Agence nationale de sécurité du médicament et des produits de santé

Surgical mesh implants for treatment of urinary incontinence and pelvic organ prolapse

ANSM review of French market between 2014 and 2017

November 2018

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Summary

Introduction

This market review concerns surgical mesh implants intended for the treatment of urinary incontinence and pelvic organ prolapse.

Female urinary incontinence is the involuntary loss of urine, especially upon physical stress. This condition, which studies have shown to affect between 25% and 40% of all women, has a major effect on sleep and quality of life, including sex life. Known risk factors in women include multiple deliveries, obstetric trauma, and pelvic surgery. Only 10%–15% of all cases of urinary incontinence are treated. Urinary incontinence may be classified as either urge or stress incontinence. Treatment for stress incontinence is adapted to the degree of patient discomfort. It may consist in re-education, injection of urethral bulking agents, or surgical treatment by a urologist or gynaecologist. The most common surgical treatment for stress incontinence is the vaginal insertion of surgical mesh implants called suburethral slings. Other implants used as second-line treatments are periurethral balloons or artificial urinary sphincters. There are also slings for the treatment of male urinary incontinence.

Pelvic organ prolapse is a hernia, via the vaginal (or more rarely anal) orifice, involving one or more abdominopelvic organs. It may affect the anterior (bladder), medial (uterus or back of vagina), or posterior (rectum and pouch of Douglas) compartment. Available treatments include re-education, pessaries, and surgical treatment, with or without insertion of surgical mesh implants. The medical practitioners involved in such treatments may be urologists, gynaecologists, or gastrointestinal surgeons. Two alternative surgical routes are adopted:
– transabdominal, often carried out laparoscopically
– transvaginal.

Over the last few years, pelvic organ surgical mesh implants have been the subject of several assessments by public institutes around the world. These devices apparently cause sometimes serious complications, like postoperative pain, implant extrusion, erosion of surrounding tissues, and infections.

In 2014, Medicine and Healthcare products Regulatory Agency (MHRA), the competent authority for medical devices in the United Kingdom, did not call into question the risk-benefit balance of vaginally inserted support devices to date, but did request that new clinical studies be conducted.

In a 2015 report, the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) indentified that surgical mesh implants for the treatment of urinary incontinence or prolapse are associated with different risks, depending on device technical characteristics and route of insertion.

In 2016, US Food and Drug Administration (FDA) reclassified vaginally inserted surgical mesh implants for the treatment of prolapse, moving them from Class II to Class III. This means that post–market approval (PMA) must be granted from the FDA before such devices may be placed on the US market.

In late 2017, Britain's National Institute for Health and Care Excellence (NICE), which supervises clinical practices, stated that surgical procedures for the treatment of vaginal wall prolapse by insertion of surgical mesh implants should be conducted within the scope of clinical research. At the same time, the Australian Therapeutic Goods Administration (TGA), the country's competent authority for medical devices, withdrew vaginally inserted surgical mesh implants for the treatment of prolapse from its register of therapeutic products.

Very recently—in July 2018—the British government and the UK National Health Service (NHS) accepted the recommendation from the Independent Medicines and Medical Devices Safety Review (IMMDSR) to pause the use of vaginally inserted surgical mesh implants (specifically, slings for stress incontinence

treatment and implants for pelvic organ prolapse treatment) to reduce the risk of injury linked to surgical procedures. The adoption of the IMMDSR recommendation was paired with a reinforced monitoring programme that aims to channel the medical use of these devices by requiring appropriate medical training and experience, report of every surgical procedures to a national database, establishment of specialist centres, reporting of complications via MHRA, and application of NICE guidelines, among other measures. In the following days, the Irish health ministry adopted a similar policy. An action plan calls for the drafting of recommendations on surgeon training, informed consent from women before surgery, and a registry of surgical procedures performed.

In France, between 2012 and July 2018, 47 vigilance reports were filed with ANSM in connection with surgical mesh implants used to treat pelvic organ prolapse (transvaginal or transabdominal route). This is a relatively small number if we consider that approximately 18,000 devices are used in France each year (between 2014 and 2018). Of these 47, only 17 concerned effects on the female patients. For slings used in the treatment of female urinary incontinence, there were 122 reported incidents between 2014 and 2017 (during which period annual sales exceeded 32,000), including 29 concerning effects on the patients.

