UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK
WHITE PLAINS DIVISION

IN RE: 13-MD-2434(CS)

MIRENA IUD PRODUCTS LIABILITY LITIGATION

AMANDA TRUITT 7:13-cv-07811-CS

Plaintiff,

v.

BAYER HEALTHCARE PHARMACEUTICALS INC., BAYER PHARMA AG, and BAYER OY

Defendants.

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANTS' MOTION TO DISMISS PLAINTIFF'S SECOND AMENDED COMPLAINT

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I. INTRODUCTION

Plaintiff Amanda Truitt's claims against Defendants are time-barred under the applicable two-year statutes of limitations of both Texas – the state in which she brought this action – and her home state of Indiana.

Plaintiff alleges four separate events occurring more than two years prior to filing her original Complaint on September 26, 2013 that would each independently trigger the accrual of her causes of action: (a) on July 7, 2011, Plaintiff was told that her Mirena's strings could not be seen and was directed to go to the emergency room promptly for further treatment; (b) on July 8, 2011, Plaintiff was diagnosed with a perforated Mirena, which had migrated out of her uterus and into her abdomen, and ovarian cysts; (c) on July 9, 2011, Plaintiff's doctor performed surgery to remove her Mirena from her abdominal cavity; and (d) on or around July 9, 2011, Plaintiff's doctor explicitly told Plaintiff that Mirena caused one or more of her alleged injuries.

Because Plaintiff admits that she was injured more than two years before filing suit, and that she discovered her injury and its connection to Mirena more than two years before filing suit, all of her claims are time-barred, and no equitable tolling doctrine in Indiana or Texas saves her claims. Each of the courts called upon to decide this question in Mirena actions alleging MDL injuries have held that diagnosis of injury and surgical removal of the Mirena triggers the statute of limitations. *See Allen v. Bayer Healthcare Pharm., Inc.*, 4:14-CV-178 CEJ, 2014 WL 655585 (E.D. Mo. Feb. 20, 2014); *Witherspoon v. Bayer HealthCare Pharm. Inc.*, 4:13CV01912 ERW, 2013 WL 6069009 (E.D. Mo. Nov. 18, 2013).

Defendants therefore respectfully request that the Court dismiss the Second Amended Complaint in its entirety.

II. FACTUAL BACKGROUND

First approved as safe and effective by the FDA in 2000 for contraception and still on the market today, Mirena is an IUD that is small (1.26 inches long), T-shaped, and made of soft, flexible plastic (*see* 2d Am. Compl. at ¶¶ 21-22). Mirena requires a doctor's prescription and is inserted into a patient's uterus during an office procedure (*see id.* at ¶ 21). Mirena "is approved ***to remain in the uterus*** for up to five (5) years" (*id.* at ¶ 24) (emphasis added).

A. Mirena Warning Label

The Mirena label in effect at the time of Plaintiff's April 30, 2009 insertion contains multiple warnings and directions relevant to Plaintiff's alleged injuries and to the discovery of her causes of action (*see* Ex. 1, July 2008 Mirena Label).[1] For example, the label contains warnings for perforation (which includes a warning for migration outside the uterine cavity) and ovarian cysts:

> 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.
>
> * * *

[1] This Court may consider the Mirena label in effect at the time of Plaintiff's insertion on this Motion to Dismiss. Plaintiff "relies heavily upon [the] terms and effect" of the Mirena label, thus rendering the label "integral" to the Second Amended Complaint. *Chambers v. Time Warner, Inc.*, 282 F.3d 147, 153 (2d Cir. 2002); *see San Leandro Emergency Med. Grp. Profit Sharing Plan v. Philip Morris Companies, Inc.*, 75 F.3d 801, 808-09 (2d Cir. 1996) (holding that on a 12(b)(6) motion, courts may consider the full text of documents partially quoted in the complaint); *see, e.g.*, 2d Am. Compl. at ¶¶ 21, 23-27, 34, 45-46, 72-83 (partially quoting the Mirena label). The Mirena label is integral to the Second Amended Complaint in this products liability action sounding primarily in failure to warn.

> 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.

(Ex. 1, July 2008 Mirena label at MIR00278293-294).

The Patient Information Booklet – which is considered part of the Mirena label, is contained in each Mirena package, and includes a consent form to be signed by the patient – also contains warnings for perforation, migration, and ovarian cysts:

> *Perforation.* Mirena may go through the uterus. This is called perforation. If your uterus is perforated, Mirena may no longer prevent pregnancy. It may move outside the uterus and can cause internal scarring, infection, or damage to other organs, and you may need surgery to have Mirena removed.
>
> * * *
>
> *Cyst on the ovary.* Approximately 12% (12 out of 100) of women using Mirena develop a cyst on the ovary. These cysts usually disappear on their own in a month or two. However, cysts can cause pain and sometimes cysts will need surgery.

(Ex. 2, July 2008 Patient Information Booklet, at MIR_CW_126604; *see also id.* at MIR_CW_126602 (Mirena consent form); 2d Am. Compl. at ¶ 34 ("Plaintiff was also given a Mirena medical consent form that she read and signed")).

The Mirena label in effect at the time of Plaintiff's 2009 insertion also contains multiple warnings and directions with respect to the threads – sometimes called strings – that are attached to the body of the Mirena. Physicians are warned that "[i]f 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" (Ex. 1, July 2008 Mirena Label, at MIR00278297). Physicians are further

instructed that "[i]f 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" (*id.*). The Mirena Patient Information Booklet directs patients to check for the threads every month (Ex. 2, July 2008 Patient Information Booklet, at MIR_CW_126604). Patients are instructed that "[i]f you cannot feel the threads at all, ask your healthcare provider to check that Mirena is still in the right place" (*id.*).

B. Plaintiff Truitt's Allegations

Plaintiff filed the instant action on September 26, 2013, in the Northern District of Texas. Pursuant to this Court's Order, in anticipation of this Motion to Dismiss, Plaintiff filed an Amended Complaint on March 24, 2014. Plaintiff filed a Second Amended Complaint on March 26, 2014. All allegations set forth below are pled in Plaintiff's Second Amended Complaint.

Plaintiff Amanda Truitt alleges that "[a]t all times relevant hereto," she "was a resident and citizen of the State of Indiana" (2d Am. Compl. at ¶ 1). On April 30, 2009, Plaintiff's Mirena was inserted (*id.* at ¶ 36). On the same day as her insertion, Plaintiff alleges that her health care providers "discussed with her the purpose, use, risks, and benefits of Mirena," and that she was given a "booklet and consent form," which she "read and signed" (*id.* at ¶ 34). "Plaintiff was instructed to check the Mirena strings monthly" (*id.* at ¶ 37).

Plaintiff allegedly understood at the time of insertion "that there was a possibility of slight risk of Mirena migration and/or perforation as a result of the implanting procedure, but that if she did not experience severe cramps, heavy bleeding, or fever over 100 degrees in the next few days then she would be passed [sic] that risk" (*id.* at ¶ 38). "Plaintiff recovered from the implant procedure and did not experience any of those complaints" (*id.*). According to Plaintiff, "[a]t no time did any healthcare provider warn or in the information provided by Defendants did

it warn Plaintiff that sometime after insertion, Mirena can spontaneously perforate her uterus and migrate to her left lower abdomen and cause medical injuries requiring hospitalization and surgical treatments" (*id.* at ¶ 45).

Due to nausea and vomiting, on July 7, 2011 Plaintiff visited her healthcare provider (*id.* at ¶ 41). On that date, Plaintiff "was told that the Mirena strings could not be seen, which meant that the IUD may have moved" (*id.*). "Plaintiff was told to promptly go [to the] nearby emergency room for further treatment, including to determine whether she was pregnant and to remove the IUD" (*id.*).

On July 8, 2011, Plaintiff visited the emergency room (*id.* at ¶ 42). After testing, Plaintiff's doctors diagnosed that Mirena "had perforated her uterus and migrated" into her "left lower abdomen" (*id.* at ¶ 43). Plaintiff was also diagnosed with "one or more ovarian cysts" (*id.*).

On July 9, 2011, Plaintiff's doctor "performed surgery to remove the Mirena" from her abdominal cavity (*id.*). Plaintiff alleges that her doctor told her "that Mirena caused her cervix to thin and caused the cysts to form" (*id.* at 44).

III. ARGUMENT

Plaintiff's claims were not brought within the two-year statutes of limitations applicable to personal injury actions both in Texas, the location of the transferor court, and in Plaintiff's home state of Indiana. Accordingly, Plaintiff's claims are time-barred and should be dismissed in their entirety.

A. Plaintiff's Claims Must Be Timely Under Both the Indiana and Texas Statutes of Limitations in Order to Survive

"When an action involving state law claims is transferred pursuant to the MDL provision of 28 U.S.C. § 1407 (2000), 'a transferee court applies the substantive state law, including

choice-of-law rules, of the jurisdiction in which the action was filed.'" *In re WorldCom, Inc. Sec. Litig.*, 03 CIV 4498, 2005 WL 2403856, at *2 (S.D.N.Y. Sept. 30, 2005) (citing *Menowitz v. Brown,* 991 F.2d 36, 40 (2d Cir.1993)). Plaintiff's action was filed on September 26, 2013 in the United States District Court for the Northern District of Texas. Therefore, the state law and choice of law rules of Texas apply to the instant action.

Texas uses a "borrowing statute" to determine the applicable statute of limitations for personal injury actions when "the wrongful act, neglect, or default causing the . . . injury takes place in a foreign state." Tex. Civ. Prac. & Rem. Code Ann. § 71.031. Under that statute, a personal injury action may only be brought in Texas if ***both*** "the action is begun in [Texas] within the time provided by the laws of [Texas] for beginning the action" ***and*** "the action is begun in [Texas] within the time provided by the laws of the foreign state or country in which the wrongful act, neglect, or default took place." *Id.* Because Plaintiff admits that "[a]t all times relevant hereto," she "was a resident and citizen of the State of Indiana" (2d Am. Compl. at ¶ 1), her claims must satisfy both the Texas and the Indiana statutes of limitations in order for them to be timely. Because each of Plaintiff's claims is time-barred under the laws of one or both states, the Second Amended Complaint should be dismissed in its entirety.

B. Plaintiff Is Time-Barred by the Indiana Statute of Limitations

Plaintiff's product liability claims sounding in negligence and strict liability (Counts I-V) are time-barred under Indiana's two-year statute of limitations for product liability actions. Ind. Code Ann. § 34-20-3-1 ("a product liability action must be commenced . . . within two (2) years after the cause of action accrues"); *see also Dague v. Piper Aircraft Corp.*, 275 Ind. 520, 525, 418 N.E.2d 207, 210 (1981) (distinguishing the ten-year statute of repose found in the same section of the Indiana Code).

"The 'general rule' is that a cause of action accrues 'when resultant damage of a negligent act is ascertainable or by due diligence could be ascertained.'" *Kazmer v. Bayer Healthcare Pharm., Inc.*, 2:07-CV-112-TS, 2007 WL 4148003, at *2 (N.D. Ind. Nov. 19, 2007) (citations omitted). "It is not necessary for accrual that 'the full extent of the damage be known or even ascertainable but only that some ascertainable damage has occurred.'" *Id.* "In essence, a cause of action accrues when the alleged negligence culminates in injury to the plaintiff and damages resulting from that injury are ascertainable." *Tolen v. A.H. Robins Co., Inc.*, 570 F. Supp. 1146, 1149 (N.D. Ind. 1983).

Under certain circumstances not present here, when an injury or its cause is not immediately knowable, the Indiana discovery rule delays the accrual of a cause of action until "the date the plaintiff knew or should have discovered that she suffered an injury or impingement, and that it was caused by the product or act of another." *Barnes v. A.H. Robins Co., Inc.*, 476 N.E.2d 84, 87-88 (Ind. 1985). Accrual of a cause of action is also triggered when an event occurs "that would cause a person of reasonable diligence to take action that would lead to the discovery of his cause of action." *Morgan v. Columbus McKinnon Corp.*, 837 N.E.2d 546, 549 (Ind. Ct. App. 2005). According to the Indiana Court of Appeals:

> [t]he exercise of reasonable diligence means simply that an injured party must act with some promptness where the acts and circumstances of an injury would put a person of common knowledge and experience on notice that some right of his has been invaded or that some claim against another party might exist. The statute of limitations begins to run from this point and not when advice of counsel is sought or a full blown theory of recovery developed.
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> Stated more succinctly, the law does not require a smoking gun in order for the statute of limitations to commence.

Perryman v. Motorist Mut. Ins. Co., 846 N.E.2d 683, 689 (Ind. Ct. App. 2006) (citations omitted). "Indiana does not require that a plaintiff uncover the legal theory for holding a defendant liable for the action to accrue. Rather, ***the plaintiff must only be aware that the***

defendant caused him injury." *Frey v. Bank One*, 91 F.3d 45, 47 (7th Cir. 1996) (emphasis added).

"Determining precisely when a cause of action accrues is a question of law for the court." *Schott v. Huntington Nat. Bank*, 914 F. Supp. 2d 933, 939 (S.D. Ind. 2012) (holding claim time-barred on a motion to dismiss, despite plaintiff's invocation of the discovery rule).

1. Plaintiff Pleads Four Different Events That Independently Trigger the Accrual of Her Causes of Action, Making This Action Time-Barred

In her Second Amended Complaint, Plaintiff pleads four different events that occurred more than two years before the filing of this action, each of which is independently sufficient to trigger the accrual of Plaintiff's products liability causes of action. Plaintiff's action is therefore time-barred.

(a) On July 7, 2011, Plaintiff was told by her healthcare provider that "the Mirena strings could not be seen, which meant that the IUD may have moved" (2d Am. Compl. at ¶ 41). "Plaintiff was told to promptly go [to the] nearby emergency room for further treatment" (*id.*).

