Desmopressin

Essential medicine status ✓

Section: 10. Medicines affecting the blood > 10.2. Medicines affecting coagulation

EMLc | ATC codes: H01BA02

Indication	Haemophilia A ICD11 code: 3B10.0
INN	Desmopressin
Medicine type	Chemical agent
List type	Complementary (EML) (EMLc)
Formulations	Parenteral > General injections > IV: 4 µg per mL in 1 mL ampoule (acetate) Local > Nasal > Spray: 10 µg per dose (acetate)
EML status history	First added in 1991 (TRS 825) Changed in 1993 (TRS 850) Removed in 2003 (TRS 920) Added in 2015 (TRS 994)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Desmopressin
DrugBank	Desmopressin

Summary of evidence and Expert Committee recommendations

An application was submitted on behalf of the World Federation of Hemophilia for the addition of desmopressin injection and nasal spray to the Model List of Essential Medicines for the treatment of select patients with type I von Willebrand disease, haemophilia A and other rare bleeding disorders. Reviews of the application were prepared by two members of the Expert Committee. Numerous public comments were received in support of the application, and are available on the WHO website. Haemophilia A is a hereditary X-linked disorder characterised by quantitative or qualitative deficiency of coagulation factor VIII (1). Haemophilia A is the most common type of haemophilia and mainly affects boys and men. It is a rare condition, affecting approximately 1 in 10 000 males (2). In addition, around 10% of female carriers of haemophilia are also at risk of bleeding. Von Willebrand disease (VWD) is the most common hereditary bleeding disorder, with an estimated prevalence of 0.6–1.3% and affecting men and women with equal frequency (3). It is caused by deficiency or dysfunction of von Willebrand factor (a coagulation factor) and is classified into three major types, which are specifically treated: partial quantitative deficiency (type 1); qualitative deficiency (type 2, with four variants – 2A, 2B, 2M and 2N); and total deficiency (type 3) (4). Acquired VWD comprises defects in von Willebrand factor concentration, structure or function arising from medical disorders or treatments. Desmopressin (or DDAVP) is an antidiuretic hormone analogue and a specific vasopressin V2 receptor agonist. It increases renal tubular reabsorption of water and is used as first-line treatment in pituitary diabetes insipidus. Desmopressin also increases factor VIII and von Willebrand factor (VWF) coagulation activity and is therefore used to control bleeding in certain types of bleeding disease including haemophilia A and type 1 VWD. In support of addition of desmopressin to the EML, the application included guidelines of the World Federation of Hemophilia (5) the European Society of Anaesthesiology (855), the British Committee for Standards in Haematology (6) and the National Heart, Lung and Blood Institute (3). The application also included reviews of the available studies in relation to the efficacy and safety of desmopressin (7-9). The Expert Committee noted that clinical experience with desmopressin is based largely