In 2016, ANSM undertook a market review for all surgical mesh implants on the French market used in the treatment of urinary incontinence and pelvic organ prolapse. The goals were to acquire an overview of the French market and to obtain data on technical characteristics and clinical evaluations of the devices from the economic operators (i.e. manufacturers, their authorized representatives, and distributors). Finally, an analysis was conducted on withdrawals of such devices from the market between 2014 and 2017.

This report presents the analysis of the data for these medical devices.

Methodology

ANSM first sought to identify the economic operators marketing such medical devices on the French market. Among the main sources of information were French database of medical devices placed on the market, manufacturers' websites, advertisements, and data from specialists' conferences. In all, 21 companies were identified.

In July 2016, these firms were surveyed about all of the surgical mesh implants for urinary incontinence and pelvic organ prolapse that were placed on the French market. They were asked on technical data, vigilance data, and clinical evaluation. In February 2018, they were again surveyed by ANSM for updates, namely data on sales volumes for 2016 and 2017.

The data collected cover the period from 2014 to 2017. Analyses excluded data for devices not on the French market in July 2016 and for other kind of devices (e.g. sutures, bulking agents, ancillary components).

It is important to note that this market review considers devices marketed in France and intended for these indications by their manufacturers. It does not account for the adaptation of surgical mesh implants not specifically intended for the treatment of urinary incontinence or pelvic organ prolapse, in the operating room, according to patients' characteristics.

When devices of identical design from the same manufacturer were sold under different proprietary names, their data were aggregated. Analyses considered surgical mesh implants for the treatment of female stress incontinence, surgical mesh implants for the treatment of male urinary incontinence, and surgical mesh implants for pelvic organ prolapse, distinguishing between transabdominal and transvaginal implants.

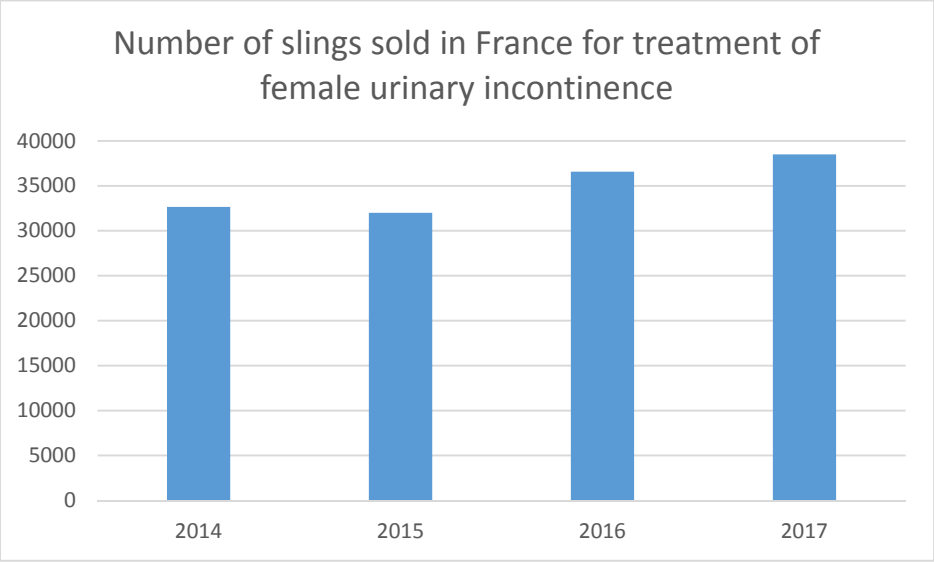
The analysis of data collected from the firms is merely descriptive.

Results and discussion

Slings for treatment of female urinary incontinence

In July 2016, ANSM identified 37 ranges of slings intended for the treatment of female urinary incontinence on the French market, manufactured by 15 different companies. A new model launched onto the market in 2017 was not taken into account (see FUI appendix).

The number of devices sold annually in France has been rising since 2014, reaching a volume of over 38,000 in 2017 (see FUI appendix).



