

HİPERLİPİDEMİDE FARMAKOLOJİK TEDAVİ AJANLARI

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Giriş

Hiperlipidemi tedavisinde yaygın olarak kullanılan başlıca ajanlar statinler, fibrik asit türevleri, ezetimib ve henüz yaygın olmasa da yeni nesil umut verici bir ajan olan PCSK9 inhibitörleridir. Bu bölümde bu sınıflar ve sınıfların alt üyeleri detaylı olarak anlatılmaktadır. Safra asidi bağlayıcıları, nikotinik asit ve probukol gibi ajanlar ise zayıf etkinlik ve yüksek yan etki profili nedeniyle çok daha nadir olarak kullanılan ajanlardır ve bu bölümde bu ajanlara yer verilmemiştir.

Statinler

Hiperlipidemi tedavisinde en etkili ve yaygın kullanılan ajanlar statinlerdir. Statinler Aseti-koenzim-A dan kolesterol yapım aşamasındaki basamaklardan biri olan HMG (hidroksimetil glutaril)-Co-A---Mevalonat basamağındaki dönüşümü sağlayan HMG Co-A redüktaz enzimini

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Kaynaklar

1. Rosenson RS, Baker SK, Jacobson TA, et. al. The National Lipid Association's Muscle Safety Expert Panel. An assessment by the Statin Muscle Safety Task Force: 2014 update. *J Clin Lipidol.* 2014 May-Jun;8(3 Suppl):S58-71. doi: 10.1016/j.jacl.2014.03.004. PMID: 24793443.
2. Kashani A, Phillips CO, Foody JM, et. al. Risks associated with statin therapy: a systematic overview of randomized clinical trials. *Circulation.* 2006 Dec 19;114(25):2788-97. doi: 10.1161/CIRCULATIONAHA.106.624890. Epub 2006 Dec 11. PMID: 17159064.
3. Vidt DG, Cressman MD, Harris S, et. al. Rosuvastatin-induced arrest in progression of renal disease. *Cardiology.* 2004;102(1):52-60. doi: 10.1159/000077704. Epub 2004 Apr 2. PMID: 15073451.
4. Wagstaff LR, Mitton MW, Arvik BM, et. al. Statin-associated memory loss: analysis of 60 case reports and review of the literature. *Pharmacotherapy.* 2003 Jul;23(7):871-80. doi: 10.1592/phco.23.7.871.32720. PMID: 12885101.
5. Collins R, Reith C, Emberson J, et. al. Interpretation of the evidence for the efficacy and safety of statin therapy. *Lancet.* 2016 Nov 19;388(10059):2532-2561. doi: 10.1016/S0140-6736(16)31357-5. Epub 2016 Sep 8. Erratum in: *Lancet.* 2017 Feb 11;389(10069):602. PMID: 27616593.
6. Carter AA, Gomes T, Camacho X, et. al. Risk of incident diabetes among patients treated with statins: population based study. *BMJ.* 2013 May 23;346:f2610. doi: 10.1136/bmj.f2610. Erratum in: *BMJ.* 2013;347:f4356. PMID: 23704171; PMCID: PMC3662830.
7. Dale KM, Coleman CI, Henyan NN, et. al. Statins and cancer risk: a meta-analysis. *JAMA.* 2006 Jan 4;295(1):74-80. doi: 10.1001/jama.295.1.74. PMID: 16391219.
8. Chalasani N, Aljadhey H, Kesterson J, et. al. Patients with elevated liver enzymes are not at higher risk for statin hepatotoxicity. *Gastroenterology.* 2004 May;126(5):1287-92. doi: 10.1053/j.gastro.2004.02.015. PMID: 15131789.
9. Uptodate (2021). Statins: Actions, side effects, and administration. (22.3.2021 tarihinde, https://www.uptodate.com/contents/statins-actions-side-effects-and-administration?search=atorvastatin&source=search_result&selectedTitle=3~133&usage_type=default&display_rank=1, adresinden ulaşılmıştır.)
10. Kasiske BL, Wanner C, O'Neill WC; National Lipid Association Statin Safety Task Force Kidney Expert Panel. An assessment of statin safety by nephrologists. *Am J Cardiol.* 2006 Apr 17;97(8A):82C-85C. doi: 10.1016/j.amjcard.2005.12.015. Epub 2006 Feb 9. PMID: 16581334.
11. Jones PH, Davidson MH, Stein EA, et. al. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR* Trial). *Am J Cardiol.* 2003 Jul 15;92(2):152-60. doi: 10.1016/s0002-9149(03)00530-7. PMID: 12860216.
12. Catapano AL. Pitavastatin - pharmacological profile from early phase studies. *Atheroscler Suppl.* 2010;11(3):3-7. doi:10.1016/S1567-5688(10)71063-1
13. Corsini A, Ceska R. Drug-drug interactions with statins: will pitavastatin overcome the statins' Achilles' heel?. *Curr Med Res Opin.* 2011;27(8):1551-1562. doi:10.1185/03007995.2011.589433
14. Vallejo-Vaz AJ, Kondapally Seshasai SR, Kurogi K, et al. Effect of pitavastatin on glucose, HbA1c and incident diabetes: A meta-analysis of randomized controlled clinical trials in individuals without diabetes. *Atherosclerosis.* 2015;241(2):409-418. doi:10.1016/j.atherosclerosis.2015.06.001
15. Mulder AB, van Lijf HJ, Bon MA, et. al. Association of polymorphism in the cytochrome CYP2D6 and the efficacy and tolerability of simvastatin. *Clin Pharmacol Ther.* 2001 Dec;70(6):546-51. doi: 10.1067/mcp.2001.120251. PMID: 11753271.