As described above, a cause of action is triggered when an event occurs "that would cause a person of reasonable diligence to take action that would lead to the discovery of his cause of action." *Morgan*, 837 N.E.2d at 549. A person of reasonable diligence who is told by her healthcare provider that her "IUD may have moved" and "to promptly go [to the] nearby emergency room for further treatment" would comply with that instruction and discover whether a perforation had occurred. That Plaintiff actually did go to the emergency room the next day and discovered the perforation confirms that she possessed constructive, or inquiry, notice as of July 7, 2011.

Even if her healthcare provider had not explicitly told Plaintiff to go to the emergency room, a person of reasonable diligence would comply with the instructions included in a

product's Patient Information Booklet. Thus, when a Mirena user discovers that her Mirena's strings are no longer protruding from her cervix, that person would "ask [her] healthcare provider to check that Mirena is still in the right place" (Ex. 2 at MIR_CW_126604). That is the case even more so here, where Plaintiff admits that she was given instructions to check the strings of her Mirena (2d Am. Compl. at ¶ 37). If a Mirena perforates a user's uterus and migrates outside of the uterus, then a person of reasonable diligence asking her healthcare provider to check that the Mirena is still in the right place will discover her injury and its cause within the limitations period. Therefore, Plaintiff's product liability causes of action accrued on July 7, 2011.

(b) On July 8, 2011, Plaintiff was diagnosed with a perforated Mirena, which had migrated out of her uterus and into her abdomen (2d Am. Compl. at ¶¶ 42-43). Plaintiff's discovery of her perforation injury triggered the accrual of her causes of action.

This case is similar to *Tolen v. A.H. Robins Co., Inc.*, in which a Dalkon Shield intrauterine device perforated a plaintiff's uterus and was found "in her lower left stomach cavity and not in her uterus where it was supposed to be." 570 F. Supp. at 1150. In *Tolen*, the plaintiff argued that the discovery rule applied, and that her cause of action did not accrue "until she discovered the causal connection between her injury and the Dalkon Shield . . . . in December 1979 when she read an article in the *Lafayette Journal and Courier* about problems concerning the Dalkon Shield." *Id.* The Court rejected that plaintiff's argument, explaining that even if the discovery rule applied, "aware[ness] of the fact that the device had not done what it was designed to do" was "sufficient information to discuss the basis of a potential cause of action." *Id.* at 1151. In *Tolen*, like here, the plaintiff's causes of action accrued when the plaintiff "had actual knowledge . . . that surgery was required to remove the Dalkon Shield, and that the

Dalkon Shield was found outside her uterus in her stomach cavity and, consequently, was not where it should be." *Id.*

Therefore, on July 8, 2011, upon learning that her Mirena was "not in her uterus where it was supposed to be," *id.*, but was in her lower abdomen, Plaintiff possessed sufficient information for her causes of action to accrue under the discovery rule (2d Am. Compl. at ¶¶ 42-43).

(c) On July 9, 2011, Plaintiff's doctor performed surgery to remove Mirena from her abdominal cavity. For the same reasons described above, the surgical removal of Plaintiff's Mirena ***intra-uterine*** device from ***outside of her uterus*** made her "aware of the fact that the device had not done what it was designed to do" and was "sufficient information to discuss the basis of a potential cause of action." *Tolen*, 570 F. Supp. at 1151.

Under these exact same circumstances, the Court in *Tolen* found that the plaintiff's causes of action accrued when the plaintiff "had actual knowledge . . . that surgery was required to remove the Dalkon Shield . . . [from] outside her uterus in her stomach cavity." *Id.* Therefore, on July 9, 2011, upon the surgical removal of Plaintiff's Mirena from outside of her uterus (2d Am. Compl. at ¶¶ 42-43), Plaintiff possessed sufficient information for her causes of action to accrue under the discovery rule.

(d) On or about July 8-9, 2011, Plaintiff was diagnosed with "one or more ovarian cysts" (*id.* at ¶ 43). Plaintiff's doctor allegedly informed her "that Mirena caused her cervix to thin and caused the cysts to form" (*id.* at ¶ 44).

"[O]nce a plaintiff's doctor expressly informs the plaintiff that there is a reasonable possibility, if not a probability, that an injury was caused by an act or product, then the statute of limitations begins to run." *Morgan v. Columbus McKinnon Corp.*, 837 N.E.2d 546, 549-50 (Ind.

Ct. App. 2005). Plaintiff admits, in no uncertain terms, that her doctor expressly informed her that her alleged ovarian cyst injury was caused by Mirena. Therefore, on July 8-9, 2011, upon the diagnosis of ovarian cysts and her doctor's express connection of that injury to Mirena (2d Am. Compl. at ¶¶ 43-44), Plaintiff possessed sufficient information for her causes of action to accrue under the discovery rule.

2. Plaintiff Does Not Plead Any Facts in Support of Application of the Discovery Rule to Toll the Statute of Limitations

Plaintiff's allegations in support of application of the discovery rule are conclusory and insufficient to toll the accrual of Plaintiff's causes of action beyond July 9, 2011. Plaintiff fails to plead a date of discovery or due diligence in an effort to discover her injury and its cause. She does not even plead the fact or facts that she did not know on July 9, but that she learned thereafter, that finally caused her causes of action to accrue. Even if a conceivable set of facts exists that could toll the statute of limitations in this action – and indeed none could – those facts are not pled. Plaintiff's claims accrued more than two years prior to the filing of this action, and they are therefore time-barred by Indiana's two-year statute of limitations.

Despite this Court granting Plaintiff "time to amend her Complaint so that she can, if she chooses, add facts relevant to the statute of limitations" (3/7/14 Order, MDL 2434 Doc. No. 736), Plaintiff's allegations in support of tolling the statute of limitations are limited to one paragraph alleging no specific facts:

> Plaintiff did not suspect, nor did she have reason to suspect, that wrongdoing had caused her injuries, nor did Plaintiff have reason to suspect the tortious nature of the conduct causing the injuries, until recently. Plaintiff had no knowledge of the defects in the Mirena® and the wrongful conduct of Defendants as set forth herein, nor did Plaintiff have access to the information regarding other injuries and complaints in the possession of Defendants. Additionally, Plaintiff was prevented from discovering this information sooner because Defendants herein misrepresented and continue to misrepresent to the public, to the medical profession and to Plaintiff that the Mirena® is safe and free from serious defects and side effects, and Defendants have fraudulently concealed facts and

> information that could have led Plaintiff to an earlier discovery of potential causes of action.

(2d Am. Compl. at ¶ 47). Not only are these allegations conclusory, but they are irrelevant to the Indiana discovery rule.

The discovery rule will only toll the statute of limitations until "the date the plaintiff knew or should have discovered that she suffered an injury or impingement, and that it was caused by the product or act of another." *Barnes*, 476 N.E.2d at 87-88. Plaintiff claims that she did not "have reason to suspect the tortious nature of the conduct causing the injuries" (2d Am. Compl. at ¶ 47), but that is irrelevant to the discovery rule analysis. "Indiana does not require that a plaintiff uncover the legal theory for holding a defendant liable for the action to accrue. ***Rather, the plaintiff must only be aware that the defendant caused him injury***." *Frey*, 91 F.3d at 47 (emphasis added). As explained above in detail, Plaintiff pleads four separate events, each of which independently caused Plaintiff, or would cause a reasonable person exercising due diligence, to believe that Mirena caused her injury.

Even if the standard was as Plaintiff implies in her Second Amended Complaint – that she be aware of every detail necessary to state a cause of action – Plaintiff possessed all the facts necessary to make a failure to warn claim at the moment she was diagnosed with perforation and migration. The Second Amended Complaint describes in detail the warnings Plaintiff alleges she was and was not given, and her belief that she was past the risk of perforation and migration that she was warned of:

- Plaintiff "understood, among other things, that there was a possibility of slight risk of Mirena migration and/or perforation as a result of the implanting procedure, but that if she did not experience severe cramps, heavy bleeding, or fever over 100 degrees in the next few days then she would be passed [sic] that risk" (2d Am. Compl. at ¶ 38).
- "Plaintiff recovered from the implant procedure and did not experience any of those complaints" (*id.*).

- "At no time did any healthcare provider warn or in the information provided by Defendants did it warn Plaintiff that sometime after insertion, Mirena can spontaneously perforate her uterus and migrate to her left lower abdomen and cause medical injuries requiring hospitalization and surgical treatments" (*id.* at ¶ 45).

At the time Plaintiff was diagnosed with a perforated Mirena, which migrated out of her uterus, she was fully aware of the risks she was warned of at the time of insertion, and that she allegedly suffered from an injury that she believed to be outside of those warnings. There is no fact that she was missing at the time of diagnosis and could have discovered at a later date that was necessary to make a failure to warn claim.

The discovery rule cannot save Plaintiff's claims under Indiana law, even if this Court applies the inaccurate reading of the discovery rule implied by the Second Amended Complaint. Plaintiff's product liability causes of action accrued more than two years prior to the filing of this action, and they are therefore time-barred by Indiana's two-year statute of limitations.

3. Plaintiff Does Not Plead Any Facts in Support of Application of the Fraudulent Concealment Doctrine to Toll the Statute of Limitations

Plaintiff's conclusory allegations regarding fraudulent concealment fail for the same reasons as her allegations in support of applying the discovery rule. Without any facts to support it, the fraudulent concealment doctrine cannot toll the two-year statute of limitations in this action, and Plaintiff's claims are therefore untimely.

Once again, after this Court granted Plaintiff an opportunity to amend her Complaint – "her only opportunity to amend" on the statute of limitations issue (3/7/14 Order, MDL 2434 Doc. No. 736) – the Second Amended Complaint contains nothing but a conclusory allegation that Bayer "fraudulently concealed facts and information that could have led Plaintiff to an earlier discovery of potential causes of action" (2d Am. Compl. at ¶ 47). Plaintiff does not allege what "facts and information" were allegedly concealed or what actions Defendants allegedly took to conceal them.

Plaintiff's conclusory allegations are insufficient to toll the statute of limitations. In evaluating a fraudulent concealment claim under Indiana law, the Seventh Circuit recently rejected similar conclusory allegations, explaining, "if the facts pleaded in the complaint establish that a claim is time barred, as they do here, a bare allegation of fraudulent concealment, without more, will not save the claim." *Logan v. Wilkins*, 644 F.3d 577, 582 (7th Cir. 2011) ("Logan has not pleaded any facts in his amended complaint that would support his contention that the defendants engaged in fraudulent concealment. He does not describe any deception or other acts by the defendants that prevented him from discovering that he was injured.").

The law narrowly defines fraudulent concealment in the products liability context. "Generally, the concealment must be active and intentional. Mere silence on the part of a defrauder will not constitute concealment absent a duty to speak." *Ludwig v. Ford Motor Co.*, 510 N.E.2d 691, 697 (Ind. Ct. App. 1987) (citations omitted). Even if Plaintiff alleged facts to support a failure to speak, silence will toll the statute of limitations only "when there is a duty to disclose, via a fiduciary or confidential relationship." *Id.* However, "there is no confidential or fiduciary relationship between . . . a consumer, and . . . a manufacturer of pharmaceutical products." *Tolen*, 570 F. Supp. at 1152.

"[T]he burden of showing a duty to speak is on the party alleging fraudulent concealment." *Ludwig*, 510 N.E.2d at 697 (citations omitted). "The affirmative acts of concealment must be calculated to mislead and hinder a plaintiff from obtaining information by the use of ordinary diligence, or to prevent inquiry or elude investigation. There must be some trick or contrivance intended by the defrauder to exclude suspicion and prevent inquiry." *Id.* "Mere lack of knowledge is not enough to constitute concealment and toll the running of the

statute. Thus, to avoid the bar of limitations by claiming fraudulent concealment, a plaintiff must show that he used due diligence to detect the fraud." *Id.*

The Court in *Tolen* rejected plaintiff's argument that fraudulent concealment is shown by alleging that defendant "misrepresented pregnancy rates, complications, side effects, hazards and dangers . . . of the Dalkon Shield in an active manner calculated to prevent the plaintiff from ascertaining that legal injury had been done to her." 570 F. Supp. at 1152. Aside from allegations similar to those rejected in *Tolen*, Plaintiff here does not allege any "affirmative acts of concealment" calculated to "prevent inquiry or elude investigation." *Ludwig*, 510 N.E.2d at 697. And even if she did, she does not allege that she "used due diligence to detect the fraud." *Id.* Moreover, as discussed above, Plaintiff alleges that she actually believed at the time of her perforation diagnosis that her injury was inconsistent with the warnings she had received. In other words, Plaintiff already knew what she claims Defendants concealed from her.

The fraudulent concealment doctrine cannot save Plaintiff's claims under Indiana law. Plaintiff's products liability causes of action accrued more than two years prior to the filing of this action, and they are therefore time-barred by Indiana's two-year statute of limitations.

4. Plaintiff's Warranty and Fraud Claims are Time-Barred

In addition to product liability causes of action alleged under negligence and strict liability theories (Counts I-V), Plaintiff also alleges claims sounding in warranty (Counts VI-VII) and fraud (Counts VIII-X). Plaintiff's warranty and fraud claims are also time-barred by the Indiana statute of limitations.

The Uniform Commercial Code governs breach of warranty claims in Indiana. "An action for breach of any contract for sale must be commenced within four (4) years after the cause of action has accrued." Ind. Code Ann. § 26-1-2-725(1). "A cause of action accrues when the breach occurs, regardless of the aggrieved party's lack of knowledge of the breach. A breach

of warranty occurs when tender of delivery is made." *Id.* at § 725(2). In *Tolen*, like here, "tender of delivery occurred . . . at the time the [IUD] was inserted into plaintiff's uterus." 570 F. Supp. at 1153. Plaintiff's Mirena was inserted on April 30, 2009, more than four years before she filed this action on September 26, 2013. Thus, her warranty claims (Counts VI-VII) are time-barred.

With respect to Plaintiff's fraud claims, "[i]t is the well established rule in Indiana that in determining what period of limitations applies the essence of the action controls rather than the form in which it is pleaded." *Tolen*, 570 F. Supp. at 1155. When, like here, the "essence of the plaintiff's complaint . . . is that the defendant manufacturer placed a defective product on the market which caused injury to plaintiff," *id.* at 1156, Plaintiff's claims for fraud are governed by the statute of limitations for product liability actions, which as noted above, is two years. Therefore, because Plaintiff discovered her injury and its cause in July 2011, her September 2013 fraud claims (Counts VIII-X) are time-barred.