Of the top 6 manufacturers by sales in 2017, the leading firm has got about 30% of total market sales, and the next 5 each account for 10%–15%. Together, these 6 manufacturers thus represent about 90% of all device sales in 2017.

For 98% of the devices sold in 2017, the first CE marking had been granted by 2011 or before, affording a relatively large period for the evaluation of these devices (see FUI appendix).

All medical devices sold in France are transvaginal implants made of monofilament polypropylene.

According to the data provided by the relevant firms for this market review, clinical evaluation has been performed for all devices, whether based on equivalent or specific clinical data. For 98% of the devices sold, the firms responded that specific clinical data (i.e. from studies with the specific device itself, implanted in women) were available. However, one manufacturer did not provide to ANSM the relevant specific clinical data for the devices (accounting for approximately 0.2% of all slings sold in France in 2017). This company has since decided to stop marketing these slings.

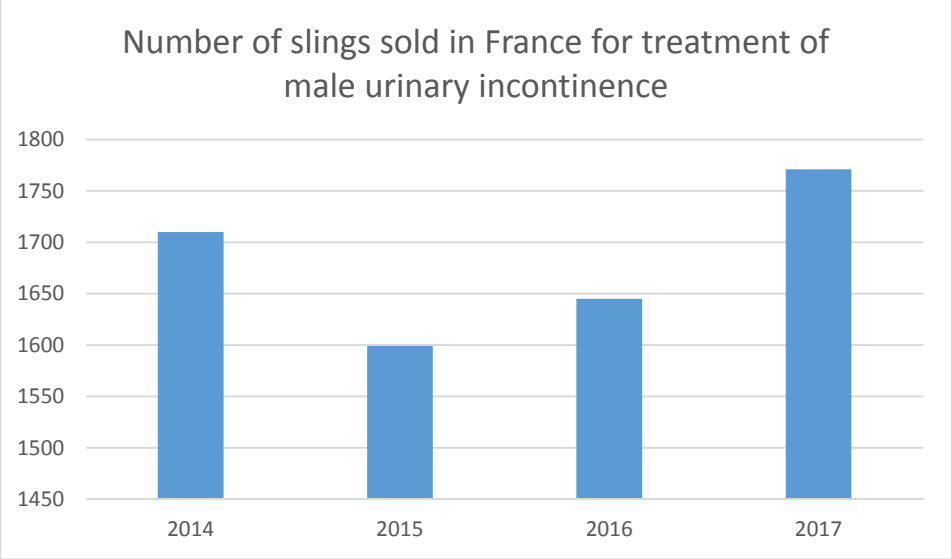
For all slings sold in France in 2017 with specific clinical evaluation claimed by their manufacturers—totalling 37,633 units sold—the quantitative analysis of the clinical studies cited by these firms is as follows:

- approximately 25% of these slings were the focus of over 10 specific clinical studies,
- nearly 90% were tested in more than 500 women (sum of all women having participated in the clinical studies),
- for nearly 95%, data from comparative clinical studies are available,
- for nearly 80%, follow-up of implanted women in the clinical studies lasted for at least 2 years.

Slings for treatment of male urinary incontinence

In July 2016, ANSM identified 6 ranges of sling intended for the treatment of male urinary incontinence on the French market, manufactured by 6 different firms (see MUI appendix).

The number of devices sold annually in France since 2014 seems to have risen in 2017, reaching a volume of over 1,700 devices. One of these manufacturers accounts for 40% of all devices sold in 2017 (see MUI appendix).



