

**National Institute for Health
and Care Excellence**

Ectopic pregnancy and miscarriage

**Technical appendices for evidence
review E on anti-D rhesus prophylaxis**

NICE guideline NG126

Technical data underpinning evidence review [E]

February 2025

Draft for consultation

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1 **Appendix A - Review protocols**

2 **Review protocol for effectiveness review of Should anti-D rhesus 3 prophylaxis be given to women with a threatened miscarriage, 4 miscarriage or ectopic pregnancy in the first trimester?**

5 The review protocol was pre-registered. The full protocol can be found at
6 <https://www.crd.york.ac.uk/PROSPERO/view/CRD420251102207>.

7 **Economic review protocol**

8

ID	Field	Content
1.	Review title	Should anti-D immunoglobulin prophylaxis be given to women with a threatened miscarriage, miscarriage or ectopic pregnancy in the first trimester?
2.	Objective	To identify economic studies relevant for the review question
3.	Inclusion criteria	<ul style="list-style-type: none">• Populations, interventions and comparators must be as specified in the effectiveness review protocol.• Relevant comparative economic study design: cost–utility analysis, cost–effectiveness analysis, cost–consequences analysis, comparative cost analysis.• Decision analytic model-based or within-trial economic analyses.• OECD countries (except USA).• Healthcare and personal social services cost perspective.• Non-comparative costing studies (such as econometric, efficiency, simulation, micro-costing and resource use, and time-series).• Studies published from 2012 – this cut off has been applied to align with the effectiveness review and to restrict the review to more recent studies which will have more applicable resource use and costs. <p>High-quality studies in line with the NICE reference case (recent UK NHS/PSS cost-utility analyses using the QALY as the measure of outcome) are the most applicable to NICE decision making. Not all studies meeting the inclusion criteria will therefore necessarily be used in decision-making - see Review strategy below for details.</p>
4.	Exclusion criteria	<ul style="list-style-type: none">• Conference posters or abstract only studies – these do not provide sufficient information for quality assessment.• Studies published before 2012 – this cut off has been applied to align with the effectiveness review and to restrict the review to more recent studies which will have more applicable resource use and costs

		<ul style="list-style-type: none"> Studies from non-OECD countries or the USA – these are considered unlikely to be applicable to the UK NHS setting due to substantial differences in healthcare delivery and unit costs. Non-comparative economic analyses including cost-of-illness studies. Letters, editorials or commentaries, study protocols or reviews of economic evaluations (recent reviews will be ordered and the bibliographies will be checked for relevant individual economic studies, which will then be ordered and checked for eligibility). Non-English language papers. Studies considering exclusively intervention costs, e.g. medicine acquisition costs, without considering wider healthcare costs associated with the management of ectopic pregnancy. Studies comparing costs of branded vs generic forms of the same medicine. Studies only focussing on productivity losses or gains.
5.	Search strategy	<p>An economic study search will be undertaken using question-specific terms.</p> <p>The searches for the cost effectiveness evidence were run on 16th July 2025. The following databases were searched: Econlit (OVID), Embase (OVID), International HTA database (INAHTA) and Medline (OVID). Limits were applied to remove conferences and to limit the date from January 2012 onwards. A broad economic search filter was used on Medline and Embase.</p> <p>For search details see appendix B below.</p>
6.	Review strategy	<ul style="list-style-type: none"> Studies meeting the inclusion and exclusion criteria will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist in appendix H of Developing NICE guidelines: the manual. The NICE economic evaluation checklist assesses: <ul style="list-style-type: none"> Applicability to the NICE guideline decision making context with consideration of the NICE reference case relevant to the guideline. Recent UK studies that use the NICE reference case methods are the most applicable when considering cost effectiveness. Methodological limitations. The aim is to present the best available economic evidence to inform committee decision-making in the context of the guideline, the current UK NHS setting and NICE methods. Therefore, the health economist may not present all studies that meet inclusion criteria. If recent high quality, UK cost-utility analyses are available for a question, it is often not

		<p>deemed informative to present studies that are less applicable or lower quality such as older UK analyses or analyses from other countries. A similar principle is deemed to apply more generally when considering applicability and methodological limitations. Some specific examples are given below:</p> <ul style="list-style-type: none"> ○ If multiple versions of a model are available for the UK and other countries it is usually reasonable to only present the UK version. ○ If multiple versions of the same UK model are available, it is usually reasonable to present only the most recent. ○ If there has been a NICE MTA or guideline model that informs current NHS practice it is usually reasonable not to present older studies, unless they address a different subpopulation or other specific issue. ○ If a UK model that includes all interventions in the decision space is available it may be reasonable not to present studies that only include individual or fewer interventions, if the analysis is sufficiently applicable and of good methodological quality. ● Quality and relevance of effectiveness data used in the economic analysis: the more closely the clinical effectiveness data used in the economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. ● Hierarchy of economic evaluation evidence based on quality assessment <ul style="list-style-type: none"> ○ 'Directly applicable' and 'Minor limitations' (only recent UK CUAs can get this rating). Usually presented and used in decision-making. ○ Directly or partially applicable combined with minor or potentially serious limitations (other than 1). Discretion over whether these are presented and used in decision-making, depending on the availability of more relevant evidence. ○ 'Not applicable' or 'Very serious limitations'. Typically not presented and not used in decision-making. <p>The health economist will make a decision based on the relative applicability and quality of the available evidence for each question, in discussion with the guideline committee if required. All decisions will be transparently reported in the evidence report. Studies that are presented to the committee and used in decision-making when formulating recommendations will be included in the summary tables and will have an evidence extraction. Other studies may not be presented to the committee in detail but will be listed, with the reason for not being presented to the committee and thus not</p>
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		used in decision-making being provided. Committee members can review and query the decision not to present studies with the health economist and will be provided with full details of these studies where requested.
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1 **Appendix B - Literature search strategies**