C. Plaintiff Is Time-Barred by the Texas Statute of Limitations

Not only are Plaintiff's products liability claims time-barred under the Indiana statute of limitations, but they are untimely under the Texas statute of limitations as well. Tex. Civ. Prac. & Rem. Code Ann. § 16.003(a) ("a person must bring suit for . . . personal injury . . . not later than two years after the day the cause of action accrues").

In Texas, "a cause of action generally is said to accrue when facts come into existence which give a claimant the right to seek remedy in the courts. In personal injury actions, it is when 'the wrongful act effects an injury, regardless of when the claimant learned of such injury.'" *Seibert v. Gen. Motors Corp.*, 853 S.W.2d 773, 776 (Tex. App. 1993).

"The discovery rule is an exception to the general rule. . . . It is not activated unless the plaintiff's injury is inherently undiscoverable." *Id.* "Because it addresses only the discovery of

the *injury,* the discovery rule is not applied to toll the statute of limitations until the time that a plaintiff discovers all the elements of his *cause of action.*" *Id.* (emphasis in original).

In *Coody v. A.H. Robins Co., Inc.*, a plaintiff's causes of action against the manufacturer of an IUD accrued when she discovered her injury "and at that time discovered that the injury was caused by her use of the IUD." 696 S.W.2d 154, 156 (Tex. App. 1985). The Court rejected Plaintiff's argument that "the limitation period began to run only in 1979, when she discovered that the IUD in question was a Dalkon Shield and that it was defectively designed." *Id.* "The discovery rule speaks only of discovery of the injury. It does not operate to toll the running of the limitation period until such time as plaintiff discovers all of the elements of a cause of action. Once appellant learned that she had been injured, the burden was on her to determine whether she should file suit." *Id.*

Plaintiff does not and cannot allege that her injuries were inherently undiscoverable beyond the date she was diagnosed with those injuries in July 2011. Indeed, she alleges the exact opposite – namely, that she was aware of multiple injuries in July 2011 (2d Am. Compl. at ¶¶ 41-44). After that time, the burden was on her to determine whether she should file suit against Bayer. Because the Texas discovery rule cannot be triggered to toll the two-year statute of limitations beyond that date, Plaintiff's claims are time-barred.

D. Other Federal Courts Have Held the Statute of Limitations to Run Upon Diagnosis of Perforation/Embedment and Surgical Removal

To date, two courts – both in the Eastern District of Missouri – have addressed the statute of limitations in cases alleging MDL-appropriate injuries of perforation, embedment, or migration. Both times, the courts held plaintiffs' claims were time-barred, reasoning that the statute begins to run upon a diagnosis of perforation or embedment, or upon surgical removal.

Witherspoon, 2013 WL 6069009; *Allen*, 2014 WL 655585. Each time, the courts' holdings were based on a standard more demanding than the motion to dismiss standard applicable here.

In both *Witherspoon* and *Allen*, plaintiffs filed multi-plaintiff suits in state court, in the Circuit Court for the City of St. Louis (93 plaintiffs in *Witherspoon*; 25 in *Allen*). In each case, a single Mirena-user plaintiff was joined that shared citizenship with Bayer, thus destroying diversity on the face of the complaints. Bayer removed both actions to the Eastern District of Missouri, arguing that the non-diverse plaintiffs were time-barred, and therefore fraudulently joined in order to defeat diversity jurisdiction. Plaintiffs in both cases filed Motions to Remand. Judge Carol E. Jackson, the same judge who found fraudulent joinder in *Allen*, describes the "standard for determining fraudulent joinder [a]s even more favorable to the plaintiff than the standard for ruling on a motion to dismiss under Fed.R.Civ.P. 12(b)(6)." *Hutton v. Teva Neuroscience, Inc.*, 4:08-CV-1010 (CEJ), 2008 WL 4862733, at *2 (E.D. Mo. Nov. 7, 2008).

In *Witherspoon*, Judge E. Richard Webber held that the high standard for fraudulent joinder was met. The Court held that "Plaintiff Casiano possessed 'reasonable medical information' connecting Mirena® to her injury in 2009, when she had the IUD removed and 'was informed at that time that the [IUD] had perforated her uterus.'" *Witherspoon*, 2013 WL 6069009 at *5. Therefore, "at the latest, Plaintiff Casiano's claim 'accrued' . . . when she was told the IUD had perforated her uterus." *Id.* at *4. Judge Webber rejected application of the New Jersey discovery rule to toll the statute of limitations past the date of diagnosis, and he also rejected the same conclusory allegations of fraudulent concealment that Plaintiff alleges here.

> Plaintiffs cite portions of the Petition, which generally allege Defendant misrepresented material facts and concealed the purportedly defective nature of Mirena®, and Plaintiffs lacked awareness of the falsity of such statements and reasonably accepted them as true. However, ***these conclusory allegations***, found under Plaintiffs' "Fraudulent Misrepresentation" and "Fraud by Concealment"

> causes of action, ***fail to suggest Plaintiff Casiano lacked awareness of her alleged injury when she had the IUD removed in 2009***.

Id. (emphasis added).

In *Allen*, the non-diverse plaintiff alleged migration and surgical removal of her Mirena. Judge Jackson held that the Delaware statute of limitations began to run on the non-diverse plaintiff's claims "when she underwent a surgical removal of her IUD" and her "injury became physically ascertainable." 2014 WL 655585, at *4. In so holding, the Court rejected plaintiff's attempt "to bypass the 2–year statute of limitations by arguing that she was not on notice of her claims against defendant until after she saw an advertisement for Mirena IUD litigation." *Id.* Judge Jackson took judicial notice of publicly available Mirena labels, and reasoned that "had Barlow engaged in a reasonable inquiry of publically available information regarding the Mirena IUD, she would have discovered product labels specifically warning of the injuries she alleged in the instant complaint. *See e.g.* Mirena IUD Product Labels . . . (warning of the risk of perforation and bleeding)." 2014 WL 655585, at *4; *see also* Ex. 1, July 2008 Mirena Label, at MIR00278293.

For the same reasons that these federal judges concluded that diagnosis of perforation and surgical removal of Mirena triggered the statute of limitations under New Jersey and Delaware law, those events trigger accrual of Plaintiff's causes of action under Indiana and Texas law.

IV. CONCLUSION

Plaintiff alleges four separate events occurring more than two years prior to filing her Complaint that would each independently trigger the accrual of her causes of action: (a) on July 7, 2011, Plaintiff was told that the Mirena strings could not be seen and was directed to go to the emergency room promptly for further treatment; (b) on July 8, 2011, Plaintiff was diagnosed with a perforated Mirena, which had migrated out of her uterus and into her abdomen; (c) on July

9, 2011, Plaintiff's doctor performed surgery to remove her Mirena from her abdominal cavity; and (d) on or around July 9, 2011, Plaintiff's doctor explicitly told Plaintiff that Mirena caused one or more of her alleged injuries.

For the foregoing reasons, Defendants' Motion to Dismiss should be granted and Plaintiff's Second Amended Complaint should be dismissed in its entirety.

Dated: April 7, 2014

Respectfully submitted,

/s/ *Shayna S. Cook*

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Lead Counsel for Defendants

DEPARTMENT OF HEALTH & HUMAN SERVICES

08036028

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-225/S-019

200806720

RECEIVED
JUL 25 2008
By

Bayer Healthcare Pharmaceuticals, Inc.
Attention: Jo-Ann Ruane
Associate Director, Global Regulatory Affairs
P.O. Box 1000
Montville, NJ 07045-1000

Dear Ms. Ruane:

Please refer to your supplemental new drug application dated November 30, 2007, received December 3, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mirena® (levonorgestrel-intrauterine releasing system).

We also acknowledge receipt of your submissions dated March 18 and June 24, 2008.

This supplemental new drug application provides for changes to the WARNINGS section, Intrauterine Pregnancy, Embedment, Perforation, Expulsion, and Ovarian Cysts subsections, and PRECAUTIONS section, Patient Evaluation and Clinical Considerations, Insertion Precautions, and Continuation and Removal subsections of the Physician Package Insert. The Patient Package Inset was updated to be consistent with the Physician Package Insert.

We have completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

Within 14 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling. Upon receipt and verification, we will transmit that version to the National Library of Medicine for public dissemination.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

If you have any questions, call Charlene Williamson, Regulatory Project Manager, at (301) 796-1025.

Sincerely,

{See appended electronic signature page}

Scott Monroe, M.D.
Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Scott Monroe
7/21/2008 02:27:36 PM

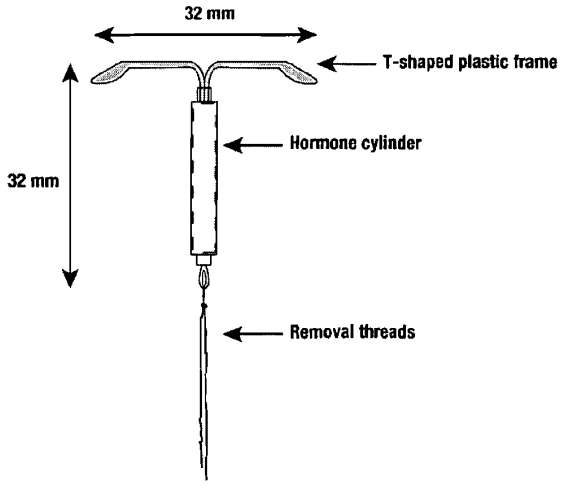
Mirena®
(levonorgestrel-releasing intrauterine system)

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

Rx only

DESCRIPTION

Mirena® (levonorgestrel-releasing intrauterine system) consists of a T-shaped polyethylene frame (T-body) with a steroid reservoir (hormone elastomer core) around the vertical stem. The reservoir consists of a white or almost white cylinder, made of a mixture of levonorgestrel and silicone (polydimethylsiloxane), containing a total of 52 mg levonorgestrel. The reservoir is covered by a semi-opaque silicone (polydimethylsiloxane) membrane. The T-body is 32 mm in both the horizontal and vertical directions. The polyethylene of the T-body is compounded with barium sulfate, which makes it radiopaque. A monofilament brown polyethylene removal thread is attached to a loop at the end of the vertical stem of the T-body.

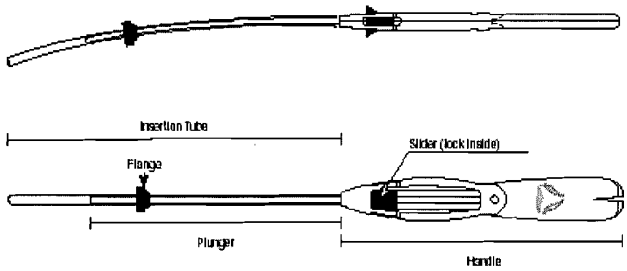


Schematic drawing of Mirena

Inserter

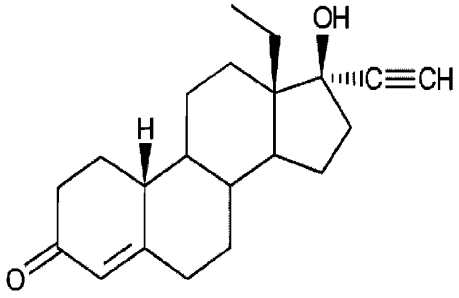
Mirena is packaged sterile within an inserter. The inserter, which is used for insertion of Mirena into the uterine cavity, consists of a symmetric two-sided body and slider that are integrated with flange, lock, pre-bent insertion tube and plunger. Once Mirena is in place, the inserter is discarded.

Diagram of Inserter



Mirena is intended to provide an initial release rate of 20 μg/day of levonorgestrel.

Levonorgestrel USP, (-)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one, the active ingredient in Mirena, has a molecular weight of 312.4, a molecular formula of $C_{21}H_{28}O_2$, and the following structural formula:



CLINICAL PHARMACOLOGY

Levonorgestrel is a progestogen used in a variety of contraceptive products. Low doses of levonorgestrel can be administered into the uterine cavity with the Mirena intrauterine delivery system. Initially, levonorgestrel is released at a rate of approximately 20 μg/day. This rate decreases progressively to half that value after 5 years.

Mirena has mainly local progestogenic effects in the uterine cavity. Morphological changes of the endometrium are observed, including stromal pseudodecidualization, glandular atrophy, a leukocytic infiltration and a decrease in glandular and stromal mitoses.

Ovulation is inhibited in some women using Mirena. In a 1-year study approximately 45% of menstrual cycles were ovulatory and in another study after 4 years 75% of cycles were ovulatory.

The local mechanism by which continuously released levonorgestrel enhances contraceptive effectiveness of Mirena has not been conclusively demonstrated. Studies of Mirena prototypes have suggested several mechanisms that prevent pregnancy: thickening of cervical mucus preventing passage of sperm into the uterus, inhibition of sperm capacitation or survival, and alteration of the endometrium.

Clinical Pharmacokinetics

Following insertion of Mirena, the initial release of levonorgestrel into the uterine cavity is 20 μg/day. A stable plasma level of levonorgestrel of 150-200 pg/mL occurs after the first few weeks following insertion of Mirena. Levonorgestrel levels after long-term use of 12, 24, and 60 months were 180±66 pg/mL, 192±140 pg/mL, and 159±59 pg/mL, respectively. The plasma concentrations achieved by Mirena are lower than those seen with levonorgestrel contraceptive implants and with oral contraceptives. Unlike oral contraceptives, plasma levels with Mirena do not display peaks and troughs.

The mean ± SD levonorgestrel endometrial tissue concentration in four women using levonorgestrel intrauterine systems releasing 30 μg/day of levonorgestrel for 36-49 days was 808 ± 511 ng/g wet tissue weight. The endometrial tissue concentration in 2 women who had been taking a 250 μg levonorgestrel–containing oral contraceptive for 7 days was 3.5 ng/g wet tissue weight. In contrast, fallopian tube and myometrial levonorgestrel tissue concentrations were of the same order of magnitude in the Mirena group and the oral contraceptive group (between 1 and 5 ng/g of wet weight of tissue).

