Kansas City

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AmniSure® for Detection of Fetal Membrane Rupture

Policy Number: 2.04.505
Origination: 12/2009
Last Review: 12/2013
Next Review: 12/2014

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for AmniSure® (AmniSure International LLC) for detection of fetal membrane rupture. This is considered investigational.

When Policy Topic is covered

Not Applicable

When Policy Topic is not covered

The use of AmniSure® is considered **investigational** for all indications including but not limited to the detection of fetal membrane rupture.

Considerations

n/a

Description of Procedure or Service

During pregnancy, the fetal membrane protects the developing fetus and its surrounding fluid from infection. Although tearing or rupture of membranes (ROM) normally occurs during labor, in approximately 10% of pregnancies, this membrane ruptures before initiation of labor. For pregnancies that are at term (≥ 37 weeks of development), labor must be induced if it doesn't begin spontaneously within 24 hours after premature ROM (PROM). Fetal membrane rupture at < 37 weeks of development is referred to as premature preterm ROM (PPROM). PPROM management is much more complex and may require hospital admission to enable frequent monitoring for infection, prolapse or compression of the umbilical cord, and other potential dangers.

Although techniques such as vaginal examination with a sterile speculum and analysis of vaginal fluids have been developed to detect both premature rupture of membranes and premature preterm rupture of membranes, a speculum exam can cause patient discomfort and standard vaginal fluid analysis techniques may give inaccurate results. The AmniSure® test has been developed to detect fetal membrane rupture based on the presence of a specific placental protein in vaginal fluid. To perform this test, a swab is used to collect vaginal fluid; then the swab is rinsed in a premeasured volume of fluid in a vial supplied in the test kit. An AmniSure test strip is then inserted into the fluid, which is slowly absorbed as it travels up the test strip. The test can usually be read in 5 to 10 minutes. Formation of a dark stripe above the center of the test strip and a second dark stripe below the center of the strip indicates a positive test that is presumably due to fetal membrane rupture. Formation of a single dark stripe indicates a negative test. The AmniSure test is typically prescribed by an obstetrician and performed by an obstetric nurse.

Rationale

The literature search identified 4 studies that compared the AmniSure test with other methods for detection of fetal membrane rupture. Although 3 of these studies enrolled more than 100 patients, 2 of

the studies evaluated the AmniSure test in pregnant women who did not match the usual clinical criteria for assessing rupture of fetal membranes and another study evaluated an older form of the test.[2,4-6]

