Desmopressin (DDAVP) for Bleeding Disorders UHL Haematology Guideline	University Hospitals of Leicester NHS NHS Trust **Trust Reference Number: C7/2020**

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, a synthetic vasopressin analogue, increases endogenous Factor VIII (FVIII) and von Willebrand factor (VWF) by releasing both from their storage pools. Baseline levels may be raised by 2-5 times with a peak level achieved after iv administration at 60 minutes and at 90-120 minutes after sub-cutaneous or intra-nasal administration. It is the treatment of choice, where sufficiently effective, for bleeding episodes and surgical prophylaxis in mild haemophilia A and some types of von Willebrand's disease to avoid the use of clotting factor concentrates, and potential exposure to blood products and animal proteins. It has also been shown to be effective in some platelet function disorders, although not currently licensed for use in these circumstances. High dose desmopressin 15 micrograms/ml (Octim®) is licensed for subcutaneous and intra-nasal administration in patients with mild and moderate haemophilia or von Willebrand's disease undergoing surgery or following trauma. It is recommended (although not licensed) for the treatment of patients with mild platelet function disorders. Tranexamic acid (orally or intra-venously) is usually used alongside desmopressin.

IMPORTANT: Desmopressin (all preparations) is absolutely contra-indicated in children under 2 years in age because of the risk of hypernatraemia and seizures.

Use of desmopressin in mild haemophilia A

Desmopressin is useful for treating mild haemophilia A and carriers of haemophilia with low Factor VIII levels providing an adequate response has been demonstrated.

Use of desmopressin in von Willebrand disease

Desmopressin is most likely to be useful in patients with Type 1 VWD. It is not useful in Type 3 VWD. In types 2A and 2M VWD, desmopressin increases the levels of the abnormal VWF and has a variable clinical effect. Desmopressin can be used in type 2N VWD but the short half-life of the FVIII response should be taken into account. The same applies to the Vicenza variant of VWD. 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. The UKHCDO guideline for the treatment of von Willebrand disease states that 'although no harmful effects have been reported, the therapeutic response is usually poor and desmopressin is not recommended for type 2B VWD.'

Use of desmopressin in platelet function disorders

Platelet function disorders (with the exception of well-defined conditions such as Glanzmann thrombasthaenia and Bernard Soulier syndrome) are a heterogeneous group of poorly characterised conditions. They have generally been described in individuals with mild bleeding symptoms and evidence of abnormal platelet function on laboratory testing such as platelet aggregometry and assessment of platelet nucleotides. Desmopressin has been shown to be beneficial in mild platelet functions disorders, in part at least, because of increased levels of large VWF multimers.

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. 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. The dose for adults over 50kg in weight is 300 micrograms (one 150microgram spray into each nostril) half an hour before surgery or at the time of bleeding. The dose for children is 4micrograms/kg which means that the dose of Octim for children (< 50kg) is 150 micrograms (i.e. one 150 microgram spray).

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

Contraindications to the use of Desmopressin:

- Uncontrolled Hypertension
- Ischaemic heart disease and cardiac failure; treatment with diuretics
- Cerebrovascular disease
- Habitual and psychogenic polydipsia

Cautions:

- Pregnancy and lactation
- Type 2B and 2N VWD see above
- Caution with older patients (> 75years)
- Avoid under 2 years of age

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 sc administration.

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 theses 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, 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 24 hour access to advice from the haemophilia team/haematologist on call.

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

10) See fluid restriction guidance in appendix 1.

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	RG	As required	

5. Supporting References (maximum of 3)

References

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6. Key Words

DDAVP, desmopressin, haemophilia , von Willebrand disease

CONTACT AND REVIEW DETAILS	
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Details of Changes made during review:	

Appendix 1:

Approximate fluid restritction 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.