

# NEW ZEALAND DATA SHEET

## **MULTILOAD**

Radio-Opaque Intrauterine Contraceptive Devices

### **Presentation**

MULTILOAD consists of a small plastic rod wound with copper wire and provided with two flexible arms and a nylon string.

MULTILOAD Cu375: length 35.0mm; width 20.5mm

MULTILOAD Cu375 SL: length 29.5mm; width 20.5mm

### **Uses**

#### **Actions**

Although the exact mechanisms by which the IUDs exert their contraceptive effect are not completely clear, there is evidence that they act primarily to prevent sperm from fertilising ova and prevention of implantation. IUDs induce a local inflammatory response, which in turn leads to lysosomal activation and other inflammatory changes that are spermicidal.

The presence of metallic copper improves the contraceptive efficacy of MULTILOAD. The plastic body of MULTILOAD contains barium sulphate to render it radio-opaque.

The flexible side arms of MULTILOAD ensure that the IUD remains in position as high as possible against the fundus, without the uterine cavity being stretched.

#### **Pharmacokinetics**

The contraceptive influence of copper is related to the oxidation of copper atoms and the subsequent dissolution of the oxides in the intrauterine milieu. For MULTILOAD Cu375 and MULTILOAD Cu375 SL the mean daily release of copper amounts to about 30 micrograms.

The intrauterine presence of copper-releasing IUDs causes neither an increase in serum copper concentrations to a measurable degree nor an increase in serum ceruloplasmin concentrations. This is to be expected since the average daily copper release of IUDs is only about one-hundredth of the average daily copper intake via food.

#### **Indications**

Intrauterine contraception.

MULTILOAD is intended for single use only, and has to be inserted by a doctor. Do not re-use, re-insert or re-sterilize Multiload.

Recommendations for the type of MULTILOAD to be fitted:

- MULTILOAD Cu375 for uteri with a sound length between 6 and 9 cm.
- MULTILOAD Cu375 SL for uteri with a sound length between 5 and 8 cm.

### **Dosage And Administration**

#### **Time For Insertion**

The optimum time for insertion of an IUD is the last days of the menstrual flow or in the first days afterwards (so-called interval insertion). This is to reduce the possibility of insertion in the presence of an existing undiagnosed pregnancy. However, it is essential that pregnancy is ruled out before insertion. An IUD may also be inserted immediately (within 10 minutes) post-abortion or post-partum, although in these cases the chances of pregnancy, translocation, and expulsion are higher.

Immediate post-abortion or post-partum insertion does not adversely affect uterine involution or breastfeeding. If a post-abortion or post-partum insertion is not done immediately, it should be delayed until involution is complete ie. at least 6 weeks after delivery or abortion (so-called delayed post-partum insertion). After caesarean section, insertion should not be attempted until 12 weeks after delivery.

#### **Postcoital IUD Use**

To prevent pregnancy after unprotected intercourse insertion of an IUD may be an effective measure, provided that intercourse has taken place no longer than 5 days before.

NB. The physician should take account of the risk of pelvic infection associated with emergency IUD insertion and should adequately inform the patient in this respect. This is particularly relevant in cases of rape.

## Recommended Insertion Procedure

It is imperative that a no-touch technique is employed throughout the insertion procedure to ensure sterile handling. The intrauterine device should not be used in the event of the inner packaging being damaged.

### A. Interval Insertion

#### **Preparation**

1. Ensure that the patient understands the contents of the patient leaflet.
2. Confirm that there are no contraindications to use of Multiload.
3. Perform a urine pregnancy test, if indicated.
4. Perform a careful bimanual examination to determine the version, flexion and uterine axis.
5. Insert a vaginal speculum to expose the cervix. Cleanse the cervix and vaginal walls with sterile cotton wool dipped in antiseptic solution (Figure a). Wipe all secretion away from the external os.
6. Grasp the anterior lip of the cervix with a single-tooth tenaculum, taking a good bite through the cervical lip so that **steady downward traction to straighten the uterine axis** can be maintained without risk of cervical laceration (Figure b).

Reflex contraction, which causes cramp of the uterus when the tenaculum is applied, can be prevented by injection of a local anaesthetic into the anterior lip or a paracervical block.

7. Carefully sound the uterus to determine its depth and to confirm the direction of its axis. If the sound meets more than normal resistance at the internal os, it may be advisable to gently dilate the cervical canal to 4-5mm, using sterile, tapered rather than cylindrical dilators. In the absence of other instruments for measurement of the internal dimensions of the uterine cavity, the sound may be used to obtain an idea of its configuration.

