CMS Clarifies Bariatric Surgery Coverage Criteria

BY JOYCE FRIEDEN
Senior Editor

Medicare will not cover bariatric surgery for beneficiaries who have type 2 diabetes but do not have a body mass index greater than 35 kg/m^2, according to a proposed decision memo issued last month.

"While recent medical reports claimed that bariatric surgery may be helpful for these patients, [the Centers for Medicare and Medicaid Services] did not find convincing medical evidence that bariatric surgery improved health outcomes for non–morbidly obese individuals," according to a CMS statement.

Dr. Barry Straube, the agency's director of its Office of Clinical Standards and Quality, said, "Limiting coverage of bariatric surgery in type 2 diabetic patients whose BMI is less than 35 is part of Medicare's ongoing commitment to ensure access to the most effective treatment alternatives with good evidence of benefit, while limiting coverage where the current evidence suggests the risks outweigh the benefits." The proposal also clarifies that type 2 diabetes is one of the comorbidities that would be acceptable criteria for surgery.

In 2006, the CMS issued a national coverage decision for bariatric surgery in morbid obesity. That decision said that Medicare would cover only three procedures—open and laparoscopic Roux-en-Y gastric bypass surgery, open and laparoscopic biliopancreatic diversion with duodenal switch, and laparoscopic adjustable gastric banding—for beneficiaries who have a BMI greater than 35, have at least one comorbidity related to obesity, and have been previously unsuccessful with medical treatment for obesity.

At that time, the agency then asked for comments on whether Medicare should cover various gastric and intestinal bypass procedures to improve diabetes status among obese, overweight, and nonoverweight diabetes patients.

The proposed decision memo is an outcome of that query; the CMS accepted comments on the memo until mid-December. The agency then has up to 30 days to issue a final decision memo. (The proposed memo is available online at www.cms.hhs.gov/mcd/index_list.asp?list_type=nca; click on "Surgery for Diabetes.")

Dr. Jeffrey Mechanick, who cochaired a bariatric surgery guidelines committee for the American Association of Clinical Endocrinologists, said that the CMS was responding to a trend in the medical literature and meeting presentations suggesting that bariatric surgery might be helpful for even those diabetes patients who are not overweight.

"A lot of surgeons began noticing that after bariatric surgery, patients with diabetes had amelioration of their hyperglycemia," he said. "At first glance, it seems pretty easy—you lose weight and so your diabetes should be getting better. But they found that a lot of the improvement was independent of weight loss; there was something else."

The theories included two hypotheses: proximal changes, such as factors in the proximal small bowel, and distal changes, such as glucagonlike protein-1 and other factors made by the small bowel in the distal ileum, said Dr. Mechanick, who is also director of metabolic support in the division of endocrinology, diabetes, and bone disease at the Mount Sinai School of Medicine, in New York.

Dr. Mechanick noted that although the CMS currently is not covering the surgery for patients with a BMI under 35, that could change if long-term follow-up data on the procedure became available. ■

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BRIEF SUMMARY
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INDICATIONS AND USAGE
Mirena is indicated for intrauterine contraception for up to 5 years. Thereafter, if continued contraception is desired, the system should be replaced.
Mirena is recommended for women who have had at least one child.

CONTRAINDICATIONS
Mirena is contraindicated when one or more of the following conditions exist:
1. Pregnancy or suspicion of pregnancy.
2. Congenital or acquired uterine anomaly including fibroids if they distort the uterine cavity.
3. Acute pelvic inflammatory disease or a history of pelvic inflammatory disease unless there has been a subsequent intrauterine pregnancy.
4. Postpartum endometritis or infected abortion in the past 3 months.
5. Known or suspected uterine or cervical neoplasia or unresolved, abnormal Pap smear.
6. Genital bleeding of unknown etiology.
7. Untreated acute cervicitis or vaginitis, including bacterial vaginosis or other lower genital tract infections until infection is controlled.
8. Acute liver disease or liver tumor (benign or malignant).
9. Conditions associated with increased susceptibility to pelvic infections.
10. A previously inserted IUD that has not been removed.
11. Hypersensitivity to any component of this product.
12. Known or suspected carcinoma of the breast.

