ETHICON
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IMPORTANT CUSTOMER COMMUNICATION
ETHICON Morcellation Devices
Product Codes MX0100, MX0200, MX0100R, MX0200R, DV0015, DV0025, MD0100, MD0200, MD0140, MD0120

April 30, 2014

Dear Healthcare Provider,

PLEASE DISTRIBUTE THIS INFORMATION TO ALL STAFF WITHIN YOUR FACILITY WHO USE ETHICON Morcellation Devices

At Ethicon, our first priority is to our customers and patients. We are committed to ensuring the safe and effective use of our products. We would like to make you aware that US FDA issued a Safety Communication on April 17, 2014 regarding Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy. The FDA Safety Communication informs health care practioners and patients that:

> "When used for hysterectomy or myomectomy in women with uterine fibroids, laparoscopic power morcellation poses a risk of spreading unsuspected cancerous tissue, notably uterine sarcomas, beyond the uterus. Health care providers and patients should carefully consider available alternative treatment options for symptomatic uterine fibroids. Based on currently available information, the FDA discourages the use of laparoscopic power morcellation during hysterectomy or myomectomy for uterine fibroids".

Based on this Safety Communication, in order to align with the FDA's recommendation and Ethicon's internal investigations, Ethicon has decided to suspend global commercialization (sales, distribution, and promotion) of its Morcellation Devices until the role of morcellation for patients with symptomatic fibroid disease is further redefined by FDA and the medical community. The April 17, 2014 FDA safety communication can be found on the FDA website at:

http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm393576.htm

This is **not** a product removal. This letter is sent to reinforce the FDA Safety Communication issued on April 17, 2014. The FDA has been notified of this letter.

Uterine fibroids (leiomyomas) represent the most common tumor in women. By the time they reach 50 years of age, as many as 70% to 80% of women will have had at least one fibroid; severe symptoms develop in 15 to 30% of these women [Bulun E. 2013].

As pointed out by FDA in its Safety Communication, many women choose to undergo laparoscopic hysterectomy or myomectomy because these procedures are associated with benefits such as a shorter post-operative recovery time and a reduced risk of infection compared to abdominal hysterectomy and myomectomy. Many of these laparoscopic

procedures have been made possible due to the availability of morcellation devices. Approximately 200,000 hysterectomies, 30,000 myomectomies, and thousands of selective uterine-artery embolizations and high-intensity focused ultrasound procedures are performed annually in the United States to remove or destroy uterine fibroids [Wu JM. et al. AJOG 2007]. Some of these procedures are performed laparoscopically using power morcellators. Morcellation may pose a risk of spreading cancerous tissue beyond the uterus. Ethicon morcellators have always carried cautionary language concerning the use of the device for morcellation of malignant tissue or tissue suspected of being malignant and dissemination of malignant tissue. Several studies have reported on the impact that tissue morcellation may impose on patients in whom uterine malignancy was found unexpectedly on post-operative histologic diagnosis. Perri T. et al., Park JY. Et al. and Oduyebo T. et al. describe an adverse effect while Morice P. et al., did not find a difference in disease free or overall survival rates [Perri T. 2009, Park JY. 2011, Oduyebo T. 2014, Morice P. 2003].

Uterine leiomyosarcoma is a rare but highly malignant disease accounting for 1.5% of all uterine malignancies and 30% of uterine sarcomas. Complete surgical excision of non-metastasized leiomyosarcoma is the only established curative treatment. Although this particular uterine malignancy is rare, statistics about just how many women in whom surgical treatment is considered may be at risk vary widely depending on the source and interpretation of the current literature (see table below). Kho K and Nezhat C. in a recent viewpoint on evaluating the risks of electric uterine morcellation stated that “pooling the data for a single risk estimate is complex and prone to error given the heterogeneity of the data, including the populations examined, and likelihood of publication bias” [Kho KA. 2014].