2 **Background and development**

4 **Search design and peer review**

5 A NICE Senior Information Specialist (SIS) conducted the literature searches
6 for the evidence review.

7 The principal search strategies were developed in MEDLINE (Ovid interface)
8 and adapted, as appropriate, for use in the other sources listed in the
9 protocol, taking into account their size, search functionality and subject
10 coverage.

11 The MEDLINE strategies below were quality assured (QA) by a trained
12 NICE SIS. All translated search strategies were peer reviewed by another
13 SIS to ensure their accuracy. Both procedures were adapted from the Peer
14 Review of Electronic Search Strategies Guideline Statement (for further
15 details see: McGowan J et al. [PRESS 2015 Guideline Statement](#). *Journal of
16 Clinical Epidemiology*, 75, 40-46).

17 This search report is based on the requirements of the PRISMA Statement for
18 Reporting Literature Searches in Systematic Reviews (for further details
19 see: Rethlefsen M et al. [PRISMA-S](#). *Systematic Reviews*, 10(1), 39).

20 **Review management**

21 The search results were managed in EPPI-Reviewer v5. Duplicates were
22 removed in EPPI-R5 using a two-step process. First, automated deduplication
23 is performed using a high-value algorithm. Second, manual deduplication is
24 used to assess "low-probability" matches. All decisions made for the review
25 can be accessed via the deduplication history.

26 **Search limits and other restrictions**

27 **Formats**

28 Limits were applied in adherence to standard NICE practice (as set out in
29 the [Identifying the evidence chapter](#) of the manual) and the eligibility
30 criteria listed in the review protocol to exclude:

- 31 • Animal studies
- 32 • Editorials, letters, news items and commentaries
- 33 • Conference abstracts and posters
- 34 • Papers not published in the English language.

35 The limit to remove animal studies in the searches was the standard NICE
36 practice, which has been adapted from:

37 Dickersin K, Scherer R & Lefebvre C. (1994) [Systematic reviews: identifying
38 relevant studies for systematic reviews](#). *BMJ*, 309(6964), 1286.

39 **Date limits**

40 A date limit of 1st January 2012 onwards was applied, as stated in the review
41 protocol, because this is an update of a previous guideline.

43 **Effectiveness searches**

44 **Database results**

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded

Cochrane Central Register of Controlled Trials (CENTRAL)	10/07/2025	Wiley	Issue 6 of 12, June 2025	4
Cochrane Database of Systematic Reviews (CDSR)	10/07/2025	Wiley	Issue 7 of 12, July 2025	2
Embase	10/07/2025	Ovid	Embase 1974 to 2025 July 09	387
Epistemonikos	10/07/2025	Epistemonikos		129
Medline ALL	10/07/2025	OVID	Ovid MEDLINE(R) ALL 1946 to July 09, 2025	101

1
2

Search strategy history

Database name: Medline

Searches

Ovid MEDLINE(R) ALL <1946 to July 09, 2025>

- 1 Pregnancy Trimester, First/ 19303
- 2 Pregnancy Complications/ 101406
- 3 Pregnancy, Ectopic/ 11934
- 4 Abortion, Spontaneous/ 23482
- 5 Abortion, Threatened/ 2364
- 6 Abortion, Induced/ 31707
- 7 abortion*.tw. 71026
- 8 (pregnan* and terminat*).tw. 20182
- 9 ((threat* or imminen*) adj2 miscarriage*).tw. 423
- 10 "surgical management of miscarriage".tw. 13
- 11 ((surgical or surgery or smm) and (miscarriage* or "pregnancy loss*")).tw. 1855
- 12 (("manual vacuum aspiration" or MVA) and (miscarriage* or "pregnancy loss*")).tw. 74
- 13 (("electric vacuum aspiration" or EVA) and (miscarriage* or "pregnancy loss*")).tw. 10
- 14 (("dilation and curettage" or D&C) and (miscarriage* or "pregnancy loss*")).tw. 183
- 15 "Dilatation and Curettage"/ 2404
- 16 "medical management of miscarriage".tw. 32
- 17 (medical adj3 (miscarriage* or "pregnancy loss*")).tw. 134
- 18 (mifepristone and (miscarriage* or "pregnancy loss*")).tw. 147
- 19 (misoprostol and (miscarriage* or "pregnancy loss*")).tw. 261
- 20 or/1-19 225683
- 21 Mifepristone/ 6672