The pharmacokinetics of levonorgestrel itself have been extensively studied and reported in the literature. Levonorgestrel in serum is primarily bound to proteins (mainly sex hormone binding globulin) and is extensively metabolized to a large number of inactive metabolites. Metabolic clearance rates may differ among individuals by several-fold, and this may account in part for wide individual variations in levonorgestrel concentrations seen in individuals using levonorgestrel–containing contraceptive products. The elimination half-life of levonorgestrel after daily oral doses is approximately 17 hours; both the parent drug and its metabolites are primarily excreted in the urine.

Pharmacokinetic studies of this product have not been conducted in special populations (pediatric, renal insufficiency, hepatic insufficiency, and different ethnic groups).

Drug-Drug Interactions

The effect of other drugs on the efficacy of Mirena has not been studied.

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.

CLINICAL STUDIES

Mirena has been studied for safety and efficacy in two large clinical trials in Finland and Sweden. In study sites having verifiable data and informed consent, 1169 women 18 to 35 years of age at enrollment used Mirena for up to 5 years, for a total of 45,000 women-months of exposure. Subjects had previously been pregnant, had no history of ectopic pregnancy, had no history of pelvic inflammatory disease over the preceding 12 months, were predominantly Caucasian, and over 70% of the participants had previously used IUDs (intrauterine devices). The reported 12-month pregnancy rates were less than or equal to 0.2 per 100 women and the cumulative 5-year pregnancy rate was approximately 0.7 per 100 women. However, due to limitations of the available data a precise estimate of the pregnancy rate is not possible.

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

	AGE GROUP					
METHODS	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 health care provider. She should also be given instructions on what other symptoms require her to call her health care 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 health care 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, pruritis, 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.

DOSAGE AND ADMINISTRATION

Mirena contains 52 mg of levonorgestrel. Initially, levonorgestrel is released at a rate of approximately 20 µg/day. This rate decreases progressively to half that value after 5 years.

Mirena is indicated for intrauterine contraception for up to 5 years. Thereafter, if continued contraception is desired, the system should be replaced.

Mirena is packaged sterile within an inserter. Information regarding insertion instructions, patient counseling and record keeping, patient follow-up, removal of Mirena and continuation of contraception after removal is provided below.

1. Insertion Instructions

NOTE: Mirena should be inserted by a trained health care provider. Health care providers are advised to become thoroughly familiar with the insertion instructions before attempting insertion of Mirena.

Mirena is inserted with the provided inserter **(Figure 1a)** into the uterine cavity within seven days of the onset of menstruation or immediately after first trimester abortion by carefully following the insertion instructions. It can be replaced by a new Mirena at any time during the menstrual cycle.

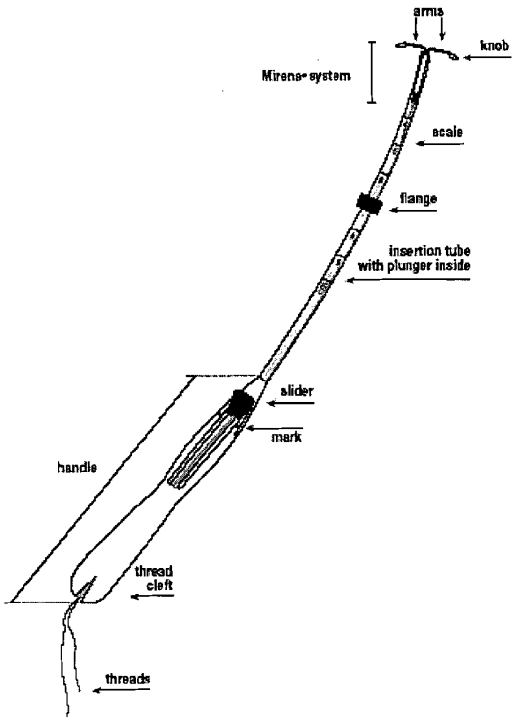


Figure 1a. Mirena and inserter

a. Preparation for insertion

- Ensure that the patient understands the contents of the Patient Information Booklet and obtain consent. A consent form that includes the lot number is on the last page of the Patient Information Booklet.
- Confirm that there are no contraindications to the use of Mirena.
- Perform a urine pregnancy test, if indicated.
- With the patient comfortably in lithotomy position, gently insert a speculum to visualize the cervix and rule out genital contraindications to the use of Mirena.
- Do a bimanual exam to establish the size and position of the uterus, to detect other genital contraindications, and to exclude pregnancy.
- Thoroughly cleanse the cervix and vagina with a suitable antiseptic solution. Perform a paracervical block, if needed.
- Prepare to sound the uterine cavity. Grasp the upper lip of the cervix with a tenaculum forceps and apply gentle traction to align the cervical canal with the uterine cavity. If the uterus is retroverted, it may be more appropriate to grasp the lower lip of the cervix. Note that the tenaculum forceps should remain in position throughout the insertion procedure to maintain gentle traction on the cervix.

- Gently insert a uterine sound to check the patency of the cervix, measure the depth of the uterine cavity, confirm its direction and exclude the presence of any uterine anomaly. If you encounter cervical stenosis, use dilatation, not force, to overcome resistance.
- The uterus should sound to a depth of 6 to 10 cm. Insertion of Mirena into a uterine cavity less than 6.0 cm by sounding may increase the incidence of expulsion, bleeding, pain, perforation, and possibly, pregnancy.
- After ascertaining that the patient is appropriate for Mirena, open the carton containing Mirena.

b. Insertion Procedure

NOTE: Ensure use of sterile technique throughout the entire procedure.

Step 1
Opening of the sterile package

- Open the sterile package completely **(Figure 1b)**.
- Place sterile gloves on your hands.
- Pick up the handle of the inserter containing Mirena and carefully release the threads so that they hang freely.
- Place your thumb or forefinger on the slider. Make sure that the slider is in the furthest position away from you, i.e., at the top of the handle towards the insertion tube (**Figure 1b**).

  NOTE: Keep your thumb or forefinger on the slider until insertion is complete.
- With the centimeter scale of the insertion tube facing up, check that the arms of Mirena are in a horizontal position. If they are not, align them on a flat, sterile surface, for example, the sterile package **(Figures 1b and 1c)**.

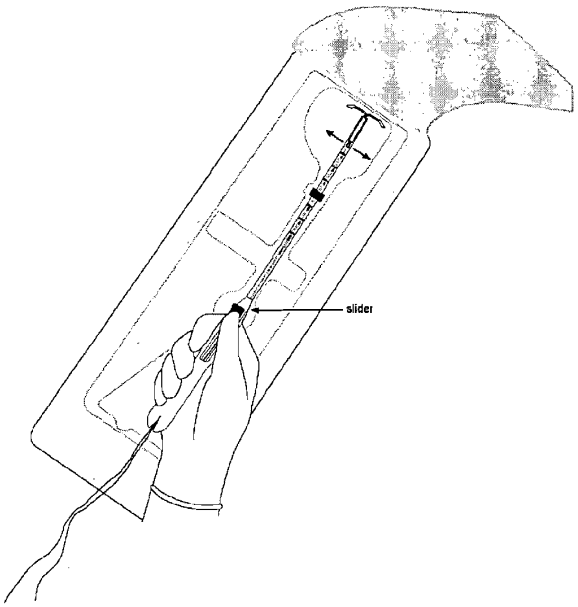


Figure 1b. Aligning the arms with the slider in the furthest position

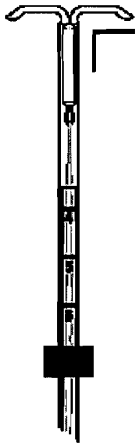


Figure 1c. Checking that the arms are horizontal and aligned with respect to the scale

Step 2
Load Mirena into the insertion tube

- Holding the slider in the furthest position, pull on both threads to load Mirena into the insertion tube **(Figure 2a)**.
- Note that the knobs at the ends of the arms now meet to close the open end of the insertion tube **(Figure 2b)**.

NOTE: If the knobs do not meet properly, release the arms by pulling the slider back to the mark (raised horizontal line on the handle) **(Figure 6a)**. Re-load Mirena by aligning the open arms on a sterile surface **(Figure 1b)**. Return the slider to its furthermost position and pull on both threads. Check for proper loading **(Figure 2b).**

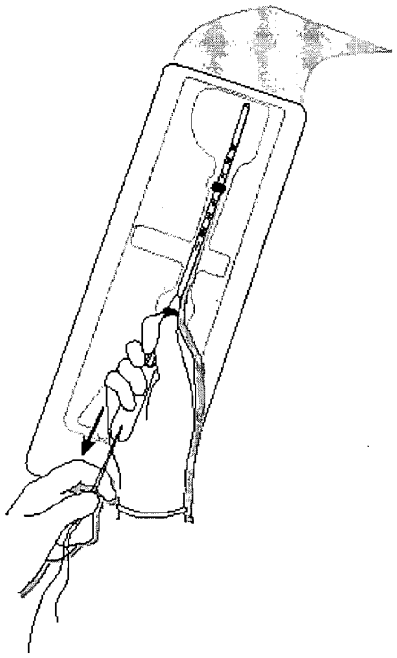


Figure 2a. Loading Mirena into the insertion tube

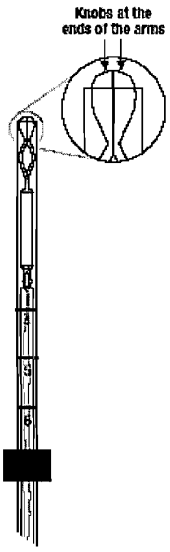


Figure 2b. Properly loaded Mirena with knobs closing the end of the insertion tube

Step 3
Secure the threads

- Secure the threads in the cleft at the bottom end of the handle to keep Mirena in the loaded position **(Figure 3)**.

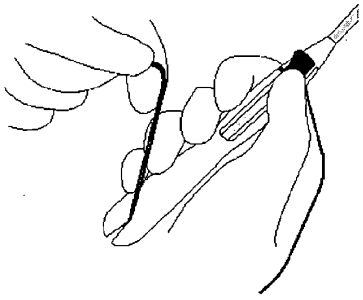


Figure 3. Threads are secured in the cleft

Step 4
Setting the flange

- Set the upper edge of the flange to the depth measured during the uterine sounding **(Figure 4)**.

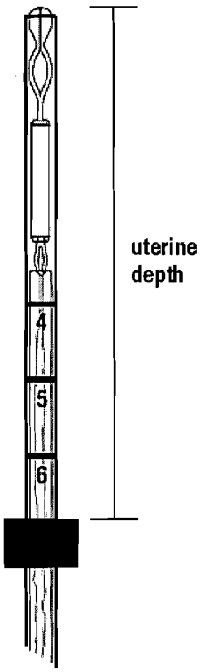


Figure 4. Setting the flange to the uterine depth

Step 5
Mirena is now ready to be inserted

- Continue to hold the slider with the thumb or forefinger firmly in the furthermost position. Grasp the tenaculum forceps with your other hand and apply gentle traction to align the cervical canal with the uterine cavity.
- While maintaining traction on the cervix, gently advance the insertion tube through the cervical canal and into the uterine cavity **UNTIL THE FLANGE IS 1.5 to 2 cm FROM THE EXTERNAL CERVICAL OS**.

  CAUTION: DO NOT ADVANCE FLANGE TO THE CERVIX AT THIS STEP. Maintaining the flange 1.5 to 2 cm from the cervical os allows sufficient space for the arms to open (when released) within the uterine cavity (**Figures 5 and 6b**).

NOTE! Do not force the inserter. If necessary, dilate the cervical canal.

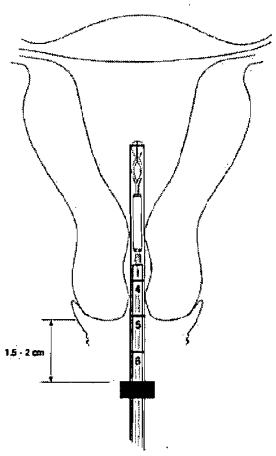


Figure 5. Advancing insertion tube until flange is 1.5 to 2 cm from cervical os

Step 6

Release the arms

- While holding the inserter steady, release the arms of Mirena by pulling the slider back until the top of the slider reaches the mark (raised horizontal line on the handle) **(Figure 6a)**.
- Wait approximately 10 seconds to allow the horizontal arms of Mirena to open and regain its T-shape **(Figure 6b)**.

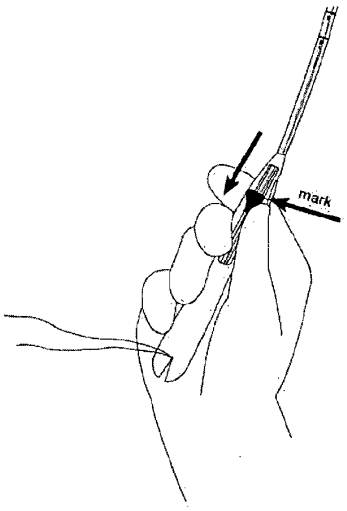


Figure 6a. Pulling the slider back to reach the mark

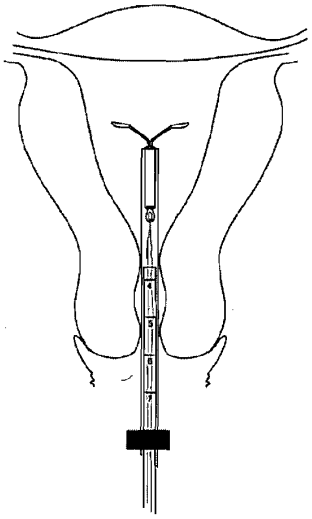


Figure 6b. Releasing the arms of Mirena

Step 7

Advance to fundal position

- Gently advance the inserter into the uterine cavity until the flange meets the cervix and you feel fundal resistance. Mirena should now be in the desired fundal position **(Figure 7)**.

