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NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Lorcaserin. [Updated 2020 Jun 5].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Lorcaserin

Updated: June 5, 2020.

OVERVIEW

Introduction

Lorcaserin is a selective serotonin agonist that was used as a weight loss agent. Lorcaserin was in clinical use for eight years when it was withdrawn because of concerns regarding an excess in cancer risk after long term use. In prelicensure studies and while in clinical use, lorcaserin was not found to be associated with serum enzyme elevations during therapy or to instances of clinically apparent liver injury.

Background

Lorcaserin (lor ka' ser in) is a serotonin agonist that is relatively selective for the serotonin 2C (5-HT2C) receptor, that is located almost exclusively in the brain. Activation of this receptor activates pathways important in hunger and satiety, including those that induce proopiomelanocortin which decreases appetite. In several premarketing controlled trials, lorcaserin was found to lead to greater weight loss than placebo. Lorcaserin was officially approved for use in the United States in 2012, but was recommended only for patients who were obese (BMI ≥30) or who were overweight (BMI ≥27-30) and had a significant obesity related condition. In early 2020, lorcaserin was withdrawn from clinical use because of long term studies suggesting an increased risk of cancer with its use. Lorcaserin was available in 10 mg tablets under the commercial name Belviq. The recommended dose was 10 mg twice daily. An extended release formulation, available as 20 mg tablets (Belviq XR), was developed which allowed for once daily administration. Commonly reported side effects were headache, dry mouth, nausea, fatigue and dizziness which occasionally required discontinuation or dose adjustment. Severe side effects were rare and possibly included depression, serotonin syndrome and cardiac valvulopathy, although these side effects were not appreciably increased among lorcaserin treated patients in prelicensure clinical trials nor were they identified in subsequent postmarketing studies. A recent reanalysis of a large, long term trial of lorcaserin identified an excess incidence of cancer with treatment, including pancreatic, colorectal and lung cancer.

Hepatotoxicity

In premarketing clinical trials, serum aminotransferase elevations were no more common among patients receiving lorcaserin than placebo. Clinically apparent liver injury due to lorcaserin has not been reported, but the numbers of patients treated has been limited.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Outcome and Management

No instances of acute liver failure or chronic liver injury have been linked to lorcaserin, but it has had limited general clinical use and now has been withdrawn because of an increased risk for cancer with long term use.

Drug Class: Weight Loss Agents

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Lorcaserin – Belviq®

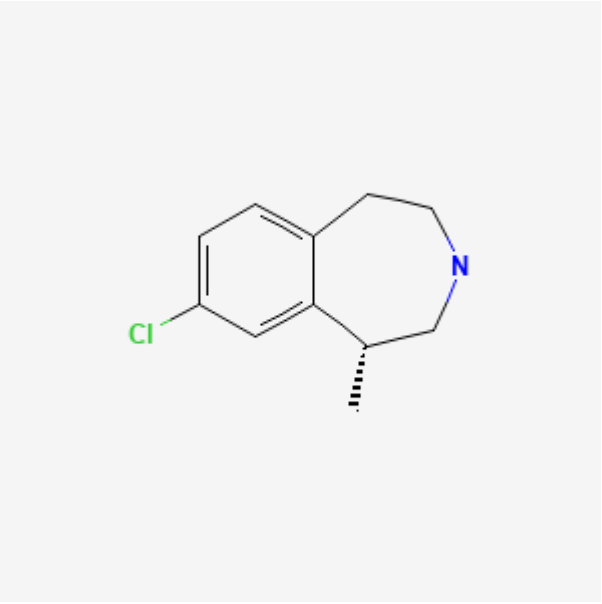
DRUG CLASS

Weight Loss Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Lorcaserin	616202-92-7	C11-H14-CI-N	

ANNOTATED BIBLIOGRAPHY

References updated: 05 June 2020

Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999.

(Review of hepatotoxicity published in 1999, well before the availability of lorcaserin).

Smith SR, Prosser WA, Donahue DJ, Morgan ME, Anderson CM, Shanahan WR; APD356-004 Study Group. Lorcaserin (APD356), a selective 5-HT (2C) agonist, reduces body weight in obese men and women. Obesity (Silver Spring). 2009;17:494–503. PubMed PMID: 19057523.

(Randomized controlled trial of 12 weeks of lorcaserin vs placebo in 469 obese subjects; no mention of ALT levels or hepatotoxicity).