22	Misoprostol/	4819
23	(miscarriage* or "pregnancy loss*").tw.	28654
24	(21 or 22) and 23	263
25	20 or 24	225689
26	Erythroblastosis, Fetal/	8826
27	("hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN).tw.	1437
28	(erythroblastosis adj2 (fetal* or foetal* or neonat*)).tw.	926
29	(rhesus adj2 disease).tw.	362
30	Rh Isoimmunization/	1840
31	(rh isoimmunization* or rh isoimmunisation* or rhesus isoimmunization* or rhesus isoimmunisation* or rh sensitization* or rh sensitisation*).tw.	827
32	((Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization)).tw.	12953
33	(anti-d or "anti d").tw.	3288
34	"Rho(D) Immune Globulin"/	1499
35	("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)).tw.	431
36	RhIg.tw.	173
37	(RhoGAM* or MICRhoGAM* or "Gamulin Rh*" or "hyoRho D*" or Rhesonativ* or "Hyper RHO*" or Rhophylac* or WinRho* or D-Gam*).tw.	470
38	or/26-37	24266
39	25 and 38	1092
40	limit 39 to english language	702
41	limit 40 to (letter or historical article or comment or editorial or news or case reports)	114
42	40 not 41	588
43	animals/ not humans/	5321352
44	42 not 43	569
45	(2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 202*).ed,dt.	18280040
46	44 and 45	101

1 Database name: Embase

Searches

Embase <1974 to 2025 July 09>

1	first trimester pregnancy/	60610
2	pregnancy complication/	75093
3	ectopic pregnancy/	22341
4	spontaneous abortion/	59058
5	imminent abortion/	2207
6	pregnancy termination/ or abortion/	48154
7	abortion*.tw.	80385
8	(pregnan* and terminat*).tw.	28856
9	((threat* or imminen*) adj2 miscarriage*).tw.	748
10	"surgical management of miscarriage".tw.	54

11	((surgical or surgery or smm) and (miscarriage* or "pregnancy loss*")).tw.	3931
12	("manual vacuum aspiration" or MVA) and (miscarriage* or "pregnancy loss*")).tw.	173
13	("electric vacuum aspiration" or EVA) and (miscarriage* or "pregnancy loss*")).tw.	22
14	("dilation and curettage" or D&C) and (miscarriage* or "pregnancy loss*")).tw.	403
15	"dilatation and curettage"/	2317
16	"medical management of miscarriage".tw.	79
17	(medical adj3 (miscarriage* or "pregnancy loss*")).tw.	287
18	(mifepristone and (miscarriage* or "pregnancy loss*")).tw.	221
19	(misoprostol and (miscarriage* or "pregnancy loss*")).tw.	508
20	or/1-19	283792
21	mifepristone plus misoprostol/ or mifepristone/	15468
22	misoprostol/	15226
23	(miscarriage* or "pregnancy loss*").tw.	48373
24	(21 or 22) and 23	755
25	20 or 24	283805
26	newborn hemolytic disease/	3492
27	("hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN).tw.	2284
28	(erythroblastosis adj2 (fetal* or foetal* or neonat*)).tw.	286
29	(rhesus adj2 disease).tw.	437
30	rhesus immunization/ or rhesus incompatibility/ or rhesus isoimmunization/	3408
31	(rh isoimmunization* or rh isoimmunisation* or rhesus isoimmunization* or rhesus isoimmunisation* or rh sensitization* or rh sensitisation*).tw.	738
32	((Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization)).tw.	18239
33	(anti-d or "anti d").tw.	5559
34	rhesus D antibody/	4913
35	("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)).tw.	664
36	Rhlg.tw.	383
37	(RhoGAM* or MICRhoGAM* or "Gamulin Rh*" or "hyoRho D*" or Rhesonativ* or "Hyper RHO*" or Rhophylac* or WinRho* or D-Gam*).tw.	718
38	or/26-37	28444
39	25 and 38	1506
40	limit 39 to english language	1221
41	nonhuman/ not (human/ and nonhuman/)	5729107
42	40 not 41	1187
43	42 not (letter or editorial).pt.	1124
44	(2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 202*).dc,dd.	23666822
45	43 and 44	642

46	conference*.db.pt.su.	6324422
47	45 not 46	387

1 **Database name: Cochrane Database of Systematic Reviews (CDSR)**

Searches

#1	[mh ^"Pregnancy Trimester, First"]	884
#2	[mh ^"Pregnancy Complications"]	2504
#3	[mh ^"Pregnancy, Ectopic"]	198
#4	[mh ^"Abortion, Spontaneous"]	804
#5	[mh ^"Abortion, Threatened"]	71
#6	[mh ^"Abortion, Induced"]	1276
#7	abortion*:ti,ab	7542
#8	(pregnan* and terminat*):ti,ab	2671
#9	((threat* or imminen*) NEAR/2 miscarriage*):ti,ab	103
#10	"surgical management of miscarriage":ti,ab	8
#11	((surgical or surgery or smm) and (miscarriage* or (pregnancy NEXT loss*)):ti,ab	435
#12	(("manual vacuum aspiration" or MVA) and (miscarriage* or (pregnancy NEXT loss*)):ti,ab	62
#13	(("electric vacuum aspiration" or EVA) and (miscarriage* or (pregnancy NEXT loss*)):ti,ab	22
#14	(("dilation and curettage" or D&C) and (miscarriage* or (pregnancy NEXT loss*)):ti,ab	49
#15	[mh ^"Dilatation and Curettage"]	295
#16	"medical management of miscarriage":ti,ab	23
#17	(medical NEAR/3 (miscarriage* or (pregnancy NEXT loss*)):ti,ab	52
#18	(mifepristone and (miscarriage* or (pregnancy NEXT loss*)):ti,ab	102
#19	(misoprostol and (miscarriage* or (pregnancy NEXT loss*)):ti,ab	237
#20	{or #1-#19}	13093
#21	[mh ^Mifepristone]	702
#22	[mh ^Misoprostol]	1979
#23	(miscarriage* or (pregnancy NEXT loss*)):ti,ab	4009
#24	{or #21-#22} and #23	116
#25	#20 or #24	13093
#26	[mh ^"Erythroblastosis, Fetal"]	65
#27	("hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN):ti,ab	54
#28	(erythroblastosis NEAR/2 (fetal* or foetal* or neonat*)):ti,ab	5
#29	(rhesus NEAR/2 disease):ti,ab	25
#30	[mh ^"Rh Isoimmunization"]	31
#31	((rh or rhesus) NEXT (isoimmunization* or isoimmunisation* or sensitization* or sensitisation*):ti,ab	29
#32	((Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization)):ti,ab	997
#33	(anti-d or "anti d"):ti,ab	186
#34	[mh ^"Rho(D) Immune Globulin"]	0