- Cousins et al. (2005) performed the largest available study[2] that evaluated the AmniSure test in women who had signs or symptoms of fetal membrane rupture. For this study, AmniSure testing was compared with standard speculum exam and vaginal fluid analysis procedures in 203 women at 15 to 42 weeks of gestation. Cousins et al. did not report any further demographic data such as mean maternal or fetal age. Based on the standard procedures, 89 (44%) women had fetal membrane rupture and the AmniSure test identified 86 of these women as having fetal membrane rupture, which corresponds to a test sensitivity of 97%. For the 114 (56%) women identified as not having fetal membrane rupture based on standard methods, the AmniSure test was negative for 110, which corresponds to a test specificity of 96%. To further investigate the 7 cases in which the AmniSure test disagreed with standard methods, repeat AmniSure and standard testing were performed with ultrasonography included for patients who had evidence of fetal membrane rupture based on standard testing. Although this confirmatory testing indicated that the AmniSure test was correct and standard testing incorrect in 6 (86%) of the 7 cases of discrepancies, the significance of this finding is difficult to interpret since membrane rupture may have occurred or worsened during the time interval between initial testing and repeat testing. A significant shortcoming of this study is that it evaluated a version of the AmniSure test that is no longer marketed, which involved use of a test slide rather than a test strip.
- Another study[4] in which the AmniSure test was evaluated in women who had signs or symptoms of fetal membrane rupture was performed by Lee et al. (2007). This study enrolled 184 pregnant women (mean fetal age 35.0 ± 0.5 weeks, range 11 to 42 weeks) who did not have active vaginal bleeding. No maternal demographics were reported. A patient was deemed to have a clinical diagnosis of fetal membrane rupture if leakage of amniotic fluid from the cervical os was observed during speculum exam or if any 2 of the following 3 tests were positive: nitrazine test, microscopic observation of ferning, or visible pooling of fluid in the posterior vaginal fornix. Based on these standard procedures, 139 (76%) women presented with fetal membrane rupture. AmniSure tests were positive for 137 of these women, which corresponds to a sensitivity of 99%. For the 45 (24%) women who did not have membrane rupture based on standard testing, AmniSure tests were negative for 21 women, which correspond to a specificity of 47%. The corresponding positive-predictive value (PPV) was 85% and the negative-predictive value (NPV) was 91%. Lee et al. reported a much higher specificity and PPV for AmniSure testing that was based on standard and AmniSure retesting performed 1 to 3 days after initial testing; however, this methodology is severely flawed since it ignores the strong possibility of new or increased membrane rupturing during the 1- to 3-day interval between initial and repeat testing.
- Lee et al. (2009) evaluated the AmniSure test in 206 pregnant women. Although this study[6] was larger than the studies described above, it did not involve AmniSure testing in women who had signs or symptoms of fetal membrane rupture, the primary population in which AmniSure testing would be performed. Absence of fetal membrane rupture was diagnosed based on a speculum exam, lack of pooling of fluid in the vaginal fornix, and negative nitrazine and ferning tests. The patients were divided into 2 groups, 125 women with full-term pregnancies who were undergoing elective Cesarean section or induction of labor (mean maternal age 30 ± 4 years, gestational age 40 ± 1 weeks, cervical dilation 0.4 ± 0.6 cm) and 81 women in labor (mean maternal age 30 ± 4 years, gestational age 40 ± 1 weeks, cervical dilation 2 ± 1 cm). The AmniSure test was positive for 6 (5%) of the 125 women not in labor and it was positive for 25 (31%) of the 81 women in labor. These findings presumably represent false-positive results of AmniSure testing; however, Lee et al. speculated that they might reflect the presence of microscopic ruptures in and/or transudation of amniotic fluid through the fetal membrane. For the 81 women in labor, there was a statistically significant correlation between a positive AmniSure test and shorter interval between admission and delivery (median 6.9 versus 9.8 hours) ($P<0.05$); however, the clinical significance of this finding is not clear.
- In a small study[5] that was sponsored by the AmniSure test manufacturer, Chen and Dudenhausen (2008) compared the AmniSure test with the Actim™ PROM test (Oy Medix Biochemica Ab) for detection of amniotic fluid as a means to detect fetal membrane rupture. The Actim PROM test is not approved for sale in the United States and it relies on detection of a different marker protein

than the AmniSure test detects. For this study, samples of amniotic fluid were collected from 20 pregnant women (median fetal age 38 weeks, range 31 to 41) who were undergoing elective Cesarean section. Serial 2-fold dilutions of the amniotic fluid were then analyzed to compare test sensitivity. Of 180 initial tests with each system, 22 (12%) AmniSure tests and 1 (1%) Actim PROM test failed. The primary reason for AmniSure test failure was insufficient wetting of the test strip, which was corrected by pushing the strip deeper into the fluid being tested. Chen and Dudenhausen reported that the mean sensitivity of the AmniSure test was 1 dilution (2-fold) higher than for the Actim PROM test (range 0-3 dilutions); however, the statistical significance of this finding was not reported. Furthermore, the testing process did not duplicate clinical testing conditions in which the amniotic fluid is mixed with vaginal secretions. In actual use, contaminants in the vaginal secretions may substantially alter the relative sensitivity of these 2 testing systems.

Summary

Results of the available studies fail to provide sufficient evidence that the AmniSure test has sufficient sensitivity and specificity for the diagnosis of fetal membrane rupture. Of the 4 available studies, 2 studies[5,6] enrolled patients who did not match the primary clinical criteria for use of the AmniSure test and a third study[2] used a version of the AmniSure test that is no longer commercially available. In the single study that used the current AmniSure test in an appropriate patient population, the AmniSure test had 99% sensitivity for detection of fetal membrane rupture; however, the AmniSure test had only 47% specificity due to a high incidence of false-positive results.[4] Additional data presented by these investigators suggest that false-positive results obtained with the AmniSure test may reflect microscopically ruptured or compromised fetal membranes that will rupture soon.[4,6] Further studies that compare the AmniSure test with standard diagnostic methods are needed to determine whether this test provides information that improves clinical management of pregnancy.

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Billing Coding/Physician Documentation Information

84112 Placental alpha microglobulin-1 (PAMG-1), cervicovaginal secretion, qualitative (effective 1/1/11)

Code S3628 was deleted effective 7/1/2011.

Additional Policy Key Words

N/A

Policy Implementation/Update Information

2/15/10 New policy; considered investigational, policy became effective 2/15/2010.
12/1/10 No policy statement changes.
12/1/11 No policy statement changes.
12/1/12 No policy statement changes.
12/1/13 No policy statement changes.