WARNINGS
1. Ectopic Pregnancy
Evaluate women who become pregnant while using Mirena for ectopic pregnancy. Up to half of pregnancies that occur with Mirena in place are ectopic. The incidence of ectopic pregnancy in clinical trials that excluded women with risk factors for ectopic pregnancy was about 1 ectopic pregnancy per 1000 users per year.
Tell women who choose Mirena about the risks of ectopic pregnancy, including the loss of fertility. Teach them to recognize and report to their physician promptly any symptoms of ectopic pregnancy. Women with a previous history of ectopic pregnancy, tubal surgery or pelvic infection carry a higher risk of ectopic pregnancy.
The risk of ectopic pregnancy in women who have a history of ectopic pregnancy and use Mirena is unknown. Clinical trials of Mirena excluded women with a history of ectopic pregnancy.

2. Intrauterine Pregnancy
If pregnancy should occur with Mirena in place, Mirena should be removed. Removal or manipulation of Mirena may result in pregnancy loss. In the event of an intrauterine pregnancy with Mirena, consider the following:
a. Septic abortion
In patients becoming pregnant with an IUD in place, septic abortion—with septicemia, septic shock, and death—may occur.
b. Continuation of pregnancy
If a woman becomes pregnant with Mirena in place and if Mirena cannot be removed or the woman chooses not to have it removed, she should be warned that failure to remove Mirena increases the risk of miscarriage, sepsis, premature labor and premature delivery. She should be followed closely and advised to report immediately any flu-like symptoms, fever, chills, cramping, pain, bleeding, vaginal discharge or leakage of fluid.
c. Long-term effects and congenital anomalies
When pregnancy continues with Mirena in place, long-term effects on the offspring are unknown. As of September 2006, 390 live births out of an estimated 9.9 million Mirena users had been reported. Congenital anomalies in live births have occurred infrequently. No clear trend towards specific anomalies has been observed. Because of the intrauterine administration of levonorgestrel and local exposure of the fetus to the hormone, the possibility of teratogenicity following exposure to Mirena cannot be completely excluded. Some observational data support a small increased risk of masculinization of the external genitalia of the female fetus following exposure to progestins at doses greater than those currently used for oral contraception. Whether these data apply to Mirena is unknown.

3. Sepsis
As of September 2006, 9 cases of Group A streptococcal sepsis (GAS) out of an estimated 9.9 million Mirena users had been reported. In some cases, severe pain occurred within hours of insertion followed by sepsis within days. Because death from GAS is more likely if treatment is delayed, it is important to be aware of these rare but serious infections. Aseptic technique during insertion of Mirena is essential. GAS sepsis may also occur postpartum, after surgery, and from wounds.

4. Pelvic Inflammatory Disease (PID)
Mirena is contraindicated in the presence of known or suspected PID or in women with a history of PID unless there has been a subsequent intrauterine pregnancy. Use of IUDs has been associated with an increased risk of PID. The highest risk of PID occurs shortly after insertion (usually within the first 20 days thereafter) (see **PRECAUTIONS, Insertion Precautions**). A decision to use Mirena must include consideration of the risks of PID.
a. Women at increased risk for PID
PID is often associated with a sexually transmitted disease, and Mirena does not protect against sexually transmitted disease. The risk of PID is greater for women who have multiple sexual partners, and also for women whose sexual partner(s) have multiple sexual partners. Women who have had PID are at increased risk for a recurrence or re-infection.
b. PID warning to Mirena users
All women who choose Mirena must be informed prior to insertion about the possibility of PID and that PID can cause tubal damage leading to ectopic pregnancy or infertility, or infrequently can necessitate hysterectomy, or cause death. Patients must be taught to recognize and report to their physician promptly any symptoms of pelvic inflammatory disease. These symptoms include development of menstrual disorders (prolonged or heavy bleeding), unusual vaginal discharge, abdominal or pelvic pain or tenderness, dyspareunia, chills, and fever.
c. Asymptomatic PID
PID may be asymptomatic but still result in tubal damage and its sequelae.
d. Treatment of PID
Following a diagnosis of PID, or suspected PID, bacteriologic specimens should be obtained and antibiotic therapy should be initiated promptly. Removal of Mirena after initiation of antibiotic therapy is usually appropriate. Guidelines for PID treatment are available from the Centers for Disease Control (CDC), Atlanta, Georgia.
Actinomycosis has been associated with IUDs. Symptomatic women with IUDs should have the IUD removed and should receive antibiotics. However, the management of the asymptomatic carrier is controversial because actinomycetes can be found normally in the genital tract cultures in healthy women without IUDs. False positive findings of actinomycosis on Pap smears can be a problem. When possible, confirm the Pap smear diagnosis with cultures.