#35 ((("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)):ti,ab 47
#36 RhIg:ti,ab 3
#37 (RhoGAM* or MICRhoGAM* or "Gamulin Rh" or "hyoRho D" or Rhesonativ* or "Hyper RHO" or Rhophylac* or WinRho* or D-Gam*):ti,ab 41
#38 {or #26-#37} 1234
#39 #25 and #38 40
#40 #39 with Cochrane Library publication date Between Jan 2012 and Jul 2025, in Cochrane Reviews 2

Database name: Cochrane Central Register of Controlled Trials (CENTRAL)

Searches

#1	[mh ^"Pregnancy Trimester, First"]	884
#2	[mh ^"Pregnancy Complications"]	2504
#3	[mh ^"Pregnancy, Ectopic"]	198
#4	[mh ^"Abortion, Spontaneous"]	804
#5	[mh ^"Abortion, Threatened"]	71
#6	[mh ^"Abortion, Induced"]	1276
#7	abortion*:ti,ab	7542
#8	(pregnan* and terminat*):ti,ab	2671
#9	((threat* or imminen*) NEAR/2 miscarriage*):ti,ab	103
#10	"surgical management of miscarriage":ti,ab	8
#11	((surgical or surgery or smm) and (miscarriage* or (pregnancy NEXT loss*)))	435
#12	(("manual vacuum aspiration" or MVA) and (miscarriage* or (pregnancy NEXT loss*)))	62
#13	(("electric vacuum aspiration" or EVA) and (miscarriage* or (pregnancy NEXT loss*)))	22
#14	(("dilation and curettage" or D&C) and (miscarriage* or (pregnancy NEXT loss*)))	49
#15	[mh ^"Dilatation and Curettage"]	295
#16	"medical management of miscarriage":ti,ab	23
#17	((medical NEAR/3 (miscarriage* or (pregnancy NEXT loss*)))	52
#18	(mifepristone and (miscarriage* or (pregnancy NEXT loss*)))	102
#19	(misoprostol and (miscarriage* or (pregnancy NEXT loss*)))	237
#20	{or #1-#19}	13093
#21	[mh ^Mifepristone]	702
#22	[mh ^Misoprostol]	1979
#23	(miscarriage* or (pregnancy NEXT loss*))	4009
#24	{or #21-#22} and #23	116
#25	#20 or #24	13093
#26	[mh ^"Erythroblastosis, Fetal"]	65
#27	("hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN)	54
#28	((erythroblastosis NEAR/2 (fetal* or foetal* or neonat*)))	5
#29	(rhesus NEAR/2 disease)	25

#30	[mh ^"Rh Isoimmunization"]	31
#31	((rh or rhesus) NEXT (isoimmunization* or isoimmunisation* or sensitization* or sensitisation*):ti,ab	29
#32	((Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization):ti,ab	997
#33	(anti-d or "anti d"):ti,ab	186
#34	[mh ^"Rho(D) Immune Globulin"]	0
#35	(("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)):ti,ab	47
#36	Rhlg:ti,ab	3
#37	(RhoGAM* or MICRhoGAM* or "Gamulin Rh" or "hyoRho D" or Rhesonativ* or "Hyper RHO" or Rhophylac* or WinRho* or D-Gam*):ti,ab	41
#38	{or #26-#37}	1234
#39	#25 and #38	40
#40	#39 with Cochrane Library publication date Between Jan 2012 and Jul 2025, in Cochrane Reviews	2
#41	"conference":pt or (clinicaltrials or trialsearch):so	835703
#42	#39 not #41	16
#43	#42 with Publication Year from 2012 to 2025, in Trials	4