on anecdotal reports and small case series, but that the number of prospective and retrospective reports is growing (7). The World Federation of Hemophilia guidelines note that desmopressin may be the treatment of choice for patients with mild or moderate haemophilia A, when factor VIII can be raised to an appropriate therapeutic level, as it avoids the expense and potential hazards of using a clotting factor concentrate (5). The guidelines also note that desmopressin is particularly useful in the treatment or prevention of bleeding in carriers of haemophilia. Desmopressin does not affect factor IX levels and is of no value in haemophilia B. According to the United Kingdom Haemophilia Centre Doctors' Organisation guidelines, desmopressin is often effective in type 1 VWD where increasing VWF levels by a factor of 2–5 is sufficient for haemostasis (10). In types 2A and 2M VWD, desmopressin increases the levels of the abnormal VWF and has a variable clinical effect. The guidelines emphasize that the use of desmopressin in type 2B VWD is controversial: it has been said to be contraindicated as the release of the abnormal VWF may induce platelet aggregation and thrombocytopenia. However, it has been argued that the thrombocytopenia may be an in vitro artefact and that desmopressin is safe and may be clinically effective in type 2B disease. According to clinical studies, desmopressin has no therapeutic use in type 3 VWD. Given the significant differences between individuals in response to desmopressin, each patient's response should be tested before therapeutic use of the drug. An individual patient's responses are usually consistent, so that patients can be labelled as responsive or not. Compared with IV administration, responses to intranasally administered desmopressin are more variable and therefore less predictable. Desmopressin may also be useful in controlling bleeding and reducing the prolongation of bleeding time associated with disorders of haemostasis, including some congenital platelet disorders. In some settings, it is used as home medication for patients with inherited bleeding disorders (9). With regard to safety, desmopressin is not licensed for use in pregnancy, but there is evidence that it can be safely used during delivery and in the postpartum period in an uncomplicated pregnancy. However, its use should be avoided in pre-eclampsia and eclampsia because of the already high levels of VWF. The major advantages of desmopressin over plasma products are the much lower cost and the absence of any risk of transmission of viral infections (10). The most common side-effects of desmopressin are tachycardia, flushing and headache, which are generally mild (9). As desmopressin is a potent antidiuretic agent, it can cause hyponatraemia and even seizures in patients receiving generous amounts of hypotonic intravenous or oral fluids, necessitating fluid restriction during desmopressin treatment. The antidiuretic effect of desmopressin is much greater when it is administered intravenously than when it is given intranasally or subcutaneously. The Expert Committee considered that the available evidence supports the efficacy and safety of desmopressin for prevention and treatment of bleeding in selected patients with haemophilia A, VWD and other congenital bleeding disorders. For selected patients, desmopressin offers a safer and more affordable alternative to plasma products and fresh blood components. The Committee noted that use of desmopressin has led to a substantial reduction in the use of blood products for the prevention and treatment of bleeding episodes and is recommended in national and international guidelines. The Committee also noted that the use of desmopressin requires access to specialist and laboratory services. While noting that the evidence of efficacy and safety in most clinical settings is largely empirical, the Expert Committee acknowledged that desmopressin is an important medicine in the haemostatic armamentarium for patients with bleeding disorders, particularly in view of the ease of administration (notably the intranasal formulation), low cost and the potential for avoidance of blood derivatives. The Expert Committee therefore recommended the inclusion of desmopressin in the complementary list of the EML and EMLc. References: 1. Boehlen F, Graf L, Berntorp E. Outcome measures in haemophilia: a systematic review. Eur J Haematol Suppl. 2014;76:2-15. 2. Haemophilia A [website]. London: The Haemophilia Society. Available from: http://www.haemophilia.org.uk/bleeding_disorders/bleeding_disorders/haemophilia_a. 3. Nichols WL, Hultin MB, James AH, Manco-Johnson MJ, Montgomery RR, Ortel TL, et al. von Willebrand disease (VWD): evidence-based diagnosis and management guidelines, the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel report (USA). Haemophilia. 2008;14(2):171-232. 4. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol. 2013;30(6):270-382. 5. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, et al. Guidelines for the management of hemophilia. Haemophilia. 2013;19(1):e1-47. 6. Laffan MA, Lester W, O'Donnell JS, Will A, Tait RC, Goodeve A, et al. The diagnosis and management of von Willebrand disease: a United Kingdom Haemophilia Centre Doctors Organization guideline approved by the British Committee for Standards in Haematology. Br J Haematol. 2014;167(4):453-65. 7. Leissinger C, Carcao M, Gill JC, Journeycake J, Singleton T, Valentino L. Desmopressin (DDAVP) in the management of patients with congenital bleeding disorders. Haemophilia. 2014;20(2):158-67. 8. Mannucci PM. Desmopressin (DDAVP) in the treatment of bleeding disorders: the first 20 years. Blood. 1997;90(7):2515-21. 9. Ozgonenel B, Rajpurkar M, Lusher JM. How do you treat bleeding disorders with desmopressin? Postgrad Med J. 2007;83(977):159-63. 10. Pasi KJ, Collins PW, Keeling DM, Brown SA, Cumming AM, Dolan GC, et al. Management of von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors' Organization. Haemophilia.

2004;10(3):218-31.