1. Introduction and Who Guideline applies to

This guideline is for use by those managing patients with bleeding disorders (haemophilia A, Von Willebrand disease, platelet function disorders).

2. Guideline Standards and Procedures

Introduction

Desmopressin (1 deamino-8-D-arginine vasopressin, also known as DDAVP) is a synthetic analogue of vasopressin that boost plasma levels of Factor VIII and Von Willebrand factor.

Indications:

1. Mild or moderate haemophilia A
2. Carriers of Haemophilia A with low Factor VIII levels
3. Type 1 Von Willebrand disease
4. Some platelet function disorders (not licensed but effective)- with the exception of well-defined conditions such as Glanzmann thrombasthaenia and Bernard Soulier syndrome

DDAVP is used in above conditions when there is need for rise in FVIII or VWF activity levels to appropriate therapeutic concentration. This has an advantage of avoiding the expenses and potential hazards of using clotting factor concentrate including risk of FVIII inhibitor development.

Note: DDAVP does not affect Factor IX levels and is of no value in haemophilia B.

Contraindications:

1. Contraindicated in children aged under 2 years of age due to risk of hyponatraemia and seizures
2. Type 3 VWD- no use
3. Uncontrolled hypertension
4. Ischemic heart disease (risk of thrombosis) and cardiac failure; treatment with diuretics
5. Cerebrovascular disease
6. Habitual and psychogenic polydipsia
7. Pre- eclampsia and eclampsia

Cautions:

1. Pregnancy and lactation- not licensed but has been used with caution
2. Aged more than 65 years
3. Type 2 B VWD - Use of DDAVP is controversial as release of abnormal VWF may induce platelet aggregation and thrombocytopenia

4. Type 2N VWD and Vincenza variant – short half- life of FVIII response should be taken into account
5. Type 2 A and 2 M, it increases the levels if abnormal VWF and has variable clinical effect.

DDAVP preparations include

- 4 microgram/ ml for Intravenous use
- 15 microgram/ml for intravenous and subcutaneous use (Octim)
- 150 microgram per metered dose nasal spray

At UHL, DDAVP for bleeding disorder patients is mostly administered through subcutaneous route.

Dose and response:

Intravenous or subcutaneous preparation: A single dose of 0.3 microgram/kg body weight can be expected to boost FVIII level 3- 6-fold.

Intranasal preparation: 150 microgram in patients with a body weight of <50 kg (one spray into one nostril) and 300 microgram in patients with a body weight of >50 kg (one spray into each nostril) at the time of bleeding or half an hour before surgery

The peak response after Intravenous administration is achieved at 60 minutes and at 90-120 minutes after subcutaneous/intranasal administration.

Tranexamic acid (orally or intra- venously) is usually used alongside desmopressin.

Route of administration

Intravenous: Desmopressin has in the past been given by slow intravenous infusion at a dose of 0.3 micrograms/kg over 20-30 minutes. This requires IV access and supervision by a trained member of staff. The administration of a more potent formulation by the subcutaneous or intra- nasal route is now more usually used.

Sub-cutaneous: The subcutaneous dose of 0.3 micrograms/kg has a comparable effect with the same IV dose, and has the advantages of not requiring IV access, and being suitable for home treatment.

Intranasal: Currently nasal preparation is not available

Useful for patients requiring frequent and regular doses of s/c desmopressin. Examples include

- Women with von Willebrand's disease or women who are carriers for Haemophilia A and have low levels of FVIII who have menorrhagia unresponsive to hormonal or other therapies.
- Patients with mild haemophilia or von Willebrand's disease who have frequent bleeding episodes unresponsive to local therapies

These patients may benefit from an alternative preparation that does not need to be given subcutaneously: nasal desmopressin (Octim® Nasal Spray). This preparation has the same licensed indications as the subcutaneous preparation. It has the advantage that frequent s/c injections can be avoided. The preparation does not require refrigeration and so is handier and more portable for patients who need to use it frequently.

Octim® nasal spray is contra-indicated in children (and adults) under 35kg in weight because of the metered dose.

Side effects:

- Precautions must be taken to avoid fluid overload. Restriction of oral fluids to 1.5L during the 24 hours following administration is recommended (see weight based guidance below)
- Headache, nausea and stomach pain may occur post treatment.
- Decreased blood pressure and facial flushing can occur after IV administration. This may be less of a problem after s/c administration.

Frequency of administration:

- Children should generally not be given DDAVP more than once per day.
- In adults under close supervision, twice daily dosing may be considered. With subsequent dosing, therapeutic response decreases (tachyphylaxis) and risk of complications rises.
- In general, DDAVP should not be used for more than 3 consecutive days

Practical guidance for the administration of desmopressin

Treatment with subcutaneous Desmopressin in hospital:

1) Baseline blood tests: FBC, U&E, Factor VIII level, von Willebrand screen, PFA (where appropriate).