1

Database name: Epistemonikos

Searches

(title:(pregnancy OR abortion OR miscarriage) OR abstract:(pregnancy OR abortion OR miscarriage)) AND (title:(("hemolytic disease of newborn" OR "haemolytic disease of newborn" OR "newborn hemolytic" OR "newborn haemolytic" OR "neonatal haemolytic" OR "neonatal hemolytic" OR HDN OR HDFN) OR abstract:(("hemolytic disease of newborn" OR "haemolytic disease of newborn" OR "newborn hemolytic" OR "newborn haemolytic" OR "neonatal haemolytic" OR "neonatal hemolytic" OR HDN OR HDFN)) OR (title:(erythroblastosis AND (fetal* OR foetal* OR neonat*)) OR abstract:(erythroblastosis AND (fetal* OR foetal* OR neonat*))) OR (title:(rhesus AND disease) OR abstract:(rhesus AND disease)) OR (title:((rh OR rhesus) AND (isoimmunization* OR isoimmunisation* OR sensitization* OR sensitisation* OR negative OR antibod* OR prophylax* OR immunoprophylax*)) OR abstract:((rh OR rhesus) AND (isoimmunization* OR isoimmunisation* OR sensitization* OR sensitisation* OR negative OR antibod* OR prophylax* OR immunoprophylax*))) OR (title:(("anti-d" OR "anti d") OR abstract:(("anti-d" OR "anti d")) OR (title:(("Rho(d)" OR "Rho (d)" OR "Rh(d)" OR "Rh (d)" OR antiRh OR "anti rhesus" OR antirhesus) AND (immune OR globulin OR immunoglobulin)) OR abstract:(("Rho(d)" OR "Rho (d)" OR "Rh(d)" OR "Rh (d)" OR antiRh OR "anti rhesus" OR antirhesus) AND (immune OR globulin OR immunoglobulin))) OR (title:(Rhlg) OR abstract:(Rhlg)) OR (title:(RhoGAM* OR MICRhoGAM* OR "Gamulin Rh*" OR "hyoRho D*" OR Rhesonativ* OR "Hyper RHO*" OR Rhophylac* OR WinRho* OR D-Gam* or "D Gam") OR abstract:(RhoGAM* OR MICRhoGAM* OR "Gamulin Rh*" OR "hyoRho D*" OR Rhesonativ* OR "Hyper RHO*" OR Rhophylac* OR WinRho* OR D-Gam* or "D Gam")))))

2

Cost-effectiveness searches

Ectopic pregnancy and miscarriage technical appendices for anti-D immunoglobulin prophylaxis DRAFT (February 2026) DRAFT

1 **Database results**

2

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Econlit	16/07/2025	OVID	Econlit 1886 to July 10, 2025	8
Embase	16/07/2025	OVID	Embase 1974 to 2025 July 15	26
International HTA Database	16/07/2025	https://database.inahta.org/	INAHTA	10
MEDLINE	16/07/2025	OVID	Ovid MEDLINE(R) ALL 1946 to July 15, 2025	6

3 **Search strategy history**

4 **Database name: Econlit**

Searches
1 ("hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN).tw. 0
2 (erythroblastosis adj2 (fetal* or foetal* or neonat*)).tw. 0
3 (rhesus adj2 disease).tw. 0
4 (rh isoimmunization* or rh isoimmunisation* or rhesus isoimmunization* or rhesus isoimmunisation* or rh sensitization* or rh sensitisation*).tw. 0
5 ((Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization)).tw. 5
6 (anti-d or "anti d").tw. 1
7 ("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)).tw. 0
8 RhIg.tw. 0
9 (RhoGAM* or MICRhoGAM* or "Gamulin Rh*" or "hyoRho D*" or Rhesonativ* or "Hyper RHO*" or Rhophylac* or WinRho* or D-Gam*).tw. 3
10 or/1-9 9
11 (2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 202*).up. 883427
12 10 and 11 8

5 **Database name: Embase**

Searches
1 first trimester pregnancy/ 60686

2	pregnancy complication/	75124
3	ectopic pregnancy/	22364
4	spontaneous abortion/	59127
5	imminent abortion/	2213
6	pregnancy termination/ or abortion/	48191
7	abortion*.tw.	80447
8	(pregnan* and terminat*).tw.	28881
9	((threat* or imminen*) adj2 miscarriage*).tw.	749
10	"surgical management of miscarriage".tw.	54
11	((surgical or surgery or smm) and (miscarriage* or "pregnancy loss**")).tw.	3940
12	(("manual vacuum aspiration" or MVA) and (miscarriage* or "pregnancy loss**")).tw.	173
13	(("electric vacuum aspiration" or EVA) and (miscarriage* or "pregnancy loss**")).tw.	22
14	(("dilation and curettage" or D&C) and (miscarriage* or "pregnancy loss**")).tw.	403
15	"dilatation and curettage"/	2316
16	"medical management of miscarriage".tw.	79
17	(medical adj3 (miscarriage* or "pregnancy loss**")).tw.	287
18	(mifepristone and (miscarriage* or "pregnancy loss**")).tw.	221
19	(misoprostol and (miscarriage* or "pregnancy loss**")).tw.	508
20	or/1-19	284039
21	mifepristone plus misoprostol/ or mifepristone/	15475
22	misoprostol/	15240
23	(miscarriage* or "pregnancy loss**").tw.	48428
24	(21 or 22) and 23	756
25	20 or 24	284052
26	newborn hemolytic disease/	3495
27	("hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN).tw.	2288
28	(erythroblastosis adj2 (fetal* or foetal* or neonat*)).tw.	286
29	(rhesus adj2 disease).tw.	437
30	rhesus immunization/ or rhesus incompatibility/ or rhesus isoimmunization/	3408
31	(rh isoimmunization* or rh isoimmunisation* or rhesus isoimmunization* or rhesus isoimmunisation* or rh sensitization* or rh sensitisation*).tw.	739
32	((Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization)).tw.	18251
33	(anti-d or "anti d").tw.	5564
34	rhesus D antibody/	4916
35	(("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)).tw.	665
36	Rhlg.tw.	383
37	(RhoGAM* or MICRhoGAM* or "Gamulin Rh*" or "hyoRho D*" or Rhesonativ* or "Hyper RHO*" or Rhophylac* or WinRho* or D-Gam*).tw.	718