Figure a

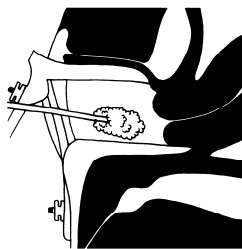
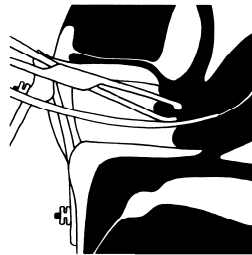


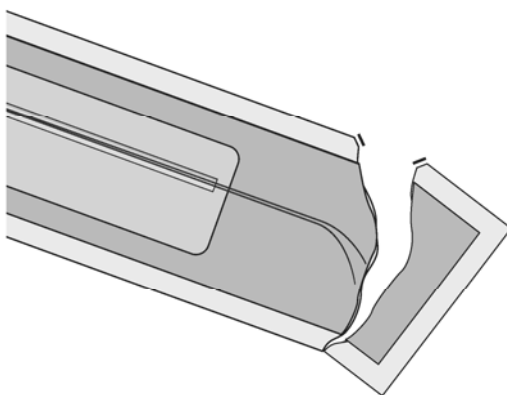
Figure b



#### **Inserting MULTILOAD**

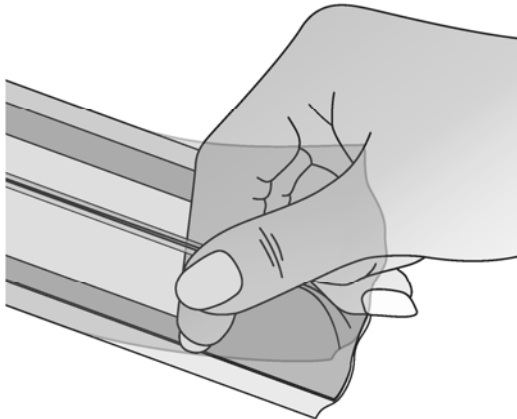
The vertical stem of MULTILOAD is already preloaded in the introducer tube. The side arms **do not** require loading into the tube. They are sufficiently flexible to adapt to the shape of the cervical canal.

1. Tear the pouch open at the indicated notch (see Figure 1).  
Figure 1

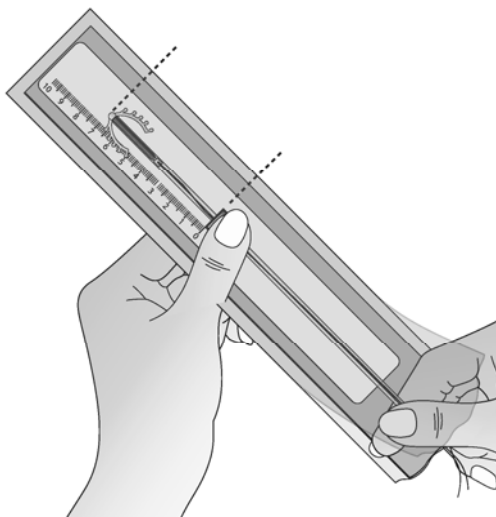


2. Peel the clear cover back so far that the introducer tube (with IUD) can be picked up at its distal end, grasping the tube and the threads, but without taking MULTILOAD out of the pouch (see Figure 2).

Figure 2



3. Hold the cervical stop with the thumb of one hand and adjust the position of the top of MULTILOAD by moving the introducer tube with the other hand until it corresponds with the mark indicating, approximately, the sounded uterine length in centimetres (see Figure 3).  
Figure 3



4. The distal end of the introducer may be held without risk of contaminating the device. Holding the threads together with the tube ensures that the device does not fall out of the introducer tube. MULTILOAD can now be taken out of the pouch.
5. Carefully insert MULTILOAD into the uterus (Figure c) until it touches the fundus and the cervical stop rests against the external os (Figure d) while **maintaining steady downward traction with the tenaculum to straighten the uterine axis**. No attempt should be made to force insertion.  
Insufficient axial straightening may, on occasion, result in a sub-endometrial insertion. This risk may be reduced by exerting an adequate downward pulling force on the cervix, thereby fully straightening the axis of the uterus against its ligamentous supports.
6. When MULTILOAD touches the fundus, it is released into the uterine cavity by simply withdrawing the introducer tube (Figure e). During this procedure continue to apply downward traction with the tenaculum. No push-rod is required to insert MULTILOAD. Check the cervical canal with the sound to ensure that the tail of MULTILOAD is entirely within the uterine cavity. Trim the threads of MULTILOAD to 2 to 3 cm measured from the external os.
7. It is imperative to follow precisely the recommended insertion procedure in order to minimise the risk of a sub-endometrial insertion, which may, in turn, lead to full or partial endometrial embedding of the IUD. Should this occur, a higher than normal force may need to be applied