Smith SR, Weissman NJ, Anderson CM, Sanchez M, Chuang E, Stubbe S, Bays H, Shanahan WR; Behavioral Modification and Lorcaserin for Overweight and Obesity Management (BLOOM) Study Group. Multicenter, placebo-controlled trial of lorcaserin for weight management. N Engl J Med. 2010;363:245–56. PubMed PMID: 20647200.

(Randomized controlled trial of 52 weeks of twice daily lorcaserin vs placebo in 3182 obese or overweight patients; serious adverse events included "hepatobiliary disorder" in 0.3% of lorcaserin and 0.3% of placebo recipient; no mention of ALT levels and no clinical details given).

Astrup A. Drug management of obesity--efficacy versus safety. N Engl J Med. 2010;363:288–90. PubMed PMID: 20647205.

(Editorial in response to Smith [2010] reviewing history of weight loss agents used in the United States, many having been withdrawn because of issues of safety of long term use).

Hurren KM, Berlie HD. Lorcaserin: an investigational serotonin 2C agonist for weight loss. Am J Health Syst Pharm. 2011;68:2029–37. PubMed PMID: 22011982.

(Review of safety and efficacy of lorcaserin for weight loss based upon 3 phase III trials; most common side effects were nausea [8.3%], headache [16.8%], and dizziness [8.5%], but discontinuations for side effects were rare; no mention of ALT levels or hepatotoxicity).

Fidler MC, Sanchez M, Raether B, Weissman NJ, Smith SR, Shanahan WR, Anderson CM; BLOSSOM Clinical Trial Group. A one-year randomized trial of lorcaserin for weight loss in obese and overweight adults: the BLOSSOM trial. J Clin Endocrinol Metab. 2011;96:3067–77. PubMed PMID: 21795446.

(Randomized controlled trial of two doses of lorcaserin vs placebo for an average of 20 weeks in 4008 obese or overweight patients: "No lorcaserin-associated changes in clinical laboratory parameters... were identified").

O'Neil PM, Smith SR, Weissman NJ, Fidler MC, Sanchez M, Zhang J, Raether B, et al. Randomized placebo-controlled clinical trial of lorcaserin for weight loss in type 2 diabetes mellitus: the BLOOM-DM study. Obesity (Silver Spring). 2012;20:1426–36. PubMed PMID: 22421927.

(Randomized controlled trial of lorcaserin vs placebo in 604 overweight or obese patients with diabetes; no mention of ALT levels or hepatotoxicity).

Chan EW, He Y, Chui CS, Wong AY, Lau WC, Wong IC. Efficacy and safety of lorcaserin in obese adults: a meta-analysis of 1-year randomized controlled trials (RCTs) and narrative review on short-term RCTs. Obes Rev. 2013;14:383–92. PubMed PMID: 23331711.

(Systematic review of results from 5 randomized controlled trials of lorcaserin, only 3 of which used the agent for more than 12 weeks; no mention of hepatotoxicity or ALT elevations).

Nigro SC, Luon D, Baker WL. Lorcaserin: a novel serotonin 2C agonist for the treatment of obesity. Curr Med Res Opin. 2013;29:839–48. PubMed PMID: 23574263.

(Review of the mechanism of action, efficacy and safety of lorcaserin as therapy of obesity; no mention of liver injury or ALT elevations).

Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. JAMA. 2014;311:74–86. PubMed PMID: 24231879.

(Systematic review of the long term efficacy of drug therapies for obesity including lorcaserin, orlistat and phentermine plus topiramate).

Lorcaserin. In obesity: unacceptable risks. Prescrire Int. 2014;23:117–20. PubMed PMID: 24926508.

(Review of the efficacy and safety of lorcaserin concludes that its weight loss effects are minimal and short lived, and that its costs and risks of adverse events do not warrant its use as therapy of obesity).

Halpern B, Halpern A. Safety assessment of FDA-approved (orlistat and lorcaserin) anti-obesity medications. Expert Opin Drug Saf. 2015;14:305–15. PubMed PMID: 25563411.

(Review of the safety and efficacy of FDA approved medications for obesity including lorcaserin).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology. 2015;148:1340–52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, none of the cases were attributed to a weight loss product such as lorcaserin).

Smith SR, Garvey WT, Greenway FL, Zhou S, Fain R, Pilson R, Fujioka K, et al. Coadministration of lorcaserin and phentermine for weight management: A 12-week, randomized, pilot safety study. Obesity (Silver Spring). 2017;25:857–65. PubMed PMID: 28440045.

(Among 235 overweight or obese, non-diabetic adults treated with lorcaserin alone or with phentermine [once or twice daily], weight loss was greater with the combination but so were side effects, but "there was no evidence of hepatic or renal toxicity").