38	or/26-37	28465
39	25 and 38	1508
40	limit 39 to english language	1223
41	nonhuman/ not (human/ and nonhuman/)	5734877
42	40 not 41	1189
43	42 not (letter or editorial).pt.	1126
44	(2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 202*).dc,dd.	23708028
45	43 and 44	643
46	conference*.db,pt,su.	6332885
47	45 not 46	388
48	Health economics/	37499
49	exp health care cost/	374822
50	exp Fee/	46935
51	exp Budget/	37007
52	Funding/	83050
53	budget*.ti,ab.	53414
54	cost*.ti.	213971
55	(economic* or pharmaco?economic*).ti.	85560
56	(price* or pricing*).ti,ab.	83133
57	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.	344982
58	(financ* or fee or fees).ti,ab.	274891
59	(value adj2 (money or monetary)).ti,ab.	4632
60	or/48-59	1212719
61	47 and 60	26

1 **Database name: International HTA database (INAHTA)**

Searches

13	#12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1	24
12	RhoGAM* or MICRhoGAM* or "Gamulin Rh*" or "hyoRho D*" or Rhesonativ* or "Hyper RHO*" or Rhophylac* or WinRho* or D-Gam*	0
11	Rhlg	1
10	("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)	2
9	"Rho(D) Immune Globulin"[mh]	0
8	anti-d or "anti d"	12
7	(Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization)	5
6	rh isoimmunization* or rh isoimmunisation* or rhesus isoimmunization* or rhesus isoimmunisation* or rh sensitization* or rh sensitisation*	13
5	"Rh Isoimmunization"[mh]	8
4	rhesus and disease	1
3	erythroblastosis and (fetal* or foetal* or neonat*)	0

2	<u>"hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN</u>	5	
1	<u>Erythroblastosis, Fetal"[mh]</u>	4	