16. Antoniou T, Macdonald EM, Yao Z, et. al. Association between statin use and ischemic stroke or major hemorrhage in patients taking dabigatran for atrial fibrillation. *CMAJ*. 2017 Jan 9;189(1):E4-E10. doi: 10.1503/cmaj.160303. Epub 2016 Nov 21. PMID: 28246253; PMCID: PMC5224945.
17. Hippisley-Cox J, Coupland C. Unintended effects of statins in men and women in England and Wales: population based cohort study using the QResearch database. *BMJ*. 2010 May 20;340:c2197. doi: 10.1136/bmj.c2197. PMID: 20488911; PMCID: PMC2874131.
18. Sidhu G, Tripp J. Fenofibrate. 2020 Jun 25. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. PMID: 32644645.
19. Uptodate (2021) Fenofibrate, Drug information. (23.3.2021 tarihinde, https://www.uptodate.com/contents/fenofibrate-drug-information?search=fenofibrate&source=panel_search_result&selectedTitle=1~43&usage_type=panel&kp_tab=drug_general&display_rank=1#F22370307, adresinden ulaşılmıştır.)
20. Quintanilla Rodriguez BS, Correa R. Gemfibrozil. 2020 Oct 12. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. PMID: 31424850.
21. Uptodate (2021) Gemfibrozil, Drug information. (23.3.2021 tarihinde, https://www.uptodate.com/contents/gemfibrozil-drug-information?search=gemfibrozil&source=panel_search_result&selectedTitle=1~61&usage_type=panel&kp_tab=drug_general&display_rank=1#F175693, adresinden ulaşılmıştır.)
22. Uptodate (2021) Low density lipoprotein cholesterol lowering with drugs other than statins and PCSK9 inhibitors. (25.3.2021 tarihinde, https://www.uptodate.com/contents/low-density-lipoprotein-cholesterol-lowering-with-drugs-other-than-statins-and-pcsk9-inhibitors?search=ezetimibe&source=search_result&selectedTitle=3~57&usage_type=default&display_rank=1, adresinden ulaşılmıştır.)
23. Uptodate (2021) Low density lipoprotein cholesterol lowering with drugs other than statins and PCSK9 inhibitors. (25.3.2021 tarihinde, https://www.uptodate.com/contents/low-density-lipoprotein-cholesterol-lowering-with-drugs-other-than-statins-and-pcsk9-inhibitors?search=ezetimibe&source=search_result&selectedTitle=3~57&usage_type=default&display_rank=1, adresinden ulaşılmıştır.)
24. Navarese EP, Kolodziejczak M, Schulze V, et. al. Effects of Proprotein Convertase Subtilisin/Kexin Type 9 Antibodies in Adults With Hypercholesterolemia: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2015 Jul 7;163(1):40-51. doi: 10.7326/M14-2957. PMID: 25915661.
25. Uptodate (2021) PCSK9 inhibitors: Pharmacology, adverse effects, and use. (25.3.2021 tarihinde, https://www.uptodate.com/contents/pcsk9-inhibitors-pharmacology-adverse-effects-and-use?search=pcsk9%20inhibitors&source=search_result&selectedTitle=2~31&usage_type=default&display_rank=1, adresinden ulaşılmıştır.)
26. Uptodate (2021) Evolcumab: Drug information. (25.3.2021 tarihinde, https://www.uptodate.com/contents/evolcumab-drug-information?search=pcsk9%20inhibitors&topic-Ref=106888&source=see_link, adresinden ulaşılmıştır.)
27. Uptodate (2021) Alirocumab: Drug information. (25.3.2021 tarihinde, https://www.uptodate.com/contents/alirocumab-drug-information?search=pcsk9%20inhibitors&topic-Ref=106888&source=see_link, adresinden ulaşılmıştır.)