to remove the IUD from this incorrect location, which may increase the risk of side-arm breakages. Furthermore, it may be clinically difficult to confirm the IUD's sub-endometrial location, since this is usually not obvious to the doctor during insertion of the device and the patient probably experiences no pain. It is anticipated that correctly inserting the device may reduce the incidence of both side-arm breakages and perforations.

Figure c

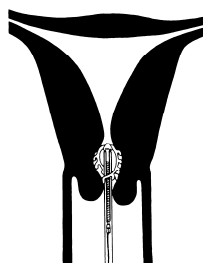


Figure d

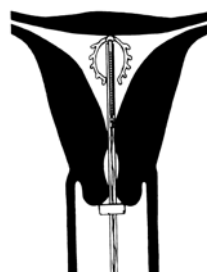
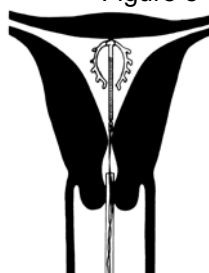


Figure e



The MULTILOAD package contains both a User Card and a Physician Card. These cards record the Lot number, the date of insertion, the intended date of removal and the address of the local Merck Sharp & Dohme distributor. It is important to fill in both cards; the User Card should be given to the user and the Physician Card should be kept in the patient's file. In case of any complaints on MULTILOAD, it is important to always mention the Lot number.

#### B. Immediate Post-Partum and Post-Abortion Insertions

1. Insert a bivalve (bayonet) speculum to expose the cervix after delivery of the placenta and membranes (no later than 10 minutes). Cleanse the cervix and vaginal walls with sterile cotton wool dipped in antiseptic solution.
2. Grasp both the anterior and the posterior lips with one or two ring forceps and draw the cervix down for close inspection.
3. Take the introducer tube (with pre-loaded IUD) and insert MULTILOAD along the palmar aspect of two fingers into the uterine cavity until it touches the fundus. Check the position of MULTILOAD with the flat hand on the abdominal wall covering the fundal region.
4. When MULTILOAD touches the fundus, it is released into the uterine cavity by very gentle withdrawal of the introducer tube. Take care not to pull on the threads which are left uncut until the first follow-up visit.

#### **Time of Removal**

The recommended *in situ* time is 5 years for each type of Cu375.

In adult women in whom it is not expected that the uterus will grow, MULTILOAD Cu375 can remain *in situ* for the full 5 years.

In young women in whom the uterus may still grow and in whom the short type of MULTILOAD has been fitted, it may be necessary to remove it within a shorter period and replace it with a larger type.

#### **Removal Procedure**

Prepare the vulva, insert the speculum and cleanse the cervix as for insertion. To facilitate removal, a tenaculum should always be used to **straighten out the uterine axis**, thereby also minimising the risk of side-arm breakages. Use a forceps to **grasp both threads of the MULTILOAD** as near to the exit from the external os as possible. Using steady downward traction with the tenaculum to straighten the uterine axis, the MULTILOAD should be able to be easily withdrawn from the uterus.

No excessive force must be used. After removal of Multiload verify that the device is intact, after this verification the IUD should be disposed if in accordance with local requirements. If Multiload is removed mid-cycle and the woman has had intercourse within the preceding week, she is at risk of pregnancy unless a new IUD is inserted immediately after removal.

### **Difficult Removal And Breakage During Removal**

Sometimes difficulties are encountered when removing the IUD. In the event of a more than usual force being required for removal, consideration should be given to the probability that the MULTILOAD is embedded. There have been reports of part of an embedded device (in particular an embedded side-arm) breaking off within the uterine cavity, when a greater than normal force needs to be applied for removal. Retained fragments may be expelled painlessly with the menstrual period and embedded side-arms may be freed by uterine contractions. There have also been some rare reports of breakage not associated with embedding.

If the device cannot be withdrawn by normal force or if a fragment has remained behind, diagnostic steps including X-rays or ultrasound, should be taken to exclude perforation or embedding. Plastic fragments, such as the side-arms, may be located using X-rays, ultrasound or hysteroscopy. The latter technique allows removal at the same time. However, reports indicate that routine curettage for removal of a fragment, whether or not located in advance, is successful in many cases. Removal of fragments should always be attempted.