1 **Database name: Medline All**

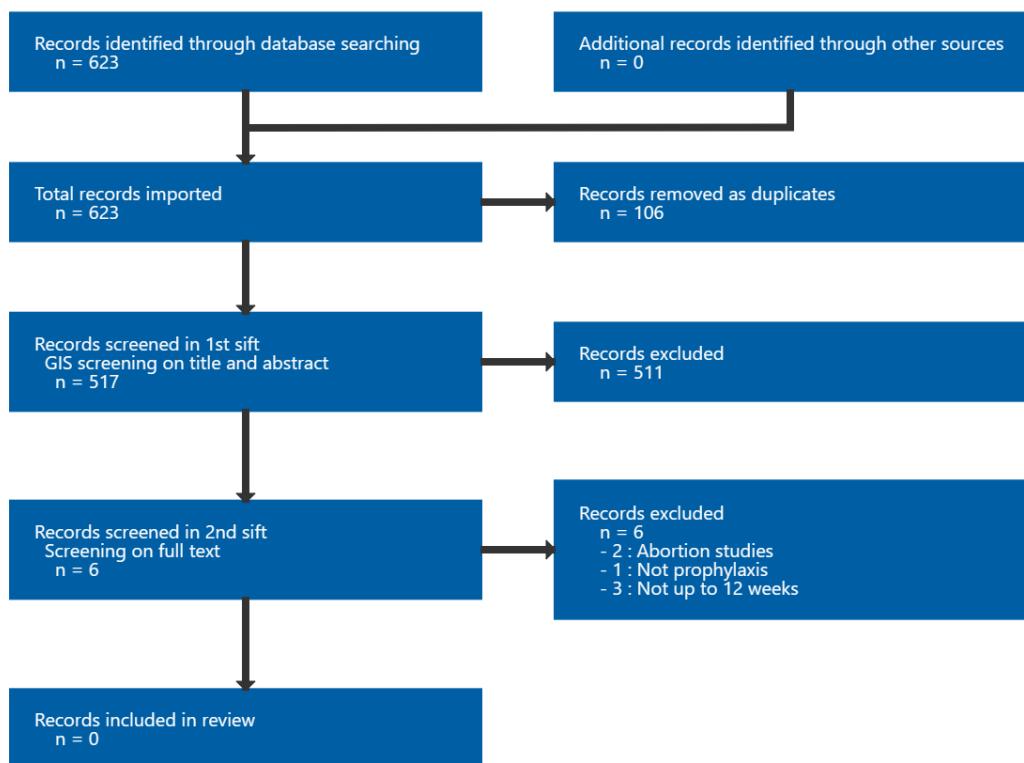
Searches

1	Pregnancy Trimester, First/	19313	
2	Pregnancy Complications/	101455	
3	Pregnancy, Ectopic/	11936	
4	Abortion, Spontaneous/	23485	
5	Abortion, Threatened/	2365	
6	Abortion, Induced/	31722	
7	abortion*.tw.	71074	
8	(pregnan* and terminat*).tw.	20198	
9	((threat* or imminen*) adj2 miscarriage*).tw.	423	
10	"surgical management of miscarriage".tw.	13	
11	((surgical or surgery or smm) and (miscarriage* or "pregnancy loss*")).tw.	1857	
12	(("manual vacuum aspiration" or MVA) and (miscarriage* or "pregnancy loss*")).tw.	74	
13	(("electric vacuum aspiration" or EVA) and (miscarriage* or "pregnancy loss*")).tw.	10	
14	(("dilation and curettage" or D&C) and (miscarriage* or "pregnancy loss*")).tw.	184	
15	"Dilatation and Curettage"/	2405	
16	"medical management of miscarriage".tw.	32	
17	(medical adj3 (miscarriage* or "pregnancy loss*")).tw.	135	
18	(mifepristone and (miscarriage* or "pregnancy loss*")).tw.	147	
19	(misoprostol and (miscarriage* or "pregnancy loss*")).tw.	262	
20	or/1-19	225801	
21	Mifepristone/	6673	
22	Misoprostol/	4822	
23	(miscarriage* or "pregnancy loss*").tw.	28715	
24	(21 or 22) and 23	264	
25	20 or 24	225807	
26	Erythroblastosis, Fetal/	8827	
27	("hemolytic disease of newborn" or "haemolytic disease of newborn" or "newborn hemolytic" or "newborn haemolytic" or "neonatal haemolytic" or "neonatal hemolytic" or HDN or HDFN).tw.	1438	
28	(erythroblastosis adj2 (fetal* or foetal* or neonat*)).tw.	926	
29	(rhesus adj2 disease).tw.	362	
30	Rh Isoimmunization/	1840	
31	(rh isoimmunization* or rh isoimmunisation* or rhesus isoimmunization* or rhesus isoimmunisation* or rh sensitization* or rh sensitisation*).tw.	827	

32	((Rh or Rhesus) and (negative or antibod* or prophylax* or immunoprophylax* or sensitisation or sensitization or isoimmunisation or isoimmunization)).tw.	12966
33	(anti-d or "anti d").tw.	3289
34	"Rho(D) Immune Globulin"/	1499
35	("Rho(d)" or "Rho (d)" or "Rh(d)" or "Rh (d)" or antiRh or "anti rhesus" or antirhesus) and (immune or globulin or immunoglobulin)).tw.	432
36	Rhlg.tw.	175
37	(RhoGAM* or MICRhoGAM* or "Gamulin Rh*" or "hyoRho D*" or Rhesonativ* or "Hyper RHO*" or Rhophylac* or WinRho* or D-Gam*).tw.	470
38	or/26-37	24280
39	25 and 38	1095
40	limit 39 to english language	705
41	limit 40 to (letter or historical article or comment or editorial or news or case reports)	115
42	40 not 41	590
43	animals/ not humans/	5323570
44	42 not 43	571
45	(2012* or 2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 202*).ed,dt.	18316103
46	44 and 45	103
47	Economics/	27548
48	Value of life/	5845
49	exp "Costs and Cost Analysis"/	280456
50	exp Economics, Hospital/	26247
51	exp Economics, Medical/	14464
52	Economics, Nursing/	4013
53	Economics, Pharmaceutical/	3168
54	exp "Fees and Charges"/	31719
55	exp Budgets/	14376
56	budget*.ti,ab.	40085
57	cost*.ti.	158854
58	(economic* or pharmaco?economic*).ti.	68419
59	(price* or pricing*).ti,ab.	60876
60	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.	248991
61	(financ* or fee or fees).ti,ab.	187726
62	(value adj2 (money or monetary)).ti,ab.	3451
63	or/47-62	826537
64	46 and 63	6