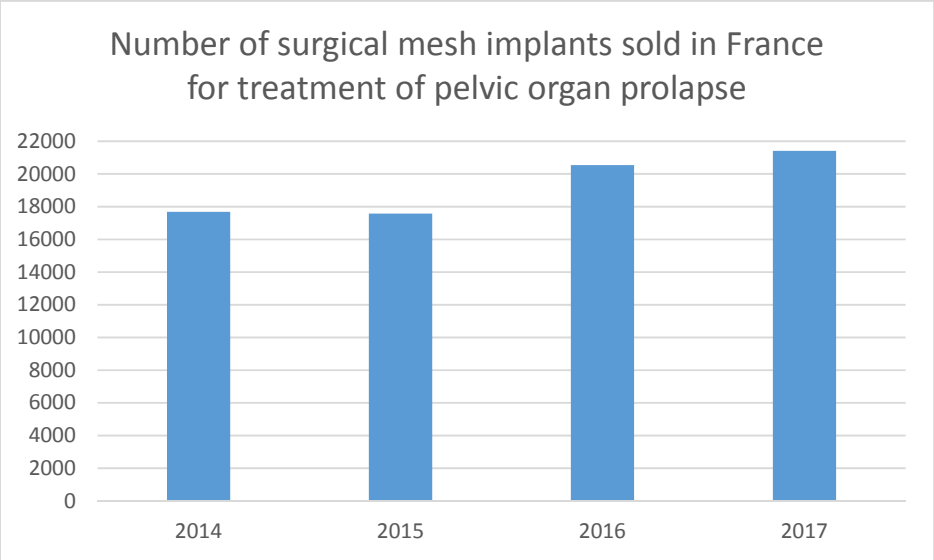
For all of these devices sold in France, the first CE marking had been granted by 2011 or before (see MUI appendix). They are all transvaginal implants made of monofilament polypropylene.

According to the information provided by the pertinent firms for this market review, clinical evaluation has been performed for all devices. These firms also responded that specific clinical data were available for each of the devices.

Surgical mesh implants for treatment of pelvic organ prolapse

In July 2016, ANSM identified 59 ranges of surgical mesh implant intended for the treatment of pelvic organ prolapse on the French market, manufactured by 18 different firms (see POP appendix).

The number of devices sold annually in France has risen since 2014, reaching a volume of over 21,000 in 2017 (see POP appendix).

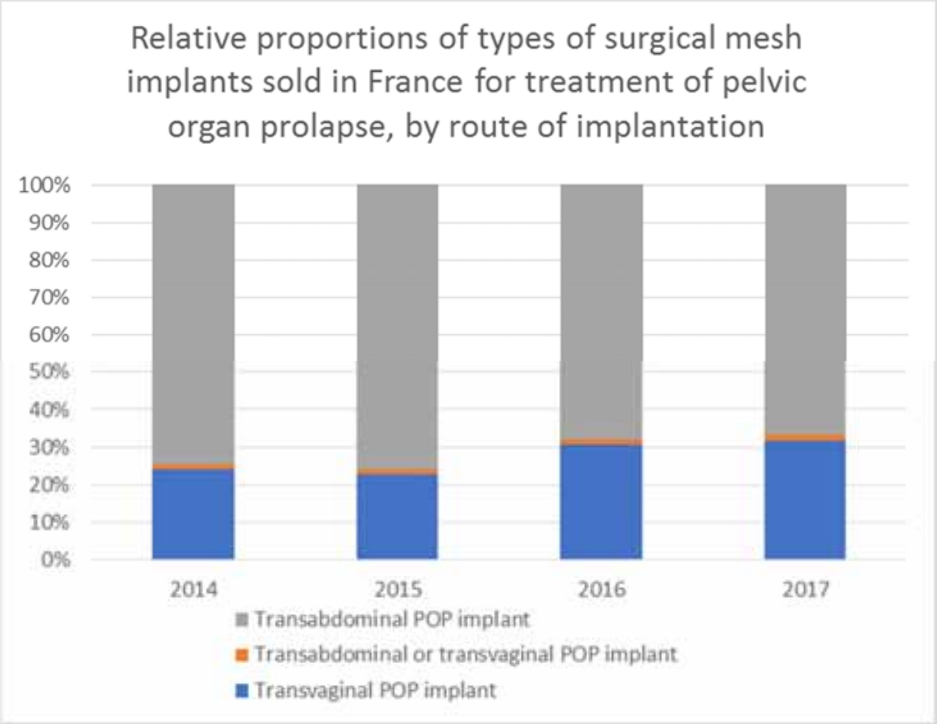


The top 7 firms by 2017 sales volumes accounted for approximately 85% of devices sold that year.

For 90% of the devices sold in 2017, the first CE marking had been granted by 2011 or before, which provides a relatively large period for the evaluation of medical devices in general (see POP appendix).