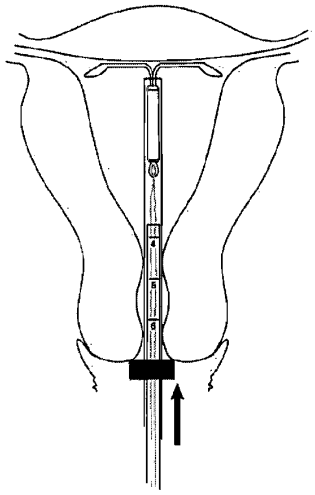


Figure 7. Mirena in the fundal position

Step 8

Release Mirena and withdraw the inserter

- While holding the inserter steady, pull the slider all the way down to release Mirena from the insertion tube **(Figure 8)**. The threads will release automatically from the cleft.
- Check that the threads are hanging freely and gently withdraw the inserter from the uterus. Be careful not to pull on the threads as this will displace Mirena.

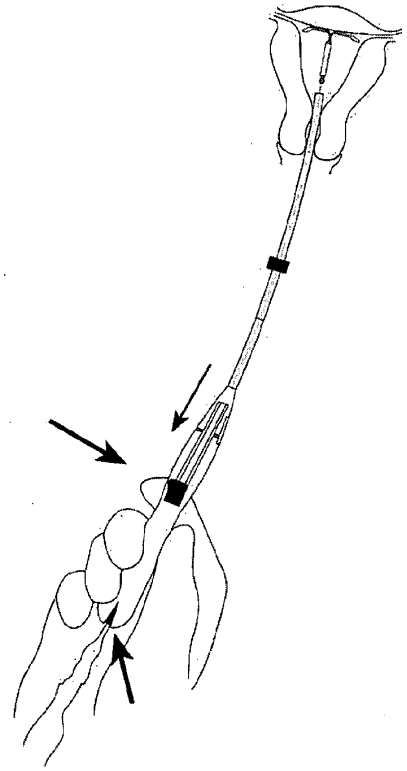


Figure 8. Releasing Mirena from the insertion tube

Step 9

Cut the threads

- Cut the threads perpendicular to the thread length, for example, with sterile curved scissors, leaving about 3 cm visible outside the cervix **(Figure 9).**
  NOTE: Cutting threads at an angle may leave sharp ends.

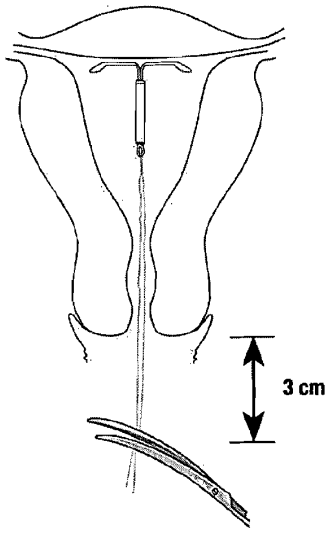


Figure 9. Cutting the threads

Mirena insertion is now complete.

IMPORTANT!

- If you suspect that Mirena is not in the correct position, check placement (for example, with transvaginal ultrasound). Remove Mirena if it is not positioned completely within the uterus. A removed Mirena must not be reinserted.
- If there is clinical concern and/or exceptional pain or bleeding during or after insertion, appropriate and timely measures and assessments, for example ultrasound, should be performed to exclude perforation.

2. Patient Counseling and Record Keeping

- Keep a copy of the consent form and lot number for your records.
- Counsel the patient on what to expect following Mirena insertion. Give the patient the Follow-up Reminder Card that is provided with the product. Discuss expected bleeding patterns during the first months of Mirena use.
- Prescribe analgesics, if indicated.

3. Patient Follow-up

- Patients should be reexamined and evaluated 4 to 12 weeks after insertion and once a year thereafter, or more frequently if clinically indicated.

4. Removal of Mirena

- Remove Mirena by applying gentle traction on the threads with forceps. The arms will fold upward as it is withdrawn from the uterus. Mirena should not remain in the uterus after 5 years.
- If the threads are not visible and Mirena is in the uterine cavity, it may be removed using a narrow forceps, such as an alligator forceps. This may require dilation of the cervical canal (see **PRECAUTIONS, Continuation and Removal**).

IMPORTANT!

- If Mirena is removed mid-cycle and the woman has had intercourse within the preceding week, she is at a risk of pregnancy unless a new Mirena is inserted immediately following removal.

5. Continuation of Contraception After Removal

- You may insert a new Mirena immediately following removal.
- If a patient with regular cycles wants to start a different birth control method, remove Mirena during the first 7 days of the menstrual cycle and start the new method.
- If a patient with irregular cycles or amenorrhea wants to start a different birth control method, or if you remove Mirena after the seventh day of the menstrual cycle, start the new method at least 7 days before removal.

HOW SUPPLIED

Mirena (levonorgestrel-releasing intrauterine system), containing a total of 52 mg levonorgestrel, is available in a carton of one sterile unit NDC# 50419-421-01. Each Mirena is packaged together with an inserter in a thermoformed blister package with a peelable lid.

Mirena is supplied sterile. Mirena is sterilized with ethylene oxide. Do not resterilize. For single use only. Do not use if the inner package is damaged or open. Insert before the end of the month shown on the label.

STORAGE AND HANDLING

Store at 25°C (77°F); with excursions permitted between 15-30°C (59-86°F) [See USP Controlled Room Temperature].

PATIENT INFORMATION

Mirena® (Mur-ā-nah)
(levonorgestrel-releasing intrauterine system)

Mirena is used to prevent pregnancy. Mirena does not protect against HIV infection (AIDS) and other sexually transmitted diseases (STDs).

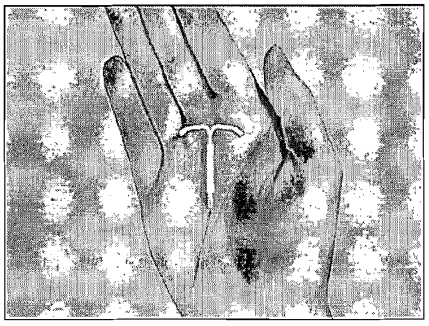
Read this Patient Information carefully before you decide if Mirena is right for you. This information does not take the place of talking with your gynecologist or other health care provider who specializes in women's health. If you have any questions about Mirena, ask your health care provider. You should also learn about other birth control methods to choose the one that is best for you.

What is Mirena?

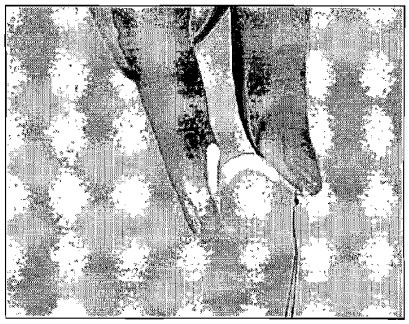
Mirena is a hormone-releasing system placed in your uterus to prevent pregnancy for up to 5 years.

Mirena is T-shaped. It is made of flexible plastic and contains a progestin hormone called levonorgestrel. Levonorgestrel is a progestin hormone often used in birth control pills; however, unlike many birth control pills, Mirena does not contain an estrogen. Mirena releases the hormone into the uterus. Only small amounts of the hormone enter your blood.

Two threads are attached to the stem of Mirena. The threads are the only part of Mirena you can feel when Mirena is in your uterus.



Mirena is small...



and flexible

What if I need birth control for more than 5 years?

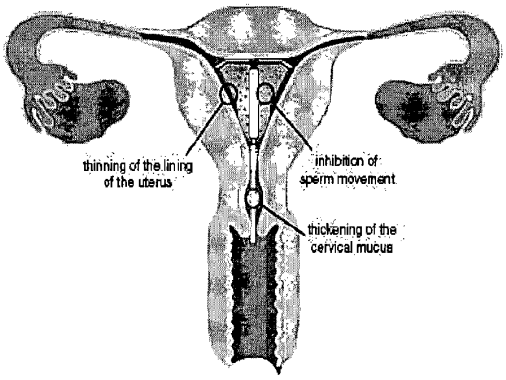
You must have Mirena removed after 5 years, but your health care provider can insert a new Mirena during the same office visit if you choose to continue using Mirena.

What if I change my mind about birth control and want to become pregnant in less than 5 years?

Your health care provider can remove Mirena at any time. You may become pregnant as soon as Mirena is removed. About 8 out of 10 women who want to become pregnant will become pregnant some time in the first year after Mirena is removed.

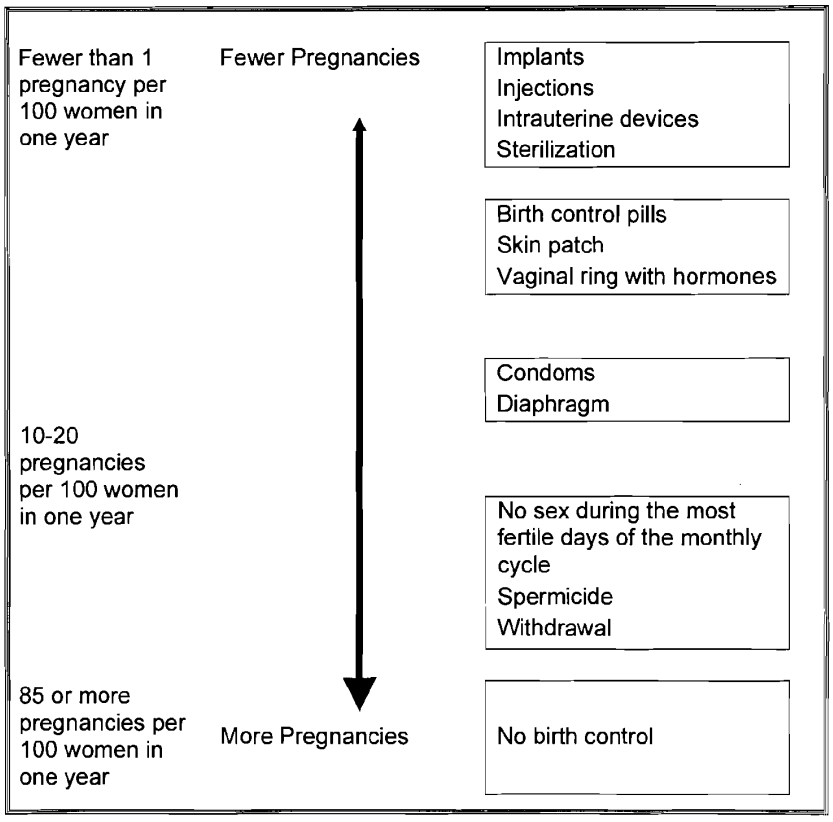
How does Mirena work?

It is not known exactly how Mirena works. Mirena may work in several ways. It may thicken your cervical mucus, thin the lining of your uterus, inhibit sperm movement and reduce sperm survival. Mirena may stop release of your egg from your ovary, but this is not the way it works in most cases. Most likely, these actions work together to prevent pregnancy.



How well does Mirena work?

The following chart shows the chance of getting pregnant for women who use different methods of birth control. Each box on the chart contains a list of birth control methods that are similar in effectiveness. The most effective methods are in the box at the top of the chart. Mirena, an intrauterine device, is in the box at the top of the chart. The box on the bottom of the chart shows the chance of getting pregnant for women who do not use birth control and are trying to get pregnant.



Who might use Mirena?

You might choose Mirena if you

- need birth control that is highly effective
- need birth control that is reversible
- need birth control that is easy to use
- have had at least one baby

Who should not use Mirena?

Do not use Mirena if you

- might be pregnant
- have had a serious pelvic infection called pelvic inflammatory disease (PID) unless you have had a normal pregnancy after the infection went away
- have an untreated pelvic infection now
- have had a serious pelvic infection in the past 3 months after a pregnancy

- can get infections easily. For example, if you have:
  - more than one sexual partner or your partner has more than one partner
  - problems with your immune system
  - leukemia
  - AIDS
  - intravenous drug abuse
- have or suspect you might have cancer of the uterus or cervix
- have bleeding from the vagina that has not been explained
- have liver disease or liver tumor
- have breast cancer now or in the past or suspect you have breast cancer
- have an intrauterine device in your uterus already
- have a condition of the uterus that changes the shape of the uterine cavity, such as large fibroid tumors
- are allergic to levonorgestrel, silicone, or polyethylene

Tell your health care provider if you

- recently had a baby or if you are breast feeding
- have diabetes (high blood sugar)
- were born with heart disease or have problems with your heart valves
- have problems with blood clotting or take medicine to reduce clotting
- have high blood pressure

How is Mirena placed?

First, your health care provider will examine your pelvis to find the exact position of your uterus. Your health care provider will then clean your vagina and cervix with an antiseptic solution, and slide a thin plastic tube containing Mirena into your uterus. Your health care provider will then remove the plastic tube, and leave Mirena in your uterus. Your healthcare provider will cut the threads to the right length. Placement takes only a few minutes during an office visit.

Some women may experience pain, bleeding and/or dizziness during and after placement. If these symptoms do not pass within half an hour while in a resting position, Mirena may not have been correctly placed. If necessary, your health care provider will examine you to determine if Mirena needs to be removed.

Should I check that Mirena is in the proper position?

Yes, you should check that Mirena is in proper position by feeling the removal threads. You should do this after each period. First, wash your hands with soap and water. Feel for the threads at the top of your vagina with your clean fingers. The threads are the only part of Mirena you should feel when Mirena is in your uterus. Be careful not to pull on the threads. If you feel more than just the threads, Mirena is not in the right position and may not prevent pregnancy. Call your health care provider to have it removed. If you cannot feel the threads at all, ask your healthcare provider to check that Mirena is still in the right place. In either case, use a non-hormonal birth control method (such as condoms or spermicide) until otherwise advised by your health care provider.

How soon after placement of Mirena should I return to my health care provider?

Call your health care provider if you have any question or concerns (see "When to call your health care provider"). Otherwise, you should return to your health care provider for a follow-up visit 4 to 12 weeks after Mirena is placed to make sure that Mirena is in the right position.

Can I use tampons with Mirena?

Tampons may be used with Mirena.

What if I become pregnant while using Mirena?

