Recurrent Pregnancy Loss
Testing and Procedures

Policy Number: HS-248

Original Effective Date: 2/5/2015
Revised Date(s): 2/4/2016, 2/2/2017; 1/4/2018

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.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). 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 CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific Medicaid mandates. Links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change. Lines of business are also subject to change without notice and are noted on www.wellcare.com. Guidelines are also available on the site by selecting 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% ofchildbearing women suffer a miscarriage.1,2
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 miscarriages.
- 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
POSITION STATEMENT

Applicable To:

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

* Consult applicable vendor for criteria for the following tests: Factor II, Factor V Leiden, Chromosomal Microarray.

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 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**

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<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>58100</td>
<td>Endometrial sampling (biopsy) with or without endocervical sampling (biopsy), without cervical dilation, any method (separate procedure)</td>
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<tr>
<td>58340</td>
<td>Catheterization and introduction of saline or contrast material for saline infusion sonohysterography (SIS) or hysterosalpingography</td>
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<tr>
<td>58555</td>
<td>Hysteroscopy, diagnostic (separate procedure)</td>
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<tr>
<td>58558</td>
<td>Hysteroscopy, surgical; with sampling (biopsy) of endometrium and/or polypectomy, with or without D &amp; C</td>
</tr>
<tr>
<td>58561</td>
<td>Hysteroscopy, surgical; with removal of leiomyomata</td>
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<tr>
<td>58563</td>
<td>Hysteroscopy, surgical; with endometrial ablation (e.g., endometrial resection, electrosurgical ablation, thermoablation)</td>
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<td>59320</td>
<td>Cerclage of cervix, during pregnancy; vaginal</td>
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<td>Cerclage of cervix, during pregnancy; abdominal</td>
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<td>74740</td>
<td>Hysterosalpingography, radiological supervision and interpretation</td>
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<td>76856</td>
<td>Ultrasound, pelvic (nonobstetric), real time with image documentation; complete</td>
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<td>76857</td>
<td>Ultrasound, pelvic (nonobstetric), real time with image documentation; limited or follow-up (eg, for follicles)</td>
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<td>81240</td>
<td>F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysisys, 20210G&gt;A Variant</td>
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<td>81241</td>
<td>Factor V Leiden gene analysis, (hereditary hypercoagulability)</td>
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<td>86146</td>
<td>Beta 2 Glycoprotein I antibody, each</td>
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<td>86147</td>
<td>Cardiolipin (phospholipid) antibody, each Ig class</td>
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<td>85302</td>
<td>Clotting inhibitors or anticoagulants; protein C, antigen</td>
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<td>88261</td>
<td>Chromosome analysis; count 5 cells, 1 karyotype, with banding</td>
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<td>88262</td>
<td>Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding</td>
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<td>88263</td>
<td>Chromosome analysis; count 45 cells for mosaicism, 2 karyotypes, with banding</td>
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**HCPCS © Codes** – No applicable codes.

**Covered ICD-10-CM Diagnosis Codes**

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<td>Recurrent pregnancy loss</td>
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<tr>
<td>O26.20</td>
<td>Pregnancy care for patient with recurrent pregnancy loss, unspecified trimester</td>
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<tr>
<td>O26.21</td>
<td>Pregnancy care for patient with recurrent pregnancy loss, first trimester</td>
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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

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal / state laws.

REFERENCES


MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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