### **Contraindications**

#### **Absolute**

- Pregnancy (established or suspected)
- Malignant disease of the corpus uteri or cervix.
- Vaginal bleeding of undiagnosed etiology.
- Ectopic pregnancy in anamnesis or the presence of predisposing factors for this condition such as salpingitis, endometritis or pelvic peritonitis.
- Congenital or acquired malformations or distortions of the uterus or the cervix; large or multiple uterine fibromyomata in the presence of excessively heavy menstrual periods; endometrial hyperplasia; cervical dysplasia.
- Genital infection (with the exception of candidiasis).
- Sexually transmitted disease during the past 12 months (with the exception of bacterial vaginitis, candidiasis, recurrent herpes virus infection, hepatitis B or cytomegalovirus infection).
- Infected abortion in the past 3 months.
- Active pelvic inflammatory disease (PID) or history of recurrent PID.
- Hypersensitivity to any of the components of the product.

#### **Relative**

- History of (partial) expulsion with Multiload or another IUD/IUS.
- Valvular heart disease. Use of an IUD in these cases may increase the risk of subacute bacterial endocarditis. Antibiotic prophylaxis should be given when inserting or removing the IUD.
- Anaemia, or a history of excessive uterine bleeding.
- Coagulopathy or current administration of anti-coagulants.
- Severe dysmenorrhoea.
- Uterine scars from previous surgery other than caesarean section or previous perforation of the uterus.
- Small uterine fibromyomata, endometrial polyps, or endometriosis. Regular pelvic examination of a patient with fibroids is advised to assess any change in size.
- Long-lasting intensive treatment with corticosteroids or non-steroidal anti-inflammatory agents (see also Interactions).
- Long-lasting intensive immunosuppressive therapy (see also Interactions).
- Disorder of copper metabolism (e.g. Wilson's disease).
- Current or recurrent lower genital tract infection.
- Multiple sexual partners (see also Interactions).

### **Warnings And Precautions**

#### **Medical Examination**

- Prior to insertion of an IUD the medical contraindications for IUD use should be excluded on the basis of both the medical history and the physical examination of the woman. Physical

examination should include a pelvic examination, cervical smear, and if possible, appropriate tests for sexually transmitted disease.

- After interval insertion IUD users should be re-examined shortly after the first period and after immediate post-abortion or post-partum insertion monthly during the first three months. Thereafter, appropriate examination should be carried out at regular intervals e.g. every six months.
- If MULTILOAD threads cannot be felt in a woman who has not noticed expulsion, examination is necessary to exclude perforation or unnoticed expulsion. Ultrasound or X-ray may be used to locate the device.

### **Nulligravity/Nulliparity**

- In nulliparous women the risks and benefits of intrauterine contraception should be assessed with special consideration of their future fertility. Pain during and after insertion is more likely to occur in nulliparous than in multiparous women.

### **Pelvic Inflammatory Disease (PID)**

- The risk of developing PID in women using an IUD is only increased in the first 20 days after insertion; thereafter the risk of PID is similar to the risk in women without an IUD. The occurrence of PID may also be due to other factors, such as contraction of a sexually transmitted disease.
- PID may lead to tubal occlusion resulting in impairment of future fertility, increase the risk of subsequent ectopic pregnancy and, if a tubo-ovarian abscess develops, may necessitate hysterectomy and oophorectomy. Therefore, in nulliparous women and in women with a recent history of treated pelvic infection, contraceptive benefits of IUD use have to be weighed against potential risks. The following clinical symptoms may be indicative of PID: pyrexia, lower abdominal tenderness or pain, abnormal vaginal discharge, deep dyspareunia, prolonged or heavy menstrual bleeding, pain on manipulation of the cervix, tenderness or pain on bi-manual examination of the uterus and uterine adnexae. If women fitted with an IUD are suspected of PID, the following is advised:
  - In mild cases the diagnosis should be established and treatment with antibiotics started. If there is no response after 24 hours the IUD should be removed.'
  - In moderate cases with more definite clinical signs the IUD should be removed before starting antibiotic therapy and the patient referred for a gynaecological opinion.
  - In severe cases associated with marked lower abdominal pain and fever the IUD should be removed and the patient should be admitted to hospital.

### **Medical Reasons For Removal**

- Pregnancy (see below)
- PID (see above)
- Excessive and persistent bleeding or cramping.
- Perforation of the cervical or uterine wall. This is extremely rare with MULTILOAD but if it should happen, the device should be removed.
- Downward displacement of MULTILOAD into the cervical canal.
- Translocation.