Bohula EA, Scirica BM, Inzucchi SE, McGuire DK, Keech AC, Smith SR, Kanevsky E, et al; CAMELLIA-TIMI 61 Steering Committee Investigators. Effect of lorcaserin on prevention and remission of type 2 diabetes in overweight and obese patients (CAMELLIA-TIMI 61): a randomised, placebo-controlled trial. Lancet. 2018;392(10161):2269–79. PubMed PMID: 30293771.

(Among 12,000 overweight or obese adults treated with lorcaserin or placebo for a median of 3.3 years, weight loss was greater with lorcaserin by approximately 2.6 kg; no mention of ALT elevations or other adverse events).

Bohula EA, Wiviott SD, McGuire DK, Inzucchi SE, Kuder J, Im K, Fanola CL, et al; CAMELLIA–TIMI 61 Steering Committee and Investigators. Cardiovascular safety of lorcaserin in overweight or obese patients. N Engl J Med. 2018;379:1107–17. PubMed PMID: 30145941.

(Further analysis of trial of lorcaserin in 12,000 overweight or obese adults focusing upon safety and adverse events mentions adverse events "possible" to include dizziness, fatigue, headache, diarrhea and nausea; no mention of ALT elevations or hepatotoxicity).

Diet, drugs, devices, and surgery for weight management. Med Lett Drugs Ther. 2018;60(1548):91–8. PubMed PMID: 29913463.

(Concise review of the medical and surgical therapies for obesity mentions that lorcaserin is a schedule IV controlled substance and only modestly effective for weight loss and that adverse effects include headache, nausea, dizziness, euphoria and impairment of attention and cognition and possibly serotonin syndrome and cardiac valvulopathy; no mention of ALT elevations or hepatotoxicity).

Tuccinardi D, Farr OM, Upadhyay J, Oussaada SM, Mathew H, Paschou SA, Perakakis N, et al. Lorcaserin treatment decreases body weight and reduces cardiometabolic risk factors in obese adults: A six-month, randomized, placebo-controlled, double-blind clinical trial. Diabetes Obes Metab. 2019;21:1487–92. PubMed PMID: 30724455.

(Among 48 obese adults treated with lorcaserin or placebo for 6 months, weight loss was greater with lorcaserin [-2 vs -0.4 kg] as were decreases in hepatic fat index, while ALT and AST levels were normal and remained normal with therapy).

Saunders KH, Umashanker D, Igel LI, Kumar RB, Aronne LJ. Obesity pharmacotherapy. Med Clin North Am. 2018;102:135–48. PubMed PMID: 29156182.

(Review of the pharmacotherapy of obesity focusing upon the 6 most commonly used medications, discusses the common side effects of lorcaserin including headache, dizziness, fatigue, nausea, dry mouth and constipation, but does not discuss hepatotoxicity).

Patel DK, Stanford FC. Safety and tolerability of new-generation anti-obesity medications: a narrative review. Postgrad Med. 2018;130:173–82. PubMed PMID: 29388462.

(Review of the history of approval and indications, efficacy and long term safety of major currently available weight loss agents including orlistat, phentermine/topiramate, lorcaserin, liraglutide and naltrexone/bupropion; does not discuss hepatotoxicity).

FDA. Information on Lorcaserin. 2020. Available at: https://www.fda.gov/media/135189/download

(FDA letter requesting the voluntary withdrawal of lorcaserin because of a secondary analysis of the CAMELLIA-TIMI trial of lorcaserin vs placebo conducted between 2014 and 2018 in 12,000 adults followed for a median of 3.3 years that showed no differences in adverse cardiovascular outcomes, but an imbalance in incidence of cancers arising in 462 patients on lorcaserin [7.7%] vs 427 [7.1%] on placebo with imbalance with several specific forms including pancreatic, colorectal and lung [liver cancer not mentioned]).

Tak YJ, Lee SY. Anti-obesity drugs: long-term efficacy and safety: an updated review. World J Mens Health. 2020 Mar 9. Epub ahead of print. PubMed PMID: 32202085.

(Review of currently available agents for long term therapy of obesity with specific discussion of mechanism of action, dosing regimen, efficacy and safety, mentions that phentermine/topiramate has the highest rates of weight loss compared to other agents, but also has a high rate of discontinuation because of side effects such as insomnia, paresthesia, dizziness, dry mouth, dysgeusia and constipation and has embryo-fetal toxicity; no mention of ALT elevations or hepatotoxicity).