The remaining analyses consider the route—transabdominal or transvaginal—for insertion of the surgical mesh implants. For some devices, both routes are possible.

We noted an upward trend in the proportion of transvaginal devices from 2014 to 2017. In 2017, approximately 30% of all surgical mesh implants sold in France were transvaginal.



All transvaginal surgical mesh implants sold in France in 2017 are made of monofilament propylene. Less than 2% of the devices sold also contained either titanium or a substance of animal origin.

Transabdominal surgical mesh implants sold in France in 2017 vary more in their composition and structure. Materials used include polypropylene, polyester, polyethylene terephthalate, and tissue of animal origin. The implants may be constructed of monofilament or multifilament.

According to the data provided by the pertinent firms for this market review, clinical evaluation has been performed for all transvaginal devices, whether based on equivalent or specific clinical data.

The manufacturers of 3 ranges of transabdominal surgical mesh implants did not claim these devices were the subject of any clinical evaluation (considering equivalent or specific data). These firms did not provide any clinical data. Their products represent 1% of all transabdominal surgical mesh implants sold in France in 2017. They will be the focus of further investigations by ANSM.

For over 80% of the devices sold—transabdominal or transvaginal devices—the firms responded that specific clinical data (i.e. from studies of the specific device itself, implanted in women) were available. These data were supplied to ANSM for all but 3 ranges of surgical mesh implants. These 3 ranges are, moreover, no longer on the market.

For all devices sold in France in 2017 with specific clinical evaluations claimed by their manufacturers—accounting for 17,609 units sold, transabdominal or transvaginal devices—the quantitative analysis of the clinical studies cited by these firms is as follows:

- approximately 1% of the transvaginal implants and 12% of the transabdominal implants were each the focus of over 5 specific clinical studies,

- approximately 45% of the transvaginal implants and 13% of the transabdominal implants were tested in more than 500 women (sum of all women having participated in the clinical studies),
- for 28% of the transvaginal implants and 55% of the transabdominal implants, comparative clinical study data are available,
- for 84% of the transvaginal implants and 56% of the transabdominal implants, follow-up of implanted women in the clinical studies lasted for at least 2 years,
- for over a third of the transvaginal implants, clinical studies were conducted before the granting of CE marking, which is not true of transabdominal implants, for which no study was conducted before the granting of the CE marking,
- for over 80% of the implants, transvaginal or transabdominal devices, clinical studies were conducted after the granting of the CE marking.

Stop of placing this kind of medical devices on the market between 2014 and 2017

Two manufacturers were not taken into account for this market review because their products were no longer on the French market in July 2016, due to complete stop of placing their devices for the treatment of urinary incontinence and pelvic organ prolapse on the market between 2014 and 2016.

Of those manufacturers with products on the French market in July 2016 whose data were taken into account for this market review, 6 nevertheless stopped commercialization of products: 2 stopped placing any medical device of this kind on the market after July 2016, and the 4 others narrowed their product ranges between 2014 and 2017. These stops of commercialisation, over half of which occurred in 2016, concerned 21 ranges of devices varying in their indications (urinary incontinence in men or women, pelvic organ prolapse) and route of insertion (transabdominal or transvaginal).

The motives for these stops of commercialisation are unknown, but it is possible that the end of certification activity by some notified bodies in 2016 and the tightening of requirements by other notified bodies had an impact.

Furthermore, over the same period (2014–2017), only 9 new medical device ranges were launched onto the French market: 8 by July 2016 or before, 1 after. We may thence deduce that there is a downward trend in the number of ranges of this kind of devices on the French market.

Conclusion

The vast majority of surgical mesh implants intended for the treatment of female urinary incontinence and pelvic organ prolapse that were sold in France in 2016 were placed on the market before 2011.

From a global perspective, sales volumes for these devices are actually growing, in spite of stops of commercialisation that mainly occurred in 2016.

They are made with materials recognized as biocompatible for these indications.

According to data provided by the economic operators, clinical evaluation has been performed for nearly all of the devices (>99%) sold in 2017, no matter the indications of use, which is based on either equivalent or specific data. The firms involved declared that specific clinical data were available for over 90% of the devices sold in 2017. ANSM has nevertheless singled out particular devices for deeper investigation into their clinical evaluation.

