health
Department:
Health
REPUBLIC OF SOUTH AFRICA

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RECOMMENDATIONS FOR RESTRICTED USE OF ANTI-D IMMUNOGLOBULIN

The Primary Health Care and Adult Hospital Level Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) currently recommends the use of Anti-D immunoglobulin for various indications. The supplier of Anti-D immunoglobulin however, is unable to meet the contractual obligation due to unforeseen operational delays[1]. The supplier anticipates that the supply of Anti-D immunoglobulin will resume at the end of July 2021.

There are no available therapeutic alternative agents for Anti-D immunoglobulin. Due to the current supply problems, restricted use of Anti-D immunoglobulin is recommended until supplies stabilise.

The following recommendations guide the restricted use of Anti-D immunoglobulin for indications listed in the Adult Hospital Level STGs and EML (2019) and the PHC STGs and EML (2020):

Indications in the Adult Hospital Level, 2019	Current recommendation in STGs and EML	Recommendation for restricted use
5.8.3 Mid-trimester miscarriage (from 13–22 weeks gestation)	If Rh-negative: • Anti-D immunoglobulin, IM, 100 mcg as a single dose.	Not applicable.
5.9.2 TOP: from the thirteenth week (12 weeks and 1 day) up to the twentieth week (19 weeks and 6 days)	If Rh-negative: • Anti-D immunoglobulin, IM, 100 mcg as a single dose.	Not applicable.
6.20 The Rhesus negative woman	After a termination of pregnancy (TOP), miscarriage, ectopic pregnancy or amniocentesis: • Anti-D immunoglobulin, IM, 50 mcg. After external cephalic version or potentially sensitizing event ≥20 weeks • Anti-D immunoglobulin, IM, 100 mcg. At birth, determine the Rh status of the cord blood and request a Coomb's test: Cord blood Rh negative - no treatment. Cord blood Rh positive, Coomb's negative: • Anti-D immunoglobulin, IM, 100 mcg. If a large feto-maternal transfusion is suspected: • Anti-D immunoglobulin, IM, 300 mcg for every 30 mL transfusion. ○ Maximum dose: 1 200 mcg. **AND**	**Try to avoid antenatal interventions that may cause trans-placental bleeding in the unsensitised Rh negative woman (e.g. amniocentesis, external cephalic version, cordocentesis or chorionic villus sampling).** • Do not use Anti-D immunoglobulin for TOPs in the 1st trimesters[3], when there are supply constraints.

[1] National Bioproducts Institute. Dear Healthcare Professional communication: Stock Out: Rhesugam IM (anti-D immunoglobulin), 25 May 2021.
[3] Schmidt-Hansen M, Lord J, Hawkins J, et al. Anti-D prophylaxis for rhesus D (RhD)-negative women having an abortion of a pregnancy up to 13+6 weeks' gestation: a systematic review and new NICE consensus guidelines. BMJ Sex Reprod Health. 2020 Jan 20:bmjsrh-2019-200536. https://pubmed.ncbi.nlm.nih.gov/31959599/

	Do a maternal blood Kleihauer test (consult a specialist). **Rh positive, Coomb's positive:** In these cases, the mother will also have antibodies. Do not administer anti-D immunoglobulin. **Maternal serum antibodies present[2].** Consult a specialist.	

Indications in the Primary Healthcare Level, 2020	Current recommendation in STGs and EML	Recommendation for restricted use
6.2 Miscarriage	In Rh-negative, non-sensitised women: • Anti-D immunoglobulin, IM, 50mcg preferably within 72 hours but may be given up to 7 days following management of miscarriage.	• Restrict the use of Anti-D immunoglobulin to miscarriages in the 2nd trimesters[4].
6.3.1 Management of termination of pregnancy at Primary Health Care level: gestation ≤ 12 Weeks and 0 days	**For both medical and surgical TOPs (MVA):** In Rh-negative, non-sensitised women: • Anti-D immunoglobulin, IM, 50mcg preferably within 72 hours but may be given up to 7 days following TOP.	• Do not use Anti-D immunoglobulin for TOPs in the 1st trimesters[3], when there are supply constraints.
6.5 Intrapartum care	**Rh-negative mother** Administer to Rh-negative mother, if baby is Rh-positive or baby's Rh group is unknown: • Anti-D immunoglobulin, IM, 100 mcg, preferably within 72 hours but can be given up to 7 days after delivery.	Obtain a fetal Rh status at birth in all cases – using onsite Rh test kit. <u>If the baby is Rh-positive:</u> • Administer Anti-D immunoglobulin, IM, 100 mcg, to Rh-negative mother, preferably within 72 hours but can be given up to 7 days after delivery. <u>If the baby is Rh negative:</u> • Do not administer Anti-D immunoglobulin, to the Rh-negative mother.