5. Irregular Bleeding and Amenorrhea
Mirena can alter the bleeding pattern and result in spotting, irregular bleeding, heavy bleeding, oligomenorrhea and amenorrhea. During the first three to six months of Mirena use, the number of bleeding and spotting days may be increased and bleeding patterns may be irregular. Thereafter the number of bleeding and spotting days usually decreases but bleeding may remain irregular. If bleeding irregularities develop during prolonged treatment, appropriate diagnostic measures should be taken to rule out endometrial pathology.
Amenorrhea develops in approximately 20% of Mirena users by one year. The possibility of pregnancy should be considered if menstruation does not occur within six weeks of the onset of previous menstruation. Once pregnancy has been excluded, repeated pregnancy tests are generally not necessary in amenorrheic women unless indicated, for example, by other signs of pregnancy or by pelvic pain.

6. Embedment
Embedment of Mirena in the myometrium may occur. Embedment may decrease contraceptive effectiveness and result in pregnancy (see **WARNINGS, Ectopic Pregnancy** and **Intrauterine Pregnancy**). An embedded Mirena should be removed. Embedment can result in difficult removal and, in some cases surgical removal may be necessary.

7. Perforation
Perforation or penetration of the uterine wall or cervix may occur during insertion although the perforation may not be detected until some time later. If perforation occurs, pregnancy may result (see **WARNINGS, Ectopic Pregnancy** and **Intrauterine Pregnancy**). Mirena must be located and removed; surgery may be required. Delayed detection of perforation may result in migration outside the uterine cavity, adhesions, peritonitis, intestinal perforations, intestinal obstruction, abscesses and erosion of adjacent viscera.
The risk of perforation may be increased in lactating women, in women with fixed retroverted uteri, and during the postpartum period. To decrease the risk of perforation postpartum, Mirena insertion should be delayed a minimum of 6 weeks after delivery or until uterine involution is complete. If involution is substantially delayed, consider waiting until 12 weeks postpartum. Inserting Mirena immediately after first trimester abortion is not known to increase the risk of perforation, but insertion after second trimester abortion should be delayed until uterine involution is complete.

8. Expulsion
Partial or complete expulsion of Mirena may occur (see **PRECAUTIONS, Continuation and Removal**).
Symptoms of the partial or complete expulsion of any IUD may include bleeding or pain. However, the system can be expelled from the uterine cavity without the woman noticing it. Partial expulsion may decrease the effectiveness of Mirena. As menstrual flow typically decreases after the first 3 to 6 months of Mirena use, an increase of menstrual flow may be indicative of an expulsion. If expulsion has occurred, Mirena may be replaced within 7 days of a menstrual period after pregnancy has been ruled out.

9. Ovarian Cysts
Since the contraceptive effect of Mirena is mainly due to its local effect, ovulatory cycles with follicular rupture usually occur in women of fertile age using Mirena. Sometimes atresia of the follicle is delayed and the follicle may continue to grow. Enlarged follicles have been diagnosed in about 12% of the subjects using Mirena. Most of these follicles are asymptomatic, although some may be accompanied by pelvic pain or dyspareunia. In most cases the enlarged follicles disappear spontaneously during two to three months observation. Persistent enlarged follicles should be evaluated. Surgical intervention is not usually required.