The FDA Safety communication cites the list of studies below and calculated that the rate of leiomyosarcoma in patients undergoing hysterectomy and myomectomy for fibroids was 1 in 498, and the rate for unsuspected uterine sarcoma was 1 in 352.

Author	Year published	Review period	No Patients	Uterine sarcoma N (%)	Leiomyosarcoma N (%)
Leibsohn et al.	1990	1983–1988	1429	7 (0.49)	7 (0.49)
Reiter et al.	1992	1986-1989	104	0	0
Parker et al.	1994	1988–1992	1332	3 (0.23)	1 (0.08)
Takamizawa et al.	1999	1983 – 1997	923	2 (0.22)	1 (0.11)
Sinha et al.	2008	1998-2005	505	2 (0.4)	2 (0.4)
Kamikabeya et al.	2010	1987-2008	1364	2 (0.15)	1 (0.07)
Rowland et al.	2011	2006-2011	1115	5 (0.45)	3 (0.27)
Leung et al.	2012	1996–2005	1297	3 (0.23)	3 (0.23)
Seidman et al.	2012	2005–2010	1091	2 (0.18)	1 (0.09)
Total			9160	26 (0.28)	19 (0.21)

Further compounding the situation is the difficulty in pre-surgical diagnosis of leiomyosarcoma, when compared to other gynecologic malignancies such as endometrial cancer [AAGL Member Update: Disseminated Leiomyosarcoma with Power Morcellation-Update #2].

The FDA issued a safety communication on April 17, 2014 discouraging the use of laparoscopic power morcellation during hysterectomy or myomectomy for uterine fibroids. In an effort to enhance understanding of the issue and provide information on the appropriate use of laparoscopic power morcellators, the FDA will convene a public meeting of the Obstetrics and Gynecological Medical Device Advisory Committee.

As a manufacturer of tissue morcellation devices, we are committed to provide health care providers with information relating to the safe and effective use of our products. Patients and doctors should discuss risks and benefits of alternatives for all procedures so that a patient is able to make an informed and voluntary decision about accepting or declining medical care [ACOG Committee Opinion 439 Informed Consent]. Until recently women were commonly advised that the risk of malignancy in a fibroid is 1 in 10,000 [Hampton T. 2014]. This rate is currently under debate.

We agree that in light of the above, the treatment algorithm of a patient confronted with symptomatic fibroid disease warrants re-evaluation. Pre-operative assessment to establish the risk of malignancy could possibly be refined. A guideline regarding preoperative workup of patients scheduled for uterine morcellation was suggested by Hagemann IS. et al. including: a Pap smear test, an endometrial biopsy and a pelvic MRI or ultrasound. [Hageman IS. 2011] Goto a. et al among others has studied the possible role magnetic resonance imaging (MRI) could have. [Goto A. 2002].

Also, as all epidemiological data sets are retrospective in nature, some going back as early as 1983, real life data from a prospective registry may shed new light on the actual incidence in the sub-population at hand. The AAGL in their second member update (March 25, 2014) stated that: “Through ACAR (the AAGL Consortium of Advanced Research), clinical questions related to issues such as disease incidence and pre-operative diagnosis can be addressed”.

The evaluation of the treatment algorithm must also include assessment of optimal safe use of the morcellators during these procedures including mitigation techniques such as the use of morcellation bags or other closed systems to eliminate or limit tissue dissemination, and appropriate perioperative tissue handling and irrigation.

We have decided to suspend the commercialization of our morcellation products until their role is redefined in an updated treatment guideline for patients with symptomatic fibroid disease. We remain committed to advancing the treatment options for women and will actively continue to gather knowledge to assess and reduce the risks associated with powered morcellation. We will also follow the evolving guidance from surgical authorities and regulators on how to optimize safe and effective use of our devices.

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<u>Actions requested on your part</u>: Distribute this notice to all users of Ethicon Morcellation Devices in your facility.

If you have any questions related to this notice, please contact XXXXXXXXXX.

Thank you for your attention and cooperation.

Sincerely,

Ethicon, Inc.

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