Recurrent Pregnancy Loss Testing and Procedures

Policy Number: HS-248

Original Effective Date: 2/5/2015

Revised Date(s): 2/4/2016

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

Clinical Coverage Guideline

Original Effective Date: 2/5/2015 - Revised: 2/4/2016
DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member’s particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member’s benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member’s Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any. Note: Lines of business (LOB) are subject to change without notice; current LOBs can be found at www.wellcare.com – select the Provider tab, then “Tools” and “Clinical Guidelines”.

BACKGROUND

Evaluation and treatment of recurrent pregnancy loss varies upon the situation of each couple. Miscarriage is defined as the spontaneous loss of pregnancy prior to a fetus reaching 24 weeks+ gestation (RCOG, 2011). Sporadic pregnancy loss is nonconsecutive pregnancy loss that occurs randomly during a woman’s reproductive years. Recurrent pregnancy loss, also referred to as recurrent spontaneous abortion (RSA) or recurrent miscarriage, is defined as two or more failed pregnancies. Estimates indicated that 1–3% of childbearing women suffer a miscarriage. Several underlying factors contribute to recurrent pregnancy loss:

- Parental chromosomal anomalies and genetic disorders
- Autoimmune disorders (e.g., antiphospholipid syndrome, systemic lupus erythematosus)
- Alloimmune disorders
- Structural uterine anomalies (e.g., bicornuate uterus, uterine septum, fibroids, intrauterine adhesions)
- Cervical incompetence
- Endocrine disorders (e.g., polycystic ovarian disease, luteal phase defect, thyroid disease)
- Prothrombotic states (e.g., antithrombin III deficiency, protein C or protein S deficiency/resistance, thrombocythaemia, factor V Leiden)
- Infectious diseases
- Embryotoxicity

Medical management of recurrent pregnancy loss typically includes diagnosis and treatment as advised by a reproductive endocrinologist and/or a high-risk obstetrician/gynecologist. In addition, members can benefit from genetic counseling to determine the potential for successful pregnancy with and without treatment.

Professional Societies/Organizations

The American College of Obstetricians and Gynecologists (ACOG) proposed key recommendations for couples with repetitive loss of pregnancies during the first or early second trimester (e.g., <15 weeks gestation):

- **Testing for lupus anticoagulant and anticardiolipin antibodies.** These special protein substances are produced by the body’s white cells to defend against foreign substances; antibodies can alter the clotting process and lead to strokes, blood clots and low platelet counts, as well as miscarriages. If tests are positive for the same antibody on two consecutive occasions six to eight weeks apart, the member may benefit from a treatment of heparin and low-dose aspirin during the next pregnancy attempt.
- **Testing for genetic abnormalities.** These tests may identify abnormalities that causing recurrent losses. This includes karyotype and microarray testing.
- **Hysteroscopy evaluation and reparative surgery.** Performed on women with recurrent miscarriage and a double uterus (uterine septum).
- **Discussion of potential pregnancy without treatment.**

The Royal College of Obstetricians and Gynaecologists (RCOG) recommends the following for the diagnosis and treatment of recurrent pregnancy loss:
Screening prior to pregnancy for antiphospholipid antibodies. For women with recurrent first-trimester miscarriage and all women with one or more second-trimester miscarriage.

Cytogenetic analysis. Performed on products of conception of the third and subsequent consecutive miscarriages(s).

Peripheral-blood karyotyping. For couples with a history of recurrent miscarriage when testing of products of conception reports an unbalanced structural chromosomal abnormality.

Pelvic ultrasound. For women with recurrent first trimester miscarriage and all women with one or more second-trimester miscarriages to assess uterine anatomy and morphology.


The American Society of Reproductive Medicine (ASRM) recommend the following for the evaluation and treatment of recurrent pregnancy loss:

- Evaluation of RSA can proceed after two consecutive clinical pregnancy losses
- Assessment of RSA focuses on screening for genetic factors and antiphospholipid syndrome, assessment of uterine anomaly hormonal and metabolic factors, and lifestyle variables – this may include:
  - Peripheral karyotypic analysis of parents
  - Screening for lupus anticoagulant, anticardiolipin antibodies, and anti-B2 glycoprotein I
  - Sonohysterogram, hysterosalpingogram, and/or hysteroscopy
  - Screening for thyroid or prolactin abnormalities
  - Karyotypic analysis of products of conception in the setting of ongoing therapy for RSA
  - Women with persistent to moderate-to-high titers of circulating antiphospholipid antibodies can be treated with a combination of prophylactic doses of unfractionated heparin and low dose aspirin
  - Psychological counseling and support.