10. Breast Cancer
Women who currently have or have had breast cancer, or have a suspicion of breast cancer, should not use hormonal contraception because breast cancer is a hormone-sensitive tumor.
Spontaneous reports of breast cancer have been received during postmarketing experience with Mirena. Because spontaneous reports are voluntary and from a population of uncertain size, it is not possible to use post-marketing data to reliably estimate the frequency or establish causal relationship to drug exposure. Two observational studies have not provided evidence of an increased risk of breast cancer during the use of Mirena.

11. Risks of Mortality
The available data from a variety of sources have been analyzed to estimate the risk of death associated with various methods of contraception. These estimates include the combined risk of the contraceptive method plus the risk of pregnancy or abortion in the event of method failure. The findings of the analysis are shown in Table 1.

Table 1: Annual Number of Birth-Related or Method-Related Deaths Associated with Control of Fertility per 100,000 Nonsterile Women, by Fertility Control Method According to Age

METHODS	AGE GROUP					
	15–19 years	20–24 years	25–29 years	30–34 years	35–39 years	40–44 years
No Birth Control Method/Term	4.7	5.4	4.8	6.3	11.7	20.6
No Birth Control Method/Abortion	2.1	2.0	1.6	1.9	2.8	5.3
IUD	0.2	0.3	0.2	0.1	0.3	0.6
Periodic Abstinence	1.4	1.3	0.7	1.0	1.0	1.9
Withdrawal	0.9	1.7	0.9	1.3	0.8	1.5
Condom	0.6	1.2	0.6	0.9	0.5	1.0
Diaphragm/Cap	0.6	1.1	0.6	0.9	1.6	3.1
Sponge	0.8	1.5	0.8	1.1	2.2	4.1
Spermicides	1.6	1.9	1.4	1.9	1.5	2.7
Oral Contraceptives	0.8	1.3	1.1	1.8	1.0	1.9
Implants/Injectables	0.2	0.6	0.5	0.8	0.5	0.6
Tubal Sterilization	1.3	1.2	1.1	1.1	1.2	1.3
Vasectomy	0.1	0.1	0.1	0.1	0.1	0.2

Harlap S. et al., *Preventing Pregnancy, protecting health: a new look at birth control choices in the US. The Alan Guttmacher Institute 1991: 1-129*

PRECAUTIONS
PATIENTS SHOULD BE COUNSELED THAT THIS PRODUCT DOES NOT PROTECT AGAINST HIV INFECTION (AIDS) AND OTHER SEXUALLY TRANSMITTED DISEASES.

1. Patient Counseling Information
Prior to insertion, give the patient the Patient Information Booklet. She should be given the opportunity to read the information and discuss fully any questions she may have concerning Mirena as well as other methods of contraception. Also, advise the patient that the prescribing information is available to her upon request.
Careful and objective counseling of the patient prior to insertion regarding the expected bleeding pattern, the possible inter-individual variation in changes in bleeding, including amenorrhea, and the etiology of the changes may have an effect on the frequency of patient-requested removal.
The patient should be informed that some bleeding such as irregular or prolonged bleeding and spotting, and/or cramps may occur during the first few weeks after insertion. If her symptoms continue or are severe she should report them to her healthcare provider. She should also be given instructions on what other symptoms require her to call her healthcare provider. She should be instructed on how to check after her menstrual period to make certain that the threads still protrude from the cervix and cautioned not to pull on the threads and displace Mirena. She should be informed that there is no contraceptive protection if Mirena is displaced or expelled.