Verification of device performance and safety on the basis of these clinical data was beyond the scope of this market review. Nevertheless, the verification of such data as part of the CE marking process is one of the responsibilities of the notified bodies.

Few vigilance reports were filed with ANSM. However, these devices—especially transvaginal implants for the treatment of pelvic organ prolapse—apparently cause sometimes serious complications, like postoperative pain, implant extrusion, erosion of surrounding tissues, and infections.

In some countries, the use of surgical mesh implants for the treatment of urinary incontinence or pelvic organ prolapse—especially transvaginal implants—is under scrutiny or subject to oversight or restrictions through measures recently taken by national institutions that primarily target surgical practices. Though this market review shows that clinical data are available for surgical mesh implants used to treat urinary incontinence and those used to treat pelvic organ prolapse, one cannot overlook the many questions now being considered internationally.

Various registries that have been created at the initiative of scientific organizations should provide answers over time, particularly with regards to clinical practices (i.e. consistency of indications for surgery, choice and quality of surgical technique, and monitoring of implanted patients).

ANSM is keeping abreast of debates on these questions and pursuing closer monitoring of these medical devices in France, especially following the apparent restructuring of the market in or around 2016.

FUI appendix: Data on slings for treatment of female urinary incontinence

List of sling product ranges for treatment of female urinary incontinence on French market in July 2016, by manufacturer, indicating year of first CE marking

	First CE marking
A.M.I	
TOA / TVA Multi-Purpose-Sling sensiTVT	2005
ABISS	
ARIS	2004
CYRENE	2008
MINI SAS	2008
SUPRIS	2013
Aspide Médical	
SLING	2006
UU SLING	2009
Bard Medical Inc.	
Ajust	2008
Align	2007
Boston Scientific	
ADVANTAGE	2003
CONSERVIA TO/SP	2015
CONSERVIA TV	2015
LYNX	2004
OBTRYX	2004
OBTRYX II	2012
SOLYX (SIS)	2008
CL Medical	
I-STOP	2002
Coloplast	
ALTIS	2011
COUSIN BIOTECH	
LIFT	2002
SOFT LIFT	2005
DIPROMED	
IGSD1245IO-EL	2008
IGSD1245WSIO-EL	2008
IGSD1250	2008
IGSD1250EL	2008
ETHICON	
GYNECARE TVT™ ABBREVO™	2010
GYNECARE TVT™ DEVICE	2006

GYNECARE TVT™ EXACT™	2010
GYNECARE TVT™ Obturator System	2006
MICROVAL	
SAFIRE / SMILE / SWIFT SLING	2007
NEOMEDIC	
KIM	2006
NEEDLELESS	2006
REMEEX FEMME	2004
PROMEDON	
OPHIRA	2008
UNITAPE	2006
SOFRADIM / MEDTRONIC	
UretexTM	2000
THT	
JUST-SWING SVS	2008
SWING-BAND SB4	2008

Slings for treatment of female urinary incontinence sold in France between 2014 and 2017

Number of slings sold in France	**2014**	**2015**	**2016**	**2017**
Total	**32 655**	**32 000**	**36 572**	**38 477**

MUI appendix: Data on slings for treatment of male urinary incontinence

List of sling product ranges for treatment of male urinary incontinence on French market in July 2016, by manufacturer, indicating year of first CE marking

	First CE marking
Aspide Médical	
M-SLING	2009
Boston Scientific	
ADVANCE MALE SLING SYSTEM	2006
CL Medical	
I-STOP TOMS	2006
Coloplast	
VIRTUE	2011
NEOMEDIC	
REMEEX HOMME	2004
THT	
SWING-BAND SB3	2008

Slings for treatment of male urinary incontinence sold in France between 2014 and 2017

Number of slings sold in France	**2014**	**2015**	**2016**	**2017**
Total	**1 134**	**1 083**	**1 052**	**1 355**

POP appendix: Data on surgical mesh implants for treatment of pelvic organ prolapse

List of surgical mesh implant product ranges for treatment of pelvic organ prolapse on French market in July 2016, by manufacturer, indicating year of first CE marking and route of surgical insertion