Call your health care provider right away if you think you are pregnant. If you get pregnant while using Mirena, you may have an ectopic pregnancy. This means that the pregnancy is not in the uterus. Unusual vaginal bleeding or abdominal pain may be a sign of ectopic pregnancy.

Ectopic pregnancy is an emergency that often requires surgery. Ectopic pregnancy can cause internal bleeding, infertility, and even death.

There are also risks if you get pregnant while using Mirena and the pregnancy is in the uterus. Severe infection, miscarriage, premature delivery, and even death can occur with pregnancies that continue with an intrauterine device (IUD). Because of this, your health care provider may try to remove Mirena, even though removing it may cause a miscarriage. If Mirena cannot be removed, talk with your health care provider about the benefits and risks of continuing the pregnancy.

If you continue your pregnancy, see your health care provider regularly. Call your health care provider right away if you get flu-like symptoms, fever, chills, cramping, pain, bleeding, vaginal discharge, or fluid leaking from your vagina. These may be signs of infection.

We do not know if Mirena can cause long-term effects on the fetus if it stays in place during a pregnancy.

How will Mirena change my periods?

For the first 3 to 6 months, your monthly period may become irregular. You may also have frequent spotting or light bleeding. A few women have heavy bleeding during this time. After your body adjusts, the number of bleeding days is likely to decrease, and you may even find that your periods stop altogether.

Is it safe to breast-feed while using Mirena?

You may use Mirena when you are breastfeeding if more than six weeks have passed since you had your baby. If you are breastfeeding, Mirena is not likely to affect the quality or amount of your breast milk or the health of your nursing baby.

Will Mirena interfere with sexual intercourse?

Neither you nor your partner should feel Mirena during intercourse, as Mirena is placed in the uterus, not in the vagina. Sometimes male partners feel the threads.

What are the possible side effects of using Mirena?

The following are serious but uncommon side effects of Mirena:

- *Pelvic inflammatory disease (PID).* Some IUD users get a serious pelvic infection called pelvic inflammatory disease. PID is usually sexually transmitted. You have a higher chance of getting PID if you or your partner have sex with other partners. PID can cause serious problems such as infertility, ectopic pregnancy or constant pelvic pain. PID is usually treated with antibiotics. More serious cases of PID may require surgery. A hysterectomy (removal of the uterus) is sometimes needed. In rare cases, infections that start as PID can even cause death.
  Tell your health care provider right away if you have any of these signs of PID: long-lasting or heavy bleeding, unusual vaginal discharge, low abdominal (stomach area) pain, painful sex, chills, or fever.
- *Life-threatening infection.* Life-threatening infection can occur within the first few days after Mirena is placed. Call your health care provider if you develop severe pain within a few hours after placement.
- *Embedment.* Mirena may adhere to the uterine wall. This is called embedment. If embedment occurs, Mirena may no longer prevent pregnancy and you may need surgery to have it removed.
- *Perforation.* Mirena may go through the uterus. This is called perforation. If your uterus is perforated, Mirena may no longer prevent pregnancy. It may move outside the uterus and can cause internal scarring, infection, or damage to other organs, and you may need surgery to have Mirena removed.

Common side effects of Mirena include:

- *Discomfort during placement.* Dizziness, faintness, bleeding or cramping may occur during placement. This is common. Let your health care provider know if the cramping is severe.
- *Expulsion.* Mirena may come out by itself. This is called expulsion. You may become pregnant if Mirena comes out. If you notice that Mirena has come out, use a backup birth control method like condoms and call your health care provider.
- *Missed menstrual periods.* About 2 out of 10 women stop having periods after 1 year of Mirena use. The periods come back when Mirena is removed. If you do not have a period for 6 weeks during Mirena use, contact your health care provider.
- *Changes in bleeding.* You may have bleeding and spotting between menstrual periods, especially during the first 3 to 6 months. Sometimes the bleeding is heavier than usual at first. However, the bleeding usually becomes lighter than usual and may be irregular. Call your health care provider if the bleeding remains heavier than usual or if the bleeding becomes heavy after it has been light for a while.

- *Cyst on the ovary*. Approximately 12% (12 out of 100) of women using Mirena develop a cyst on the ovary. These cysts usually disappear on their own in a month or two. However, cysts can cause pain and sometimes cysts will need surgery.

This is not a complete list of possible side effects with Mirena. For more information, ask your health care provider.

Call your doctor for medical advice about side effects. You may report side effects to the manufacturer at 1-888-842-2937, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

When should I call my health care provider?

Call your health care provider if you have any concerns about Mirena. Be sure to call if you

- think you are pregnant
- have pelvic pain or pain during sex
- have unusual vaginal discharge or genital sores
- have unexplained fever
- might be exposed to sexually transmitted diseases (STDs)
- cannot feel Mirena 's threads
- develop very severe or migraine headaches
- have yellowing of the skin or whites of the eyes. These may be signs of liver problems.
- have a stroke or heart attack
- or your partner becomes HIV positive
- have severe vaginal bleeding or bleeding that lasts a long time
- miss a menstrual period

General advice about prescription medicines

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. This leaflet summarizes the most important information about Mirena. If you would like more information, talk with your health care provider. You can ask your health care provider for information about Mirena that is written for health providers.

Manufactured for:

Bayer HealthCare
Pharmaceuticals

Bayer HealthCare Pharmaceuticals Inc.
Wayne, NJ 07470

Telephone number: 1-888-842-2937

Manufactured in Finland

This patient information booklet was updated July 2008.

Fill out the following checklist. Your answers will help you and your health care provider decide if Mirena is a good choice for you.

Do you have any of these conditions?

	Yes	No	Don't know— will discuss with my health care provider
Abnormalities of the uterus	☐	☐	☐
Acquired immune deficiency syndrome (AIDS)	☐	☐	☐
Anemia or blood clotting problems	☐	☐	☐
Bleeding between periods	☐	☐	☐
Cancer of the uterus or cervix	☐	☐	☐
History of other types of cancer	☐	☐	☐
Steroid therapy (for example, prednisone)	☐	☐	☐
Possible pregnancy	☐	☐	☐
Diabetes	☐	☐	☐
Ectopic pregnancy in the past	☐	☐	☐
Fainting attacks	☐	☐	☐
Genital sores	☐	☐	☐
Heart disease	☐	☐	☐
Heart murmur	☐	☐	☐

Heavy menstrual flow	☐	☐	☐
Hepatitis or other liver disease	☐	☐	☐
Infection of the uterus or cervix	☐	☐	☐
IUD in place now or in the past	☐	☐	☐
IV drug abuse now or in the past	☐	☐	☐
Leukemia	☐	☐	☐
More than one sexual partner	☐	☐	☐
A sexual partner who has more than one sexual partner	☐	☐	☐
Pelvic infection	☐	☐	☐
Abortion or miscarriage in the past 2 months	☐	☐	☐
Pregnancy in the past 2 months	☐	☐	☐
Severe menstrual cramps	☐	☐	☐
Severe headache	☐	☐	☐
Sexually transmitted disease (STD), such as gonorrhea or chlamydia	☐	☐	☐
Stroke	☐	☐	☐
Abnormal Pap smear	☐	☐	☐
Unexplained genital bleeding	☐	☐	☐
Uterine or pelvic surgery	☐	☐	☐
Vaginal discharge or infection	☐	☐	☐
HIV infection	☐	☐	☐
Breastfeeding	☐	☐	☐
High blood pressure	☐	☐	☐

Manufactured for:

Bayer HealthCare
Pharmaceuticals

Bayer HealthCare Pharmaceuticals Inc.
Wayne, NJ 07470

Telephone number: 1-888-842-2937

Manufactured in Finland

component codes July 2008

LOT:

Mirena®
(levonorgestrel-releasing intrauterine system)
(sistema intrauterino liberador de levonorgestrel)

CONSENT FORM
FORMULARIO DE CONSENTIMIENTO

I have read the patient information booklet and have had my questions about Mirena answered. I choose to have Mirena inserted by
He leído el folleto de información para pacientes y he recibido respuesta a todas mis preguntas sobre el dispositivo Mirena. He decidido que el dispositivo Mirena sea colocado por

Healthcare Provider's Name
Nombre del médico

Patient's Signature / Date/Fecha
Firma de la paciente

The patient has signed this consent form in my presence after I counseled her and answered her questions.
La paciente ha firmado este formulario de consentimiento en mi presencia después de haberla asesorado y respondido a sus preguntas.

Healthcare Provider's Signature / Date/Fecha
Firma del médico

The system is scheduled for removal on / Date/Fecha
El dispositivo debe ser retirado por el médico el

Manufactured for:
Fabricado para:
Bayer HealthCare Pharmaceuticals

Bayer HealthCare Pharmaceuticals Inc.
Wayne, NJ 07470

Manufactured in Finland
Fabricado en Finlandia

81179515 6795102 July 2008

Patient Information Booklet
Folleto de información para pacientes

Mirena®
(levonorgestrel-releasing intrauterine system)
(sistema intrauterino liberador de levonorgestrel)

PATIENT INFORMATION

MIRENA® (Mur-ā-nah)
(levonorgestrel-releasing intrauterine system)

Mirena is used to prevent pregnancy. Mirena does not protect against HIV infection (AIDS) and other sexually transmitted diseases (STDs).

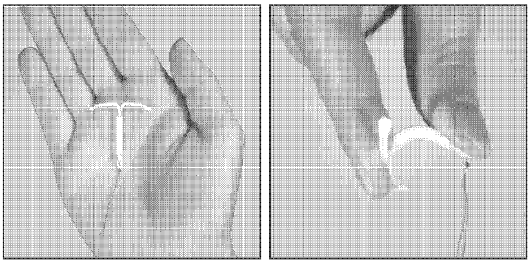
Read this Patient Information carefully before you decide if Mirena is right for you. This information does not take the place of talking with your gynecologist or other healthcare provider who specializes in women's health. If you have any questions about Mirena, ask your healthcare provider. You should also learn about other birth control methods to choose the one that is best for you.

What is Mirena?

Mirena is a hormone-releasing system placed in your uterus to prevent pregnancy for up to 5 years.

Mirena is T-shaped. It is made of flexible plastic and contains a progestin hormone called levonorgestrel. Levonorgestrel is a progestin hormone often used in birth control pills; however, unlike many birth control pills, Mirena does not contain an estrogen. Mirena releases the hormone into the uterus. Only small amounts of the hormone enter your blood.

Two threads are attached to the stem of Mirena. The threads are the only part of Mirena you can feel when Mirena is in your uterus.



Mirena is small... and flexible

What if I need birth control for more than 5 years?

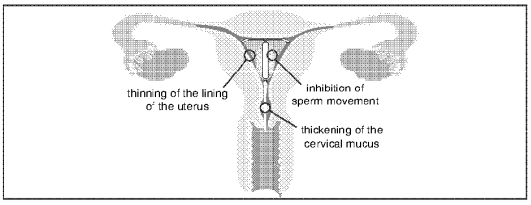
You must have Mirena removed after 5 years, but your healthcare provider can insert a new Mirena during the same office visit if you choose to continue using Mirena.

What if I change my mind about birth control and want to become pregnant in less than 5 years?

Your healthcare provider can remove Mirena at any time. You may become pregnant as soon as Mirena is removed. About 8 out of 10 women who want to become pregnant will become pregnant some time in the first year after Mirena is removed.

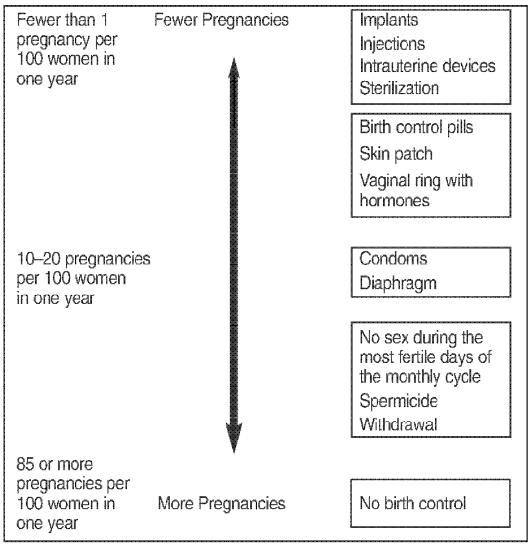
How does Mirena work?

It is not known exactly how Mirena works. Mirena may work in several ways. It may thicken your cervical mucus, thin the lining of your uterus, inhibit sperm movement and reduce sperm survival. Mirena may stop release of your egg from your ovary, but this is not the way it works in most cases. Most likely, these actions work together to prevent pregnancy.



How well does Mirena work?

The following chart shows the chance of getting pregnant for women who use different methods of birth control. Each box on the chart contains a list of birth control methods that are similar in effectiveness. The most effective methods are in the box at the top of the chart. Mirena, an intrauterine device, is in the box at the top of the chart. The box on the bottom of the chart shows the chance of getting pregnant for women who do not use birth control and are trying to get pregnant.



Who might use Mirena?

You might choose Mirena if you

- need birth control that is highly effective
- need birth control that is reversible
- need birth control that is easy to use
- have had at least one baby

Who should not use Mirena?

Do not use Mirena if you

- might be pregnant
- have had a serious pelvic infection called pelvic inflammatory disease (PID) unless you have had a normal pregnancy after the infection went away
- have an untreated pelvic infection now
- have had a serious pelvic infection in the past 3 months after a pregnancy
- can get infections easily. For example, if you have:
  - more than one sexual partner or your partner has more than one partner
  - problems with your immune system
  - leukemia
  - AIDS
  - intravenous drug abuse
- have or suspect you might have cancer of the uterus or cervix
- have bleeding from the vagina that has not been explained
- have liver disease or liver tumor
- have breast cancer now or in the past or suspect you have breast cancer
- have an intrauterine device in your uterus already
- have a condition of the uterus that changes the shape of the uterine cavity, such as large fibroid tumors
- are allergic to levonorgestrel, silicone, or polyethylene

Tell your healthcare provider if you

- recently had a baby or if you are breast feeding
- have diabetes (high blood sugar)
- were born with heart disease or have problems with your heart valves
- have problems with blood clotting or take medicine to reduce clotting
- have high blood pressure

How is Mirena placed?