For other indications not listed in the STGs and EML:

- In women who are Rh negative, after delivery of the baby clamp the cord on the fetal side only. Let the placental side bleed freely. Avoid manual removal of the placenta if at all possible[5].
- Do not administer routine antenatal Anti-D immunoglobulin prophylaxis at 28 and 34 weeks to unsensitised Rh negative women[6].
- A woman with "weak D" (also known as Du-positive) should not receive Anti-D immunoglobulin[7].
- Consider omitting Anti-D immunoglobulin to unsensitised Rh negative women who undergo postpartum tubal ligation[8].

[2] Anti-D is not effective once alloimmunization to the D antigen has occurred and will not prevent a rise in maternal titer.
Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 181: Prevention of Rh D Alloimmunization. Obstet Gynecol. 2017 Aug;130(2):e57-e70. https://www.ncbi.nlm.nih.gov/pubmed/28742673

[4] The risk of transmission is greater the more advanced the pregnancy. There is insufficient data available to evaluate the practice of routine administration of anti-D in an unsensitised Rh negative mother after spontaneous miscarriage.
Karanth L, Jaafar SH, Kanagasabai S, et al. Anti-D administration after spontaneous miscarriage for preventing Rhesus alloimmunisation. Cochrane Database Syst Rev. 2013 Mar 28;(3):CD009617. https://www.ncbi.nlm.nih.gov/pubmed/2354358

[5] This may minimise the risk of trans-placental bleeding.
Cronje HS, Cilliers JBF, Pretorius MS. Clinical Obstetrics: A South African Perspective. Van Schaik Publishers; 2010. p 810.

[6] There is no difference in risk of immunisation when routine administration of Anti-D immunoglobulin at 28 and 34 weeks, compared to placebo.
McBain RD, Crowther CA, Middleton P. Anti-D administration in pregnancy for preventing Rhesus alloimmunisation. Cochrane Database Syst Rev. 2015 Sep 3;(9):CD000020. https://www.ncbi.nlm.nih.gov/pubmed/26334436

[7] *Fung Kee Fung K, Eason E, et al; Maternal-Fetal Medicine Committee, Genetics Committee. Prevention of Rh alloimmunization. J Obstet Gynaecol Can. 2003 Sep;25(9):765-73.* https://www.ncbi.nlm.nih.gov/pubmed/12970812

[8] **Ensure that the family is indeed complete, and no more children is expected. Anti-D antibodies will only be a risk in a subsequent pregnancy. Women who do not receive Anti-D immunoglobulin after sterilization/ tubal ligation should be advised that they need to check for antibodies prior to any investigations for sterilization reversal in future.**

Note: It is important to inform women suspected of sensitisation and who were not administered Anti-D immunoglobulin prophylaxis of the current supply constraints. These women require a follow-up examination that includes testing for antibodies 3 months' post-delivery, as well as prior to any future pregnancy.

Provinces and Health Care Facilities are requested to distribute and communicate this information in consultation with the Pharmaceutical and Therapeutics Committees.

The National Department of Health will provide updated communication as soon as the supply of Anti-D immunoglobulin is confirmed by National Bioproducts Institute.

Queries may be submitted to:

Clinical queries
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E-mail: SAEDP@health.gov.za

Supply queries
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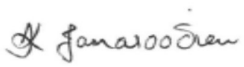
Kind regards



MS K JAMALOODIEN
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