Loratadine

Essential medicine status ✓

Section: 3. Antiallergics and medicines used in anaphylaxis

EMLc | ATC codes: R06AX13

Indication	Allergic or hypersensitivity conditions of unspecified type ICD11 code: 4A8Z
INN	Loratadine
Medicine type	Chemical agent
List type	Core *there may be a role for sedating antihistamines for limited indications (EMLc)
Formulations	Oral > Liquid: 1 mg per mL oral liquid Oral > Solid: 10 mg tablet
EML status history	First added in 2013 (TRS 985)
Sex	All
Age	Also recommended for children
Therapeutic equivalence	Medicines within the same pharmacological class can be used
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Loratadine
DrugBank	Loratadine

Summary of evidence and Expert Committee recommendations

The 18th meeting of the Expert Committee (2011) requested a comparative review of the safety and efficacy of chlorphenamine (which is listed in both the EML and the EMLc) and diphenhydramine, to provide information regarding the possible inclusion of diphenhydramine. Given the possible favourable clinical effects and side-effect profile of second-generation systemic antihistamines (SGAHs), three over-the-counter SGAHs (cetirizine, loratadine and fexofenadine) were also reviewed and compared with chlorphenamine and diphenhydramine (which are first-generation antihistamines, or FGAHs). The use in children and elderly people was specifically considered in the review, and the national essential medicines lists of 15 countries were checked for the availability of SGAHs. Evidence of the efficacy and safety of these five antihistamines in allergic rhinitis and urticaria was provided. Overall, there was a lack of high-quality data to compare the two FGAHs. The review found no randomized controlled trials that satisfactorily compared efficacy and safety of chlorphenamine and diphenhydramine for use in allergic rhinitis or urticarial conditions. The evidence from five randomized controlled trials comparing them with placebo or other medicines show similar effectiveness and side-effect profiles of the two medications for both allergic rhinitis and urticaria (1). Fifteen randomized controlled trials showed similar efficacy of FGAHs and SGAHs in treating allergic rhinitis, with significantly fewer side-effects (in frequency and severity) with SGAHs. For treatment of urticaria, nine randomized controlled trials showed similar efficacy between FGAHs and SGAHs, with lower incidence of side-effects with SGAHs. Six randomized controlled trials, three retrospective studies and one systematic review provided evidence establishing the safety profile of SGAHs as superior to that of FGAHs (2). Significant sedation and psychomotor impairment were observed with FGAHs compared with SGAHs. Due to the anticholinergic side-effects and the reduced drug clearance in elderly people, the use of FGAHs in this population is strongly discouraged. Evidence from five randomized controlled trials, two pharmacokinetic studies, a systematic review and from guidelines, recommends against the use of FGAHs in infants and children, due to risk of sedation and death (1, 3). The review provided a detailed discussion on the use of antihistamines in anaphylaxis and concluded that there was no strong evidence to recommend the use of antihistamines for this indication. The review also found that the monthly treatment cost of loratadine was lower than that of chlorphenamine and that

53% of the 15 low- and middle-income countries surveyed already had an SGAH on their respective national essential medicines lists. The Expert Committee further considered the evidence on safety. The FGAHs are referred to as “sedating” and the SGAHs as “non-sedating”. This broad distinction is based on two primary differences between these medicine classes: (1) SGAHs are more specific to H-1 receptors than are FGAHs and (2) FGAHs are able to cross the blood–brain barrier while the SGAHs are not. These differences in receptor specificity and liphophilicity cause FGAHs to display significant central nervous system, cardiovascular system and gastrointestinal system side-effects. These effects were seen during clinical trials. Based on considerations of inferior safety, especially in children and elderly people, and the equal efficacy of SGAHs and FGAHs, the Expert Committee decided to delete chlorphenamine from the EML and EMLc, and to recommend the addition of loratadine tablets (10 mg) and oral liquid (1 mg/mL) to the EML and EMLc with a square box. A lower age limit of 2 years for loratadine may be applied, although use below this age has occurred in some settings (4-9).

References: 1. Simons FE. Advances in H1-antihistamines. N Engl J Med. 2004;351(21):2203-17. http://dx.doi. org/10.1056/NEJMra033121 PMID:15548781 2. Yanai K, Rogala B, Chugh K, Paraskakis E, Pampura AN, Boev R. Safety considerations in the management of allergic diseases: focus on antihistamines. Curr Med Res Opin. 2012;28(4):623-42. http://dx.doi.org/10.1185/03007995.2012.672405 PMID:22455874 3. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al.; World Health Organization; GA(2)LEN; AllerGen. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008;63 Suppl 86:8-160. http://dx.doi.org/10.1111/j.1398-9995.2007.01620.x PMID:18331513 4. Kavosh ER, Khan DA. Second-generation H1-antihistamines in chronic urticaria: an evidencebased review. Am J Clin Dermatol. 2011;12(6):361-76. http://dx.doi.org/10.2165/11591130- 000000000-00000 PMID:21967114 5. Sheikh A, ten Broek Vm, Brown SGA, Simons FER. H1-antihistamines for the treatment of anaphylaxis with and without shock. Cochrane Database Syst Rev. 2007;(1):CD006160. http:// dx.doi.org/10.1002/14651858.CD006160.pub2 PMID:17253584 6. Simons FER, Ardusso LRF, Bilo MB, El-Gamal YM, Ledford DK, Ring J, et al.; World Allergy Organization. World Allergy Organization anaphylaxis guidelines: summary. J Allergy Clin Immunol. 2011;127(3):587, e22. http://dx.doi.org/10.1016/j.jaci.2011.01.038 PMID:21377030 7. Holgate ST, Canonica GW, Simons FER, Taglialatela M, Tharp M, Timmerman H, et al.; Consensus Group on New-Generation Antihistamines. Consensus Group on New-Generation Antihistamines (CONGA): present status and recommendations. Clin Exp Allergy. 2003;33(9):1305-24. http://dx.doi.org/10.1046/j.1365-2222.2003.01769.x PMID:12956754 8. Pawankar R, Canonica GW, Holgate ST, Lockey RF, editors. WAO white book on allergy. Milwaukee (WI): World Allergy Organization; 2011. 9. Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. BMJ. 1998;317(7173):1624-9. http://dx.doi.org/10.1136/bmj.317.7173.1624 PMID:9848901