2. Patient Evaluation and Clinical Considerations
a. A complete medical and social history, including that of the partner, should be obtained to determine conditions that might influence the selection of an IUD for contraception (see **CONTRAINDICATIONS**).
NOTE: Special attention must be given to ascertaining whether the woman is at increased risk of infection (for example, leukemia, acquired immune deficiency syndrome (AIDS), I.V. drug abuse), or has a history of PID unless there has been a subsequent intrauterine pregnancy. Mirena is contraindicated in these women.
b. A physical examination should include a pelvic examination, a Pap smear, examination of the breasts, and appropriate tests for any other forms of genital or other sexually transmitted diseases, such as gonorrhea and chlamydia laboratory evaluations, if indicated. Use of Mirena in patients with vaginitis or cervicitis should be postponed until proper treatment has eradicated the infection and until it has been shown that the cervicitis is not due to gonorrhea or chlamydia (see **CONTRAINDICATIONS**).
c. Irregular bleeding may mask symptoms and signs of endometrial polyps or cancer. Because irregular bleeding/spotting is common during the first months of Mirena use, exclude endometrial pathology prior to the insertion of Mirena in women with persistent or uncharacteristic bleeding. If unexplained bleeding irregularities develop during the prolonged use of Mirena, appropriate diagnostic measures should be taken. (See **WARNINGS, Irregular Bleeding and Amenorrhea.**)
d. **The healthcare provider should determine that the patient is not pregnant.** The possibility of insertion of Mirena in the presence of an existing undetermined pregnancy is reduced if insertion is performed within 7 days of the onset of a menstrual period. Mirena can be replaced by a new system at any time in the cycle. Mirena can be inserted immediately after first trimester abortion.
e. Mirena should not be inserted until 6 weeks postpartum or until involution of the uterus is complete in order to reduce the incidence of perforation and expulsion. If involution is substantially delayed, consider waiting until 12 weeks postpartum (see **WARNINGS, Perforation**).
f. Patients with certain types of valvular or congenital heart disease and surgically constructed systemic-pulmonary shunts are at increased risk of infective endocarditis. Use of Mirena in these patients may represent a potential source of septic emboli. Patients with known congenital heart disease who may be at increased risk should be treated with appropriate antibiotics at the time of insertion and removal.
g. Patients requiring chronic corticosteroid therapy or insulin for diabetes should be monitored with special care for infection.
h. Mirena should be used with caution in patients who have:
- coagulopathy or are receiving anticoagulants
- migraine, focal migraine with asymmetrical visual loss or other symptoms indicating transient cerebral ischemia
- exceptionally severe headache
- marked increase of blood pressure
- severe arterial disease such as stroke or myocardial infarction

3. Insertion Precautions
a. Observe strict asepsis during insertion. The presence of organisms capable of establishing PID cannot be determined by appearance, and IUD insertion may be associated with introduction of vaginal bacteria into the uterus. Administration of antibiotics may be considered, but the utility of this treatment is unknown.
b. Carefully sound the uterus prior to Mirena insertion to determine the degree of patency of the endocervical canal and the internal os, and the direction and depth of the uterine cavity. In occasional cases, severe cervical stenosis may be encountered. Do not use excessive force to overcome this resistance.
c. Fundal positioning of Mirena is important to prevent expulsion and maximize efficacy. Therefore, follow the instructions for the insertion carefully.
d. If the patient develops decreased pulse, perspiration, or pallor, have her remain supine until these signs resolve. Insertion may be associated with some pain and/or bleeding. Syncope, bradycardia, or other neurovascular episodes may occur during insertion of Mirena, especially in patients with a predisposition to these conditions or cervical stenosis.

4. Continuation and Removal
a. Reexamine and evaluate patients 4 to 12 weeks after insertion and once a year thereafter, or more frequently if clinically indicated.
b. If the threads are not visible, they may have retracted into the uterus or broken, or Mirena may have broken, perforated the uterus, or been expelled (see **WARNINGS, Perforation and Expulsion**). If the length of the threads has changed from the length at time of insertion, the system may have become displaced. Pregnancy must be excluded and the location of Mirena verified, for example, by sonography, X-ray, or by gentle exploration of the uterine cavity with a probe. If Mirena is displaced, remove it. A new Mirena may be inserted at that time or during the next menses if it is certain that conception has not occurred. If Mirena is in place with no evidence of perforation, no intervention is indicated.
c. Promptly examine users with complaints of pain, odorous discharge, unexplained bleeding (see **WARNINGS, Irregular Bleeding and Amenorrhea**), fever, genital lesions or sores.
d. Consider the possibility of ectopic pregnancy in the case of lower abdominal pain especially in association with missed periods or if an amenorrheic woman starts bleeding (see **WARNINGS, Ectopic Pregnancy**).
e. In the event a pregnancy is confirmed during Mirena use:
- Determine whether pregnancy is ectopic and, if so, take appropriate measures.
- Inform patient of the risks of leaving Mirena in place or removing it during pregnancy and of the lack of data on long-term effects on the offspring of women who have had Mirena in place during conception or gestation (see **WARNINGS, Intrauterine Pregnancy**).
- If possible, Mirena should be removed after the patient has been warned of the risks of removal. If removal is difficult, the patient should be counseled and offered pregnancy termination.
- If Mirena is left in place, the patient's course should be followed closely.