First, your healthcare provider will examine your pelvis to find the exact position of your uterus. Your healthcare provider will then clean your vagina and cervix with an antiseptic solution, and slide a thin plastic tube containing Mirena into your uterus. Your healthcare provider will then remove the plastic tube, and leave Mirena in your uterus. Your healthcare provider will cut the threads to the right length. Placement takes only a few minutes during an office visit.

Some women may experience pain, bleeding and/or dizziness during and after placement. If these symptoms do not pass within half an hour while in a resting position, Mirena may not have been correctly placed. If necessary, your healthcare provider will examine you to determine if Mirena needs to be removed.

Should I check that Mirena is in the proper position?

Yes, you should check that Mirena is in proper position by feeling the removal threads. You should do this after each period. First, wash your hands with soap and water. Feel for the threads at the top of your vagina with your clean fingers. The threads are the only part of Mirena you should feel when Mirena is in your uterus. Be careful not to pull on the threads. If you feel more than just the threads, Mirena is not in the right position and may not prevent pregnancy. Call your healthcare provider to have it removed. If you cannot feel the threads at all, ask your healthcare provider to check that Mirena is still in the right place. In either case, use a non-hormonal birth control method (such as condoms or spermicide) until otherwise advised by your healthcare provider.

How soon after placement of Mirena should I return to my healthcare provider?

Call your healthcare provider if you have any question or concerns (see "When to call your healthcare provider"). Otherwise, you should return to your healthcare provider for a follow-up visit 4 to 12 weeks after Mirena is placed to make sure that Mirena is in the right position.

Can I use tampons with Mirena?

Tampons may be used with Mirena.

What if I become pregnant while using Mirena?

Call your healthcare provider right away if you think you are pregnant. If you get pregnant while using Mirena, you may have an ectopic pregnancy. This means that the pregnancy is not in the uterus. Unusual vaginal bleeding or abdominal pain may be a sign of ectopic pregnancy.

Ectopic pregnancy is an emergency that often requires surgery. Ectopic pregnancy can cause internal bleeding, infertility, and even death.

There are also risks if you get pregnant while using Mirena and the pregnancy is in the uterus. Severe infection, miscarriage, premature delivery, and even death can occur with pregnancies that continue with an intrauterine device (IUD). Because of this, your healthcare provider may try to remove Mirena, even though removing it may cause a miscarriage. If Mirena cannot be removed, talk with your healthcare provider about the benefits and risks of continuing the pregnancy.

If you continue your pregnancy, see your healthcare provider regularly. Call your healthcare provider right away if you get flu-like symptoms, fever, chills, cramping, pain, bleeding, vaginal discharge, or fluid leaking from your vagina. These may be signs of infection.

We do not know if Mirena can cause long-term effects on the fetus if it stays in place during a pregnancy.

How will Mirena change my periods?

For the first 3 to 6 months, your monthly period may become irregular. You may also have frequent spotting or light bleeding. A few women have heavy

bleeding during this time. After your body adjusts, the number of bleeding days is likely to decrease, and you may even find that your periods stop altogether.

Is it safe to breast-feed while using Mirena?

You may use Mirena when you are breastfeeding if more than six weeks have passed since you had your baby. If you are breastfeeding, Mirena is not likely to affect the quality or amount of your breast milk or the health of your nursing baby.

Will Mirena interfere with sexual intercourse?

Neither you nor your partner should feel Mirena during intercourse, as Mirena is placed in the uterus, not in the vagina. Sometimes male partners feel the threads.

What are the possible side effects of using Mirena?

The following are serious but uncommon side effects of Mirena:

- *Pelvic inflammatory disease (PID).* Some IUD users get a serious pelvic infection called pelvic inflammatory disease. PID is usually sexually transmitted. You have a higher chance of getting PID if you or your partner have sex with other partners. PID can cause serious problems such as infertility, ectopic pregnancy or constant pelvic pain. PID is usually treated with antibiotics. More serious cases of PID may require surgery. A hysterectomy (removal of the uterus) is sometimes needed. In rare cases, infections that start as PID can even cause death.

  Tell your healthcare provider right away if you have any of these signs of PID: long-lasting or heavy bleeding, unusual vaginal discharge, low abdominal (stomach area) pain, painful sex, chills, or fever.
- *Life-threatening infection.* Life-threatening infection can occur within the first few days after Mirena is placed. Call your healthcare provider if you develop severe pain within a few hours after placement.
- *Embedment.* Mirena may adhere to the uterine wall. This is called embedment. If embedment occurs, Mirena may no longer prevent pregnancy and you may need surgery to have it removed.
- *Perforation.* Mirena may go through the uterus. This is called perforation. If your uterus is perforated, Mirena may no longer prevent pregnancy. It may move outside the uterus and can cause internal scarring, infection, or damage to other organs, and you may need surgery to have Mirena removed.

Common side effects of Mirena include:

- *Discomfort during placement.* Dizziness, faintness, bleeding or cramping may occur during placement. This is common. Let your healthcare provider know if the cramping is severe.
- *Expulsion.* Mirena may come out by itself. This is called expulsion. You may become pregnant if Mirena comes out. If you notice that Mirena has come out, use a backup birth control method like condoms and call your healthcare provider.
- *Missed menstrual periods.* About 2 out of 10 women stop having periods after 1 year of Mirena use. The periods come back when Mirena is removed. If you do not have a period for 6 weeks during Mirena use, contact your healthcare provider.
- *Changes in bleeding.* You may have bleeding and spotting between menstrual periods, especially during the first 3 to 6 months. Sometimes the bleeding is heavier than usual at first. However, the bleeding usually becomes lighter than usual and may be irregular. Call your healthcare provider if the bleeding remains heavier than usual or if the bleeding becomes heavy after it has been light for a while.
- *Cyst on the ovary.* Approximately 12% (12 out of 100) of women using Mirena develop a cyst on the ovary. These cysts usually disappear on their own in a month or two. However, cysts can cause pain and sometimes cysts will need surgery.

This is not a complete list of possible side effects with Mirena. For more information, ask your healthcare provider.

Call your doctor for medical advice about side effects. You may report side effects to the manufacturer at 1-888-842-2937, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

When should I call my healthcare provider?

Call your healthcare provider if you have any concerns about Mirena. Be sure to call if you

- think you are pregnant
- have pelvic pain or pain during sex
- have unusual vaginal discharge or genital sores
- have unexplained fever
- might be exposed to sexually transmitted diseases (STDs)
- cannot feel Mirena 's threads
- develop very severe or migraine headaches
- have yellowing of the skin or whites of the eyes. These may be signs of liver problems.
- have a stroke or heart attack
- or your partner becomes HIV positive
- have severe vaginal bleeding or bleeding that lasts a long time
- miss a menstrual period

General advice about prescription medicines

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. This leaflet summarizes the most important information about Mirena. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider for information about Mirena that is written for health providers.

Manufactured for:

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Bayer HealthCare Pharmaceuticals Inc.
Wayne, NJ 07470

Manufactured in Finland

Telephone number: 1-888-842-2937

This patient information booklet was updated July 2008.

Fill out the following checklist. Your answers will help you and your healthcare provider decide if Mirena is a good choice for you.

Do you have any of these conditions?

	Yes	No	Don't know—will discuss with my healthcare provider
Abnormalities of the uterus	❑	❑	❑
Acquired immune deficiency syndrome (AIDS)	❑	❑	❑
Anemia or blood clotting problems	❑	❑	❑
Bleeding between periods	❑	❑	❑
Cancer of the uterus or cervix	❑	❑	❑
History of other types of cancer	❑	❑	❑
Steroid therapy (for example, prednisone)	❑	❑	❑
Possible pregnancy	❑	❑	❑
Diabetes	❑	❑	❑
Ectopic pregnancy in the past	❑	❑	❑
Fainting attacks	❑	❑	❑
Genital sores	❑	❑	❑
Heart disease	❑	❑	❑
Heart murmur	❑	❑	❑
Heavy menstrual flow	❑	❑	❑
Hepatitis or other liver disease	❑	❑	❑
Infection of the uterus or cervix	❑	❑	❑
IUD in place now or in the past	❑	❑	❑
IV drug abuse now or in the past	❑	❑	❑
Leukemia	❑	❑	❑
More than one sexual partner	❑	❑	❑
A sexual partner who has more than one sexual partner	❑	❑	❑
Pelvic infection	❑	❑	❑
Abortion or miscarriage in the past 2 months	❑	❑	❑
Pregnancy in the past 2 months	❑	❑	❑
Severe menstrual cramps	❑	❑	❑
Severe headache	❑	❑	❑
Sexually transmitted disease (STD), such as gonorrhea or chlamydia	❑	❑	❑
Stroke	❑	❑	❑
Abnormal Pap smear	❑	❑	❑
Unexplained genital bleeding	❑	❑	❑
Uterine or pelvic surgery	❑	❑	❑
Vaginal discharge or infection	❑	❑	❑
HIV infection	❑	❑	❑
Breastfeeding			
High blood pressure	❑	❑	❑

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81179515 6795102 July 2008

INFORMACIÓN PARA LA PACIENTE

Mirena® (Mi-re-na)

(sistema de administración intrauterina de levonorgestrol)

La Mirena se utiliza para prevenir el embarazo. La Mirena no protege contra la infección por VIH (SIDA) y otras enfermedades transmitidas sexualmente (ETS).

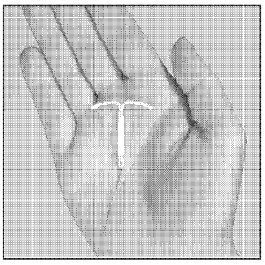
Lea cuidadosamente esta información para la paciente, antes de decidir si la Mirena es adecuada para usted. Esta información no reemplaza la consulta con su ginecólogo u otro proveedor de atención médica, que se especialice en la salud femenina. Si desea hacer cualquier pregunta relativa a la Mirena, diríjase a su proveedor de atención médica. También debe conocer otros métodos de control de la natalidad, para escoger el que sea óptimo para usted.

¿Qué es la Mirena?

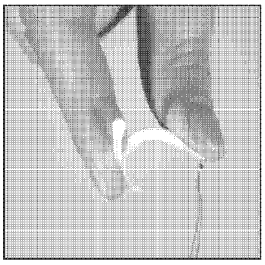
La Mirena es un sistema de administración de hormonas, colocado en su útero para prevenir el embarazo, durante un máximo de 5 años.

La Mirena tiene forma de T. Está hecha de plástico flexible y contiene una hormona progestina llamada "levonorgestrol". El Levonorgestrol es una hormona progestina, utilizada frecuentemente en las píldoras de control de la natalidad. No obstante, a diferencia de muchas de estas píldoras, la Mirena no contiene estrógenos. La Mirena administra la hormona dentro del útero. Solamente pequeñas cantidades de la hormona entran a su sangre.

Los dos cordoncillos están acheridos al eje de la Mirena. Los cordoncillos son la única parte de la Mirena que usted puede sentir, cuando ésta se encuentra en su útero.



La Mirena es pequeña...



y flexible

¿Necesidad del control de la natalidad durante más de 5 años?

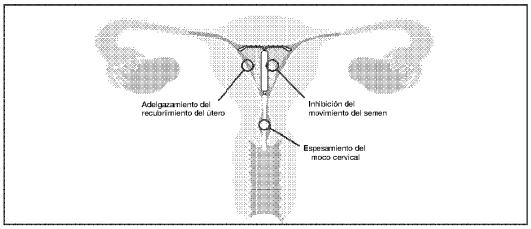
5 años después de la inserción, deberá hacerse extraer la Mirena, pero su proveedor de atención médica podrá insertar una nueva Mirena durante la misma consulta, si usted opta por continuar utilizándola.

¿Cambio de opinión y deseo de quedar embarazada, en menos de 5 años?

Su proveedor de atención médica podrá extraer la Mirena en cualquier momento. Podrá quedar embarazada, en cuanto se extraiga la Mirena. Aproximadamente 8 de cada 10 mujeres que desean quedar embarazadas, quedarán embarazadas en algún momento del primer año siguiente a la extracción de la Mirena.

¿Cómo obra la Mirena?

No se sabe exactamente cómo obra la Mirena. Quizá obre de varias maneras. Es posible que espese el moco cervical, adelgace el recubrimiento de su útero, inhiba el movimiento del semen y reduzca su supervivencia. La Mirena quizá detenga la liberación de su óvulo del ovario, pero ésta no es la forma en la cual obra en la mayoría de los casos. Lo más probable es que estas acciones obren conjuntamente para evitar el embarazo.



¿Eficacia de la Mirena?

El siguiente cuadro muestra las probabilidades de quedar embarazadas, para las mujeres que utilizan diferentes métodos de control de la natalidad. Cada casilla del cuadro contiene una lista de métodos de control de la natalidad, cuya eficacia es similar. Los métodos más eficaces se encuentran en la casilla superior del cuadro. La Mirena, un dispositivo intrauterino, se encuentra en la casilla de la parte superior del cuadro. La casilla del pie del cuadro muestra las probabilidades de quedar embarazadas, para las mujeres que no utilizan el control de la natalidad y están tratando de quedar embarazadas.

Menos de 1 embarazo en un año, por cada 100 mujeres	Menos embarazos	Implantes Inyecciones Dispositivos intrauterinos Esterilización
		Píldoras de control de la natalidad Parche cutáneo Anillo vaginal, con hormonas
De 10 a 20 embarazos en 1 año, por cada 100 mujeres		Condones Diafragma
		Abstención sexual, durante los días más fértiles del ciclo mensual Espermicida Abstinencia
85 o más embarazos en 1 año, por cada 100 mujeres	Más embarazos	Ningún control de la natalidad

¿Quién puede usar la Mirena?

Puede escoger la Mirena, si:

- Necesita un control de la natalidad altamente eficaz.
- Necesita un control de la natalidad reversible.
- Necesita un control de la natalidad de fácil uso.
- Ha tenido un bebe, por lo menos.