1 Appendix C - Study selection – effectiveness evidence

2 Figure 1 Effectiveness evidence study selection



3
4

1 **Appendix D - Effectiveness evidence tables**

2 No evidence identified that matched protocol.

3

4 **Appendix E - Forest plots**

5 No evidence identified that matched protocol.

6

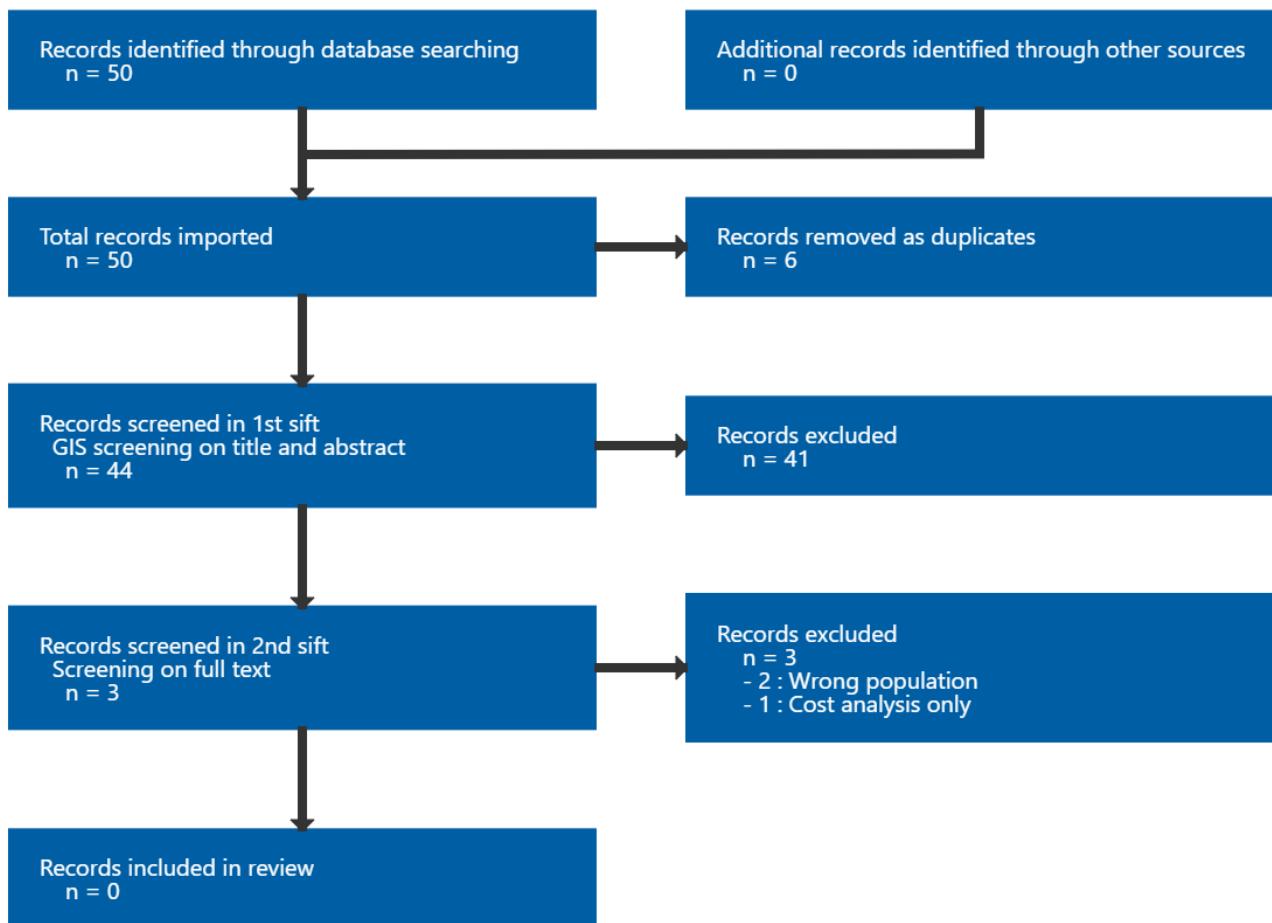
7

1 **Appendix F - GRADE summary**

- 2 No evidence identified that matched protocol.

1 Appendix G - Economic evidence study selection

2 Figure 2: Economic evidence study selection flow chart



3

- 1 **Appendix H - Economic evidence tables**
- 2 No evidence was identified which was applicable to this review question.
- 3

1 Appendix I - Excluded studies

2 Effectiveness

3 Table 1 Studies excluded from the effectiveness review

Study	Reason for exclusion
<u>Chan, Michelle C; Gill, Roopan Kaur; Kim, Caron Rahn (2022) Rhesus isoimmunisation in unsensitised RhD-negative individuals seeking abortion at less than 12 weeks' gestation: a systematic review.</u> BMJ sexual & reproductive health 48(3): 163-168	- Systematic review of 2 studies from (Goldman 1972 and Gavin 1972); both were abortion studies.
<u>Horvath, Sarah, Huang, Zhen-Yu, Koelper, Nathanael C et al. (2023) Induced Abortion and the Risk of Rh Sensitization.</u> JAMA 330(12): 1167-1174	- Abortion study
<u>Karanth, Laxminarayan, Jaafar, Sharifah Halimah, Kanagasabai, Sachchithanantham et al. (2013) Anti-D administration after spontaneous miscarriage for preventing Rhesus alloimmunisation.</u> The Cochrane database of systematic reviews: cd009617	- Not up to 12 weeks (up to 24 weeks)
<u>Neovius, M, Tiblad, E, Westgren, M et al. (2016) Cost-effectiveness of first trimester non-invasive fetal RHD screening for targeted antenatal anti-D prophylaxis in RhD-negative pregnant women: a model-based analysis.</u> BJOG : an international journal of obstetrics and gynaecology 123(8): 1337-46	- Not up to 12 weeks: screening at 12 weeks but anti-D given at 29 weeks.
<u>Slootweg, Y M, Zwiers, C, Koelewijn, J M et al. (2022) Risk factors for Rhd immunisation in a high coverage prevention programme of antenatal and postnatal RhIg: a nationwide cohort study.</u> BJOG : an international journal of obstetrics and gynaecology 129(10): 1721-1730	- Not prophylaxis, risk factors for RhD immunisation.
<u>Thorup, E., Clausen, F.B., Brodersen, T. et al. (2025) Evaluation of the clinical effect of a nationwide implementation of targeted routine antenatal anti-D prophylaxis in Denmark.</u> Transfusion 65(1): 29	- Not up to 12 weeks

1

2 **Economic**

3 No economic study was reviewed at full text and excluded from this review.

4

1 **Appendix J - Methods**

2 This was an update of one question, focusing on whether anti-D prophylaxis
3 should be provided to people with miscarriage, threatened miscarriage or
4 ectopic pregnancy, who are sensitised to anti-D in their first trimester. A short
5 scope and protocol were created for this updated question in the guideline. A
6 guideline search and scoping search was conducted to search for evidence to
7 focus the protocol. Following creation of the protocol a full search was
8 conducted for the question. As no evidence was found to answer the protocol
9 studies from the search which were relevant to the topic were described
10 narratively as supporting information to aid the GC discussion.

11

1 **Appendix K - Research recommendations**

2 **Research recommendation**

3 No research recommendations were made.