f. Should the patient's relationship cease to be mutually monogamous, or should her partner become HIV positive, or acquire a sexually transmitted disease, she should be instructed to report this change to her clinician immediately. The use of a barrier method as a partial protection against acquiring sexually transmitted diseases should be strongly recommended. Removal of Mirena should be considered.
g. Mirena should be removed for the following medical reasons:
- menorrhagia and/or metrorrhagia producing anemia
- acquired immune deficiency syndrome (AIDS)
- sexually transmitted disease
- pelvic infection; endometritis
- symptomatic genital actinomycosis
- intractable pelvic pain
- severe dyspareunia
- pregnancy
- endometrial or cervical malignancy
- uterine or cervical perforation

h. Removal of the system should also be considered if any of the following conditions arise for the first time:
- migraine, focal migraine with asymmetrical visual loss or other symptoms indicating transient cerebral ischemia
- exceptionally severe headache
- jaundice
- marked increase of blood pressure
- severe arterial disease such as stroke or myocardial infarction

i. Removal may be associated with pain and/or bleeding or neurovascular episodes.

5. Glucose Tolerance
Levonorgestrel may affect glucose tolerance, and the blood glucose concentration should be monitored in diabetic users of Mirena.

6. Drug Interactions
The influence of drugs on the contraceptive efficacy of Mirena has not been studied. The metabolism of progestogens may be increased by concomitant use of substances known to induce drug-metabolizing liver enzymes, specifically cytochrome P450 enzymes.

7. Carcinogenesis
Long-term studies in animals to assess the carcinogenic potential of levonorgestrel releasing intrauterine system have not been performed (see **WARNINGS**).

8. Pregnancy
Pregnancy Category X (see **WARNINGS**).

9. Nursing Mothers
In general, no adverse effects have been found on breastfeeding performance or on the health, growth, or development of the infant. However, isolated post-marketing cases of decreased milk production have been reported. Small amounts of progestins pass into the breast milk of nursing mothers, resulting in detectable steroid levels in infant plasma. Also, see **WARNINGS, Perforation.**

10. Pediatric Use
Safety and efficacy of Mirena have been established in women of reproductive age. Use of this product before menarche is not indicated.

11. Geriatric Use
Mirena has not been studied in women over age 65 and is not currently approved for use in this population.

12. Return to Fertility
About 80% of women wishing to become pregnant conceived within 12 months after removal of Mirena.

ADVERSE REACTIONS
The most serious adverse reactions associated with the use of Mirena are discussed above in the **WARNINGS** and **PRECAUTIONS** sections. Very common adverse reactions (>1/10 users) include uterine/vaginal bleeding (including spotting, irregular bleeding, heavy bleeding, oligomenorrhea and amenorrhea) and ovarian cysts. Other adverse events are listed below using MedDRA (9.0) terms. Adverse reactions reported by 5% or more of clinical trial subjects include:
Abdominal/pelvic pain
Vaginal discharge
Nausea
Headache
Nervousness
Vulvovaginitis
Dysmenorrhea
Back pain
Weight increase
Breast pain/tenderness
Acne
Decreased libido
Depressed mood
Cervicitis/Papanicolaou smear normal, class II
Hypertension
Other relevant reported adverse reactions occurring in less than 5% of subjects include: migraine, vomiting, anemia, dyspareunia, alopecia, eczema, pruritus, rash, urticaria, abdominal distension, altered mood, hirsutism, edema.

Postmarketing Experience
The following adverse reactions have been identified during post approval use of Mirena: device breakage and angioedema. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

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