¿Quién no debe usar la Mirena?

No use la Mirena, si:

- Puede estar embarazada.
- Ha tenido una enfermedad pélvica grave, llamada "enfermedad inflamatoria pélvica", (EIP) a menos que haya tenido un embarazo normal, después de la cura de la infección.
- Tiene actualmente una infección pélvica sin tratar.
- Ha tenido una infección pélvica grave, en los 3 meses siguientes a un embarazo.

- Puede contraer infecciones fácilmente. Por ejemplo, si:
  - Tiene más de una pareja sexual o si su pareja la tiene.
  - Tiene problemas con su sistema inmunitario.
  - Tiene leucemia.
  - Si tiene SIDA.
  - Consume drogas intravenosas.
- Tiene o sospecha tener cáncer de la matriz o el cuello.
- Tiene hemorragias vaginales inexplicables.
- Tiene una enfermedad o tumor hepático.
- Tiene actualmente o ha tenido anteriormente cáncer de seno o sospecha que lo tiene.
- Ya tiene en el útero un dispositivo intrauterino.
- Tiene un problema del útero que cambia la forma de la cavidad uterina, tal como grandes tumores fibroides.
- Es alérgica al levonorgestrol, la silicona o el polietileno.

Informe a su proveedor de atención médica, si:

- Ha tenido recientemente un bebe o está lactando.
- Tiene diabetes (azúcar alta en la sangre).
- Nació con una enfermedad cardiaca o tiene problemas con sus válvulas cardiacas.
- Tiene problemas de coagulación o le administran medicinas para reducirla.
- Tiene una tensión arterial alta.

¿Cómo se coloca la Mirena?

En primer lugar, su proveedor de atención médica examinará su pelvis, para hallar la posición exacta de su útero. Su proveedor de atención médica limpiará a continuación su vagina y cuello con una solución antibiótica, y hará deslizar en su matriz un fino tubo plástico, que contiene la Mirena. Su proveedor de atención médica extraerá a continuación el tubo plástico y dejará la Mirena en su útero. Su proveedor de atención médica cortará los corconcillos a la longitud correcta. La colocación requiere unos pocos minutos, durante una consulta.

Algunas mujeres quizá experimenten dolor, hemorragia, mareos o todos ellos, durante la colocación y después de ella. Si estos síntomas no cesan en media hora en posición de descanso, quizá la Mirena no fue colocada correctamente. Si es necesario, su proveedor de atención médica la examinará, para ver si es necesario extraer la Mirena.

¿Verificación por la paciente de la posición de la Mirena?

Usted debe verificar que la Mirena se encuentre en la posición apropiada, tocando los cordoncillos de extracción. Deberá hacerlo después de cada período. En primer lugar, lávese las manos con agua y jabón. Toque los corconcillos en la parte superior de la vagina, con los dedos limpios. Los corconcillos son la única parte de la Mirena que usted deberá poder tocar, cuando la Mirena se encuentre en su útero. Tenga cuidado de no tirar de los cordoncillos. Si puede tocar algo más que los cordoncillos, la Mirena no estará en la posición correcta, y quizá no prevenga el embarazo. Llame a su proveedor de atención médica, para que se la extraiga. Si no puede tocar los cordoncillos en absoluto, pida a su proveedor de atención médica verificar que la Mirena se encuentre aún en la posición correcta. En cualquiera de los casos, utilice un método de control de la natalidad no hormonal (tal como condones o espermicida), hasta que su proveedor de atención médica la aconseje otra cosa.

¿Consulta después de la colocación de la Mirena?

Llame a su proveedor de atención médica, si desea plantear cualquier pregunta o problema (vea "Cuándo debe llamar a su proveedor de atención médica"). De lo contrario, deberá consultar nuevamente a su proveedor de atención médica durante un control, de 4 a 12 semanas después de la colocación de la Mirena, para verificar que la Mirena se encuentre en la posición correcta.

¿El uso de tampones y la Mirena?

Puede usar tampones con la Mirena.

¿Embarazo, mientras se está utilizando la Mirena?

Llame inmediatamente a su proveedor de atención médica, si cree que está embarazada. Si queda embarazada mientras está utilizando la Mirena, puede tener un embarazo ectópico. Esto significa que el embarazo no se encuentra en el útero. Las hemorragias vaginales anormales o el dolor abdominal pueden ser síntomas de embarazo ectópico.

El embarazo ectópico es una emergencia, que frecuentemente requiere cirugía. El embarazo ectópico puede causar hemorragia interna, esterilidad, y aun la muerte.

También hay riesgos, si queda embarazada mientras utiliza la Mirena y el embarazo está en el útero. Las infecciones graves, los abortos espontáneos, los partos prematuros y aun la muerte pueden presentarse en los embarazos que continúan con un dispositivo intrauterino (DIU). Debido a esto, quizá su proveedor de atención médica trate de extraer la Mirena, aunque la extracción puede causar un aborto espontáneo. Si la Mirena no se puede extraer, discuta con su proveedor de atención médica las ventajas y los riesgos de continuar el embarazo.

Si continúa su embarazo, consulte regularmente a su proveedor de atención médica. Llámelo de inmediato, si presenta síntomas similares a los de la gripe, fiebre, escalofríos, contracciones dolorosas, dolor, hemorragia, secreción vaginal o si escapa líquido de su vagina. Éstos pueden ser síntomas de infección.

No sabemos si la Mirena puede causar efectos a largo plazo sobre el feto, si continúa colocada durante el embarazo.

¿Cambio de los períodos por la Mirena?

Durante los primeros 3 a 6 meses, su período mensual puede volverse irregular. Quizá presente también frecuentes manchas o hemorragias ligeras. Unas pocas mujeres presentan también hemorragias copiosas durante este período. Después de que su cuerpo se adapte, es probable que el número de días de hemorragia disminuya, e inclusive es posible que sus períodos cesen por completo.

¿La lactación, durante el uso de la Mirena?

Podrá usar la Mirena mientras esté lactando, si han transcurrido más de seis semanas desde el nacimiento de su bebe. Si está amamantando, no es probable que la Mirena afecte la calidad o cantidad de su leche, ni la salud de su bebe lactante.

¿Interferencia de la Mirena con las relaciones sexuales?

Ni usted ni su pareja deberán sentir la Mirena durante las relaciones sexuales, pues la Mirena se coloca en el útero, no en la vagina. A veces, los hombres sienten los cordoncillos.

¿Posibles efectos secundarios del uso de la Mirena?

Los siguientes son graves (pero raros) efectos secundarios del uso de la Mirena:

- *Enfermedad inflamatoria pélvica (EIP):* algunas mujeres que usan la Mirena contraen una grave inflamación pélvica, llamada "enfermedad inflamatoria pélvica". La EIP generalmente se transmite sexualmente. Tiene mayores probabilidades de contraer la EIP, si usted o su pareja tienen relaciones sexuales con otras parejas. La EIP puede causar graves problemas, tales como esterilidad, embarazo ectópico o dolor pélvico constante. La EIP se trata habitualmente con antibióticos. Los casos más graves de EIP pueden requerir cirugía. A veces se requiere una histerectomía (extirpación del útero). En casos raros, infecciones que se inician como EIP pueden llegar a causar la muerte.
- Informe inmediatamente a su proveedor de atención médica, si tiene cualquiera de los siguientes síntomas de EIP: hemorragia prolongada o copiosa, secreción vaginal inusitada, dolor en el bajo vientre (área del estómago), relaciones sexuales dolorosas, escalofríos o fiebre.
- *Infección que amenace la vida:* puede presentarse pocos días después de la colocación de la Mirena. Llame a su proveedor de atención médica, si presenta un dolor intenso, unas pocas horas después de la colocación de la Mirena.
- *Incrustación:* la Mirena puede adherirse a la pared uterina. Esto se llama "incrustación". Si se produce la incrustación, la Mirena no podrá prevenir el embarazo, y quizá usted necesite cirugía para extraerla.
- *Perforación:* la Mirena puede atravesar el útero. Esto se llama "perforación". Si se le perfora el útero, la Mirena ya no podrá impedir el embarazo. La Mirena puede salirse del útero y causar escaras internas, infección o daños a los demás órganos, y quizá usted requiera cirugía para extraérsela.

Los efectos secundarios comunes de la Mirena comprenden:

- *Molestias, durante la colocación:* pueden presentarse mareos, desmayos, hemorragias o contracciones dolorosas, durante la colocación. Esto es común. Informe a su proveedor de atención médica, si las contracciones dolorosas son intensas.
- *Expulsión:* la Mirena puede salirse por sí sola. Esto se llama "expulsión". Usted puede quedar embarazada, si la Mirena se sale. Si

nota que la Mirena se ha salido, utilice un método de control de la natalidad de refuerzo, tal como condones, y llame a su proveedor de atención médica.

- *Ausencia de períodos menstruales:* aproximadamente 2 de cada 10 mujeres dejan de tener períodos, tras un año de uso de la Mirena. Los períodos se reinician cuando se extrae la Mirena. Si no tiene el período durante 6 semanas, durante el uso de la Mirena, comuníquese con su proveedor de atención médica
- *Cambios en las hemorragias:* quizá presente hemorragias o manchas entre los períodos menstruales, especialmente durante los primeros 3 a 6 meses. A veces la hemorragia es inicialmente más copiosa que la habitual. No obstante, la hemorragia generalmente se hace más ligera que de costumbre, y puede ser irregular. Llame a su proveedor de atención médica, si la hemorragia sigue siendo más copiosa que la habitual, o si se vuelve más copiosa después de haber sido más ligera durante un tiempo.
- *Quiste ovárico:* aproximadamente el 12% (12 de cada 100) de las mujeres que utilizan la Mirena, presentan quistes ováricos. Estos quistes habitualmente desaparecen por sí solos, en uno o dos meses. No obstante, los quistes pueden causar dolor, y a veces requieren cirugía.

Esta no es una lista completa de los efectos secundarios posibles de la Mirena. Para obtener información adicional, pregunte a su proveedor de atención médica.

Llame a su médico, para pedir consejo respecto a los efectos secundarios. Puede informar de los efectos secundarios al fabricante, en el 1-888-842-2937, o a la Administración de Alimentos y Drogas (Food and Drug Administration, FDA) en el 1-800-FDA-1088 o en www.fda.gov/medwatch.

Cuándo debe llamar a su proveedor de atención médica

Llame a su proveedor de atención médica, si tiene cualquier problema con la Mirena. No olvide llamarle, si:

- Cree que está embarazada.
- Tiene dolor pélvico o dolor durante las relaciones sexuales.
- Tiene una secreción vaginal inusitada o llagas genitales.
- Tiene una fiebre inexplicable.
- Puede estar expuesta a las enfermedades transmitidas sexualmente.
- No puede sentir los cordoncillos de la Mirena.
- Presenta dolores de cabeza muy intensos o migrañas.
- La piel o el blanco de los ojos se le vuelve amarillo. Éstos pueden ser síntomas de problemas hepáticos.
- Sufre un derrame o ataque cardiaco.
- Si usted o su pareja contrae el VIH.
- Si tiene hemorragia vaginal copiosa o muy prolongada.
- No tiene un período menstrual.

Consejo general sobre las medicinas recetadas

Las medicinas se recetan a veces para problemas que no se mencionan en los folletos de información para los pacientes. Este folleto compendia la información más importante sobre la Mirena. Si desea obtener información adicional, hable con su proveedor de atención médica. Puede pedir a su proveedor de atención médica información sobre la, escrita para los profesionales de la salud.

Fabricado para:

Bayer HealthCare Pharmaceuticals

Bayer HealthCare Pharmaceuticals Inc.
Wayne, NJ 07470

Fabricado en Finlandia

Número telefónico: 1-888-842-2937

Este folleto de información para la paciente fue actualizado en julio del 2008.

Llene la siguiente lista de comprobación. Sus respuestas les ayudarán a usted y a su proveedor de atención médica a decidir si la Mirena es una buena alternativa para usted.

¿Tiene usted alguno de estos problemas?

	Sí	No	No lo sabe. Lo discutirá con su proveedor de atención médica
Anomalías del útero	❑	❑	❑
Síndrome de inmunodeficiencia adquirida (SIDA)	❑	❑	❑
Anemia o problemas de coagulación	❑	❑	❑
Hemorragias entre períodos	❑	❑	❑
Cáncer del útero o el cuello	❑	❑	❑
Antecedentes de otros tipos de cáncer	❑	❑	❑
Terapia de esteroides (v. gr., prednisona)	❑	❑	❑
Posible embarazo	❑	❑	❑
Diabetes	❑	❑	❑
Embarazo ectópico anterior	❑	❑	❑
Desmayos	❑	❑	❑
Llagas genitales	❑	❑	❑
Enfermedad cardiaca	❑	❑	❑
Soplo cardiaco	❑	❑	❑
Flujo menstrual copioso	❑	❑	❑
Hepatitis u otra enfermedad hepática	❑	❑	❑
Infección del útero o el cuello	❑	❑	❑
DIU actual o anterior	❑	❑	❑
Consumo de drogas IV actual o anterior	❑	❑	❑
Leucemia	❑	❑	❑
Varias parejas sexuales	❑	❑	❑
Una pareja sexual, que tenga a su vez varias parejas	❑	❑	❑
Infección pélvica	❑	❑	❑
Aborto provocado o espontáneo en los 2 meses anteriores	❑	❑	❑
Embarazo, en los 2 meses anteriores	❑	❑	❑
Cólicos menstruales intensos	❑	❑	❑
Dolor de cabeza intenso	❑	❑	❑
Enfermedad transmitida sexualmente (ETS), tal como gonorrea o clamidia	❑	❑	❑
Derrame	❑	❑	❑
Frotis de Papanicolaou anormal	❑	❑	❑
Hemorragia genital inexplicable	❑	❑	❑
Cirugía uterina o pélvica	❑	❑	❑
Secreción o infección vaginal	❑	❑	❑
Infección por VIH	❑	❑	❑
Lactación	❑	❑	❑
Tensión arterial alta	❑	❑	❑