2) Take blood pressure and pulse pre-injection.

3) Desmopressin dose is 0.3 micrograms/kg of body weight by subcutaneous injection.

4) Take blood pressure and pulse 30 min post injection after initial 3 uses. Consider these assessments for subsequent doses, depending on patient and clinical circumstances.

5) Follow up blood samples (Factor VIII level, von Willebrand screen) 90-120 minutes post injection, when used as part of a "DDAVP trial/challenge".

6) For Desmopressin trials further samples may be taken at 4 hours, and sometimes 24 hours post injection to assess duration of response.

7) See fluid restriction guidance in appendix 1.

Home treatment with subcutaneous Desmopressin:

1) An adequate therapeutic response to Desmopressin must have been documented following a supervised trial in hospital.

2) The supervising clinician must agree with the patient/ carer, clear indications for home treatment with Desmopressin.

3) The patient will be instructed in storage, preparation, and administration of Desmopressin by Haemophilia unit staff (see Appendix 1).

4) Supplies of Desmopressin will be prescribed by Haemophilia Unit staff and obtained

from the pharmacy.

5) The patient will keep a record of administration of Desmopressin

6) The patient's usage of Desmopressin will regularly be reviewed by the supervising clinician.

7) The patient will have 24 hour access to advice from the haemophilia team/haematologist on call.

8) See fluid restriction guidance in **appendix 1**

Home treatment with nasal Desmopressin:

1) An adequate therapeutic response to desmopressin must have been documented following a supervised trial in hospital.

2) The supervising clinician must agree clear indications with the patient for home treatment with desmopressin.

3) There must be documentation in the patient's notes that frequent treatment is required (see above).

4) The patient will be instructed in the administration of nasal desmopressin by Haemophilia unit staff.

5) Supplies of desmopressin will be prescribed by Haemophilia Unit staff and obtained from the pharmacy.

6) The patient will keep a record of administration of desmopressin.

7) The patient's usage of desmopressin will regularly be reviewed by the supervising clinician.

8) The patient will have 24hour access to advice from the haemophilia team/haematologist on call.

9) Parents of children will be given specific instructions about fluid restriction post desmopressin.

3. Education and Training

None

4.Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
No active monitoring	Review of relevant DATIX	SM	As required	

5. Supporting References (maximum of 3):

1. WFH guidelines for the Management of Haemophilia, 3rd edition 2020: Alok Srivastava1 | Elena Santagostino2 | Alison Dougall3 | Steve Kitchen4 | Megan Sutherland5 | Steven W. Pipe6 | Manuel Carcao7 | Johnny Mahlangu8 | Margaret V. Ragni9 | Jerzy Windyga10 | Adolfo Llinás11 | Nicholas J. Goddard12 | Richa Mohan13 | Pradeep M. Poonnoose14 | Brian M. Feldman15 | Sandra Zelman Lewis16 | H. Marijke van den Berg17 | Glenn F. Pierce18
2. ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease: Nathan T. Connell,1,* Veronica H. Flood,2,* Romina Brignardello-Petersen,3 Rezan Abdul-Kadir,4 Alice Arapshian,5 Susie Couper,6 Jean M. Grow,7 Peter Kouides,8 Michael Laffan,9 Michelle Lavin,10 Frank W. G. Leebeek,11 Sarah H. O'Brien,12 Margareth C. Ozelo,13 Alberto Tosetto,14 Angela C. Weyand,15 Paula D. James,16 Mohamad A. Kalot,17 Nedaa Husainat,17 and Reem A. Mustafa17
3. 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 Mike A. Laffan, Will Lester, James S. O'Donnell, Andrew Will, Robert Campbell Tait, Anne Goodeve, Carolyn M. Millar and David M. Keeling. B J Haem 2014.

Key Words

DDAVP, desmopressin, haemophilia, von Willebrand disease

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Dr Sandhya Munireddy and Dr Styliani Salta Consultant in Haemostasis and Thrombosis	**Executive Lead**
Details of Changes made during review: **1. References reduced to 3** **2. Different types of VWD included under Indications, cautions and contraindication heading** **3. Dosing of intranasal spray included under dosing heading as opposed to previous route of administration**	

NB: Paper copies of this document may not be most recent version. The definitive version is held in the trust's Policies and Guidelines Library

Appendix 1:

Approximate fluid restriction post DDAVP:

Weight (kg)	Maximum fluid in first 0-12 hours (mls)	Maximum fluid in next 12 hours (i.e. 12-24 hours post DDAVP)
10	330	470
20	470	710
30	560	830
40	620	950
50	710	1065
60	800	1180
70	860	1300
80	950	1420
90	1035	1540
100	1100	1660

Neff et al, Current controversies in the diagnosis and management of Von Willebrand disease 2014, ASH Education program. Adapted from US Fluid oz to ml.