POSITION STATEMENT

Applicable To:

- Medicaid – Hawaii
- Medicaid – Florida, Georgia, Illinois, Kentucky, New Jersey, New York and South Carolina

Exclusions

The following tests and studies are considered experimental and investigational due to a lack of evidence to support their use for detection of recurrent pregnancy loss:

- Antibodies to phosphatidylserine, phosphatidylethanolamine, or other anti-phospholipid antibodies other than anti-cardiolipin and lupus anticoagulant
- Determination of the percentage of circulating natural killer (NK) cells
- Embryo toxicity assay (ETA)
- Genetic association studies of inflammatory cytokine polymorphisms
- Inter-α trypsin inhibitor-heavy chain 4 (ITI-H4) (as a biomarker for recurrent pregnancy loss)
- Luteal phase biopsy to determine the status of natural killer (NK)-like cells
- Maternal antiparental antibodies
- Parental human leukocyte antigen (HLA) status
- Pre-implantation genetic screening
- Reproductive immunophenotype (CD3+, CD4+, CD5+, CD8+, CD16+, CD19+, CD56+)
- Tests for embryotoxic factor
• Tests for maternal antileukocytic antibodies to paternal leukocytes
• Tests for serum “blocking factor”
• Cytokine polymorphisms analysis (Th1/Th2 intra-cellular cytokine ratio)
• X-chromosome inactivation study

Further, the following treatments and therapies are considered experimental and investigational due to a lack of evidence to support their use for detection of recurrent pregnancy loss:

• Intravenous immunoglobulin (IVIG) therapy
• Leukocyte immunization (immunizing the female partner with the male partner's leukocytes)
• Low-molecular-weight heparin

Coverage

WellCare considers the following tests for members with recurrent pregnancy loss* medically necessary and a covered benefit:

• Endometrial biopsies for assessment of luteal phase defect;
• Hysterosalpingography, hysteroscopy or sonohysteroscopy/sonohysterography to diagnose uterine anatomic abnormalities;
• Karyotype (cytogenetic analysis) of parents to detect balanced chromosomal anomalies;
• Karyotype of abortus tissue when a couple with recurrent pregnancy loss experiences a subsequent spontaneous abortion;
• Measurement of anti-beta2-glycoprotein I (IgG or IgM) antibodies, anti-cardiolipin (IgG or IgM) antibodies, and lupus anticoagulant, using standard assays, for diagnosis of antiphospholipid syndrome;
• Pelvic ultrasound scan to assess ovarian morphology and the uterine cavity;
• Prenatal genetic diagnosis for all couples in which 1 partner has been found to have a balanced translocation or inversion;
• Tests for inherited thrombophilic disorders: factor V Leiden, prothrombin G20210A mutation, serum homocysteine, and deficiencies of the anticoagulants protein C, protein S, and antithrombin II;
• Tests for thyroid stimulating hormone (TSH) and thyroid antibodies.

WellCare considers the following treatments for members with recurrent pregnancy loss* medically necessary and a covered benefit:

• Administration of low-dose heparin and aspirin as a treatment for clearly established antiphospholipid syndrome
• Antenatal transvaginal cervical cerclage
• Antenatal transabdominal cervical cerclage for an individual with a prior failed or contraindication to transvaginal cerclage
• Surgical treatment of structural uterine abnormalities

* Recurrent pregnancy loss is defined as 2 or more consecutive spontaneous abortions.

Coding

Covered CPT® Codes
58100 Endometrial sampling (biopsy) with or without endocervical sampling (biopsy), without cervical dilation, any method (separate procedure)
58340 Catheterization and introduction of saline or contrast material for saline infusion sonohysterography (SIS) or hysterosalpingography
58555 Hysteroscopy, diagnostic (separate procedure)
58558 Hysteroscopy, surgical; with sampling (biopsy) of endometrium and/or polypectomy, with or without D & C
58561  Hysteroscopy, surgical; with removal of leiomyomata
58563  Hysteroscopy, surgical; with endometrial ablation (e.g., endometrial resection, electrosurgical ablation, thermoablation)

HCPCS © Codes – No applicable codes.

Covered ICD-9-CM Diagnosis Codes
- 629.81  Recurrent pregnancy loss without current pregnancy
- 646.30  Recurrent pregnancy loss, unspecified as to episode of care or not applicable
- 646.31  Recurrent pregnancy loss, delivered, with or without mention of antepartum condition
- 646.33  Recurrent pregnancy loss, antepartum condition or complication
- V26.35  Encounter for testing of male partner of female with recurrent pregnancy loss

Covered ICD-10-CM Diagnosis Codes
- N96  Recurrent pregnancy loss
- O26.20  Pregnancy care for patient with recurrent pregnancy loss, unspecified trimester
- O26.21  Pregnancy care for patient with recurrent pregnancy loss, first trimester
- O26.22  Pregnancy care for patient with recurrent pregnancy loss, second trimester
- O26.23  Pregnancy care for patient with recurrent pregnancy loss, third trimester
- O26.21  Pregnancy care for patient with recurrent pregnancy loss, first trimester
- O26.22  Pregnancy care for patient with recurrent pregnancy loss, second trimester
- O26.23  Pregnancy care for patient with recurrent pregnancy loss, third trimester
- Z31.441  Encounter for testing of male partner of patient with recurrent pregnancy loss


REFERENCES

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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<td>02/05/2015</td>
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