	Route of insertion	First CE marking
A.M.I		
BSC Mesh	Transvaginal	2012
CR-Mesh	Transvaginal	2008
EndoGYNious	Transabdominal	2013
InGYNious	Transvaginal	2012
PelviGYNious	Transabdominal	2014
ABISS		
NOVASILK / URAFLOR	Transvaginal or transabdominal	2006
OPUR	Transvaginal	2010
Aspide Médical		
Kit UU cystocèle Transvaginal	Transvaginal	2012
Cystocèle / Rectocèle Transabdominal	Transabdominal	2007
Cystocèle Transvaginal	Transvaginal	2006
Cystocèle Transabdominal	Transabdominal	2005
Rectocèle Transvaginal	Transvaginal	2006
Rectocèle Transabdominal	Transabdominal	2006
Bard Medical Inc.		
Alyte	Transabdominal	2009
Avaulta Plus	Transvaginal	2007
Avaulta Solo	Transvaginal	2007
Nuvia	Transvaginal	2011
Boston Scientific		
PINNACLE LITE	Transvaginal	2014
POLYFORM	Transvaginal or transabdominal	2005
UPHOLD LITE	Transvaginal	2013
UPSYLON	Transabdominal	2013
XENFORM	Transvaginal	2007
CL Medical		
Pelvi-STOP	Transabdominal	2008
Coloplast		
RESTORELLE	Transabdominal	2011
RESTORELLE DIRECTFIX	Transvaginal	2011

COUSIN BIOTECH		
BIOMESH ®SOFT PROLAPS (RECTO)	Transvaginal	2006
BIOMESH® SOFT PROLAPS (CYSTO)	Transvaginal	2006
SACROMESH ®SOFT PROLAPS	Transabdominal	2005
DIPROMED		
CSP0517	Transabdominal	2008
IGPELB1524	Transvaginal or transabdominal	2008
IGPELB18348	Transabdominal	2008
IGPROAML	Transvaginal	2008
IGPROPML	Transvaginal	2008
ETHICON		
GYNECARE GYNEMESH™ PS GPSL	Transabdominal	2003
GYNECARE GYNEMESH™ PS GPSXL3	Transabdominal	2003
I.B.I Israel Biomedical Innovations Ltd.		
Endofast Reliant SCP	Transabdominal	2013
Endofast Reliant System	Transvaginal	2007
MECCELLIS BIOTECH		
CELLIS CR618EP	Transabdominal	2015
MICROVAL		
GYNE-PRO	Transabdominal	2004
PROCUR	Transabdominal	2004
PROLAFIX	Transabdominal	2004
PROLAFIX-V	Transvaginal	2009
S-SWIFT	Transabdominal	2004
SWIFT	Transvaginal	2009
NEOMEDIC		
SURELIFT / SURELIFT MIPS / SURELIFT LINK	Transvaginal	2011
UPLIFT	Transabdominal	2011
PFM MEDICAL		
TiLOOP	Transabdominal	2007
TiLOOP PRO PLUS	Transvaginal	2015
TiLOOP Total PLUS	Transvaginal	2007
PROMEDON		
CALISTAR	Transvaginal	2011
SPLENTIS	Transvaginal	2012
SOFRADIM / MEDTRONIC		
ProSupTM	Transabdominal	1996
UgytexTM	Transvaginal	2002
THT		
CYSTO-SWING CS3	Transvaginal	2008
CYSTO-SWING CS4	Transvaginal	2008

PRO-SWING PS2	Transabdominal	2003
PRO-SWING PS4	Transabdominal	2008
RECO-SWING RS3	Transvaginal	2008
RECTO-SWING RS4	Transvaginal	2008

Surgical mesh implants for treatment of pelvic organ prolapse sold in France between 2014 and 2017, by route of surgical insertion

Number of surgical mesh implants sold in France	**2014**	**2015**	**2016**	**2017**
Transvaginal	*4 225*	*4 000*	*6 321*	*6 781*
Transvaginal or transabdominal	*252*	*241*	*237*	*350*
Transabdominal	*13 200*	*13 340*	*13 985*	*14 286*
Total	**17 677**	**17 581**	**20 543**	**21 417**