [^] Huang PH, McBride WG (1997). Interaction of (glutarimide-2-14C)-thalidomide with rat embryonic DNA in vivo". *Teratogenesis, Carcinogenesis, and Mutagenesis* **17** (1): 1–5. doi:10.1002/(SICI)1520-6866(1997)17:1<1::AID-TCM2>3.0.CO;2-L. PMID 9249925.
37. [^] Therapontos C, Erskine L, Gardner ER, Figg WD, Vargesson N (May 2009). "Thalidomide induces limb defects by preventing angiogenic outgrowth during early limb formation". *Proceedings of the National Academy of Sciences of the United States of America* **106** (21): 8573–8. doi:10.1073/pnas.0901505106. PMID 19433787.
38. [^] Search of: pomalidomide - ClinicalTrials.gov
39. [^] Courtenay-Smith, Natasha (2008-04-23). "A truly special love story: Two married thalidomide survivors living happily 50 years after drug's launch". London: The Daily Mail. http://www.dailymail.co.uk/news/article-561360/A-truly-special-love-story-Two-married-thalidomide-survivors-living-happily-50-years-drugs-launch.html. Retrieved 2009-06-18.
40. [^] Orpheus lives: A small good thing in Quastoff Retrieved on 2008-10-22
41. [^] David Lega personal website

Further reading

[edit]

- Stephens, Trent; Brynner, Rock (2001-12-24). *Dark Remedy: The Impact of Thalidomide and Its Revival as a Vital Medicine*. Perseus. ISBN 0-7382-0590-7.
- Knightley, Phillip; Evans, Harold. Potter, Elaine. Wallace, Marjorie. (1979). *Suffer The Children: The Story of Thalidomide*. New York: The Viking Press. ISBN 0-670-68114-8.

External links

[edit]

- Thalidomide product monograph (Needs registration)
- Multiple Myeloma Research Foundation article on Thalidomide
- International Myeloma Foundation article on Thalidomide
- Thalidomide — Annotated List of Links (covering English and German pages)
- WHO Pharmaceuticals Newsletter No. 2, 2003 - See page 11, Feature Article
- Grünenthal GmbH - Thalidomide
- Celgene website on Thalomid
- The Return of Thalidomide - BBC

- [CBC Digital Archives – Thalidomide: Bitter Pills, Broken Promises](#)
- [Thalidomide UK](#)
- [The Thalidomide Trust](#)
- "The Big Pitch: How would you conduct a campaign for the new Thalidomide Drugs?", forum of pharmaceutical and medical marketing professionals commenting on how they would address the Thalidomine controversies.

v • d • e		Immunomodulators: Immunosuppressive drugs / Immunosuppressants (L04)		[hide]
Intracellular (signal initiation)	Antimetabolites	purine synthesis inhibitor	: Azathioprine · Mycophenolic acid	
		pyrimidine synthesis inhibitor	: Leflunomide · Teriflunomide	
		antifolate	: Methotrexate	
	Macrolides/ other IL-2 inhibitors	FKBP / Cyclophilin / Calcineurin	: Tacrolimus	
· Ciclosporin · Pimecrolimus				
	TNF-α inhibitor	Thalidomide · Lenalidomide		
Intracellular (signal reception)	IL-1 receptor antagonists	Anakinra		
	mTOR	Sirolimus · Deforolimus · Everolimus · Temsirolimus · Zotarolimus		
Extracellular	Antibodies	Monoclonal	Serum target (noncellular)	Complement component 5 (Eculizumab)
				· TNFs (Infliximab, Adalimumab, Certolizumab pegol, Afelimomab, Golimumab)
				· Interleukin 5 (Mepolizumab)
				· Immunoglobulin E (Omalizumab) · BAYX
				(Nerelimomab)
				Interferon (Faralimomab)
				IL-6 (Elsilimomab)
				IL-12 and IL-13 (Ustekinumab)
				CD3 (Muromonab-CD3, Otelixizumab, Teplizumab, Visilizumab) · CD4 (Clenoliximab, Keliximab, Zanolimumab) · CD11a (Efalizumab) · CD18 (Erlizumab) · CD20 (Afutuzumab, Ocrelizumab, Pascolizumab) · CD23 (Lumiliximab) · CD40 (Teneliximab, Toralizumab) · CD62L/L-selectin (Aselizumab) · CD80
				(Galiximab) · CD147/Basigin (Gavilimomab, Ziralimumab) · CD154 (Ruplizumab)

				<i>BlyS</i>	(Belimumab) · <i>CTLA-4</i>	(Ipilimumab, Tremelimumab) · <i>CAT</i>
				(Bertilimumab, Lerdelimumab, Metelimumab) · <i>Integrin</i>		(Natalizumab
) · <i>Interleukin-6 receptor</i>		(Tocilizumab
) · <i>LFA-1</i>	(Oculimomab)	
				<i>IL-2 receptor/CD25</i>		(Basiliximab, Daclizumab, Inolimomab)
				<i>T-lymphocyte</i>		(Zolimomab aritox)
				Atlizumab, Atorolimumab, Cedelizumab, Dorlimomab aritox , Dorlizumab, Fontolizumab		
			Unsorted	, Gantenerumab, Gomiliximab, Lebrilizumab, Maslimomab, Morolimumab, Pexelizumab, Reslizumab		
				, Rovelizumab, Siplizumab, Talizumab, Telimomab aritox, Vapaliximab, Vepalimomab		
		Polyclonal	Anti-thymocyte globulin · Anti-lymphocyte globulin			
	-cept (Fusion protein)	<i>CTLA-4</i>	(Abatacept, Belatacept) · Aflibercept · Alefacept · Riloncept · TNF inhibitor (Etanercept)			

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