NB. For the removal procedure and the possible complications encountered therewith see the **Dosage and Administration** section.

### **Additional Warnings**

- IUDs do not protect against HIV infection (AIDS) or any other sexually transmitted disease.
- Insertion of an IUD may precipitate a seizure in women suffering from epilepsy. Special care is therefore recommended during insertion.
- In women fitted with an IUD menstrual blood loss is often increased and occasionally this may lead to iron deficiency anaemia.

### **Use During Breastfeeding**

MULTILOAD may be inserted in breast-feeding women. However, in view of reports suggesting an increased risk of uterine perforation during lactation, particular care should be taken.

## **Pregnancy Despite IUD Use**

IUDs are more protective against intrauterine than against extrauterine pregnancy, but there are indications that the chance of the latter is also decreased as a result of the use of an IUD. Should a pregnancy occur with an IUD *in situ*, it is necessary to determine, e.g. by ultrasonography, whether this pregnancy is intrauterine or ectopic.

### **1. Intrauterine Pregnancy**

If intrauterine pregnancy occurs with an IUD *in situ* the following is strongly recommended:

- up to 12 weeks gestation, the device should be removed if the threads are visible.
- beyond 12 weeks, or if no threads are visible, termination of pregnancy should be considered and offered to the woman as an option, bearing in mind that the risks associated with elective abortion increase with gestational age.

If the woman insists on continuing the pregnancy with the IUD *in situ*, refer early for antenatal care. Some reports indicate an increased incidence of septic abortion in patients becoming pregnant with an IUD *in situ*. In some instances septic abortion has been complicated by septicaemia, sometimes with fatal outcome. The onset of septicaemia may be insidious. If pregnancy is continued with the IUD *in situ*, the woman must be closely observed and advised to report immediately all abnormal symptoms such as flu-like syndrome, fever, abdominal cramping and pain, dyspareunia, bleeding or vaginal discharge.

If left *in situ* throughout pregnancy the device is usually expelled prior to or concomitantly with delivery of placenta and membranes. If not, X-ray or ultrasound should be used early in the puerperium to locate it.

So far, there is no evidence that, when a pregnancy continues to term with an IUD *in situ*, this will lead to birth defects.

### **2. Ectopic Pregnancy**

If ectopic pregnancy is suspected early diagnosis is vital. If ectopic pregnancy is established immediate gynaecological intervention is required. Clinical features include amenorrhoea for 6-8 weeks accompanied by symptoms of pregnancy and (severe) unilateral pelvic pain with or without vaginal bleeding which is often scanty and black. However, these symptoms are not always present. The period may not even be late. In addition shouldertip pain or the recent onset of dizziness or fainting may be present.

## **Effects on Ability to Drive and Use Machines**

No observed effects.

## **Patient Counselling**

- Every potential IUD user should be fully informed of the risks and benefits of IUDs. Any user of MULTILOAD should be given the "Package insert" containing the "Information for the User".
- The physician should inform the user about:
  - the necessity to read the "Information for the User" very carefully and to follow the instructions to the letter. This is particularly relevant with regard to the possibility of device failure and pregnancy and the paragraph in the section "Possible complications", covering the early symptoms of genito-urinary infection. Women desiring future pregnancy should be made aware of the slightly increased risk of PID and its possible interference with future fertility.
  - the necessity to carefully keep the User Card for future reference
  - how to feel for the threads of MULTILOAD after the end of each period and at any time she would experience unusual contractions in the lower abdomen during her period.
  - how to feel the cervix each month after the end of her period and to ensure that no firm plastic is protruding.
  - the necessity to contact a doctor:
    - if she cannot feel the thread(s) of MULTILOAD.
    - if she feels the plastic end of MULTILOAD protruding.
    - if she experiences heavy menstrual bleeding or troublesome intermenstrual bleeding or spotting as a new complaint occurring after the first few months after insertion, or post-coital bleeding.
    - if she experiences dysmenorrhoea or dyspareunia.
    - if she misses a period.
    - if signs or symptoms of a genito-urinary infection or of an extrauterine pregnancy appear, ie. prolonged or heavy menstrual bleeding, (persistent) lower abdominal pain or shouldertip

pain, deep dyspareunia, fever in excess of 38°C and/or flu-like syndrome, abnormal vaginal discharge, dizziness or fainting.

### **Adverse Effects**

The table\* below lists the undesirable effects that have been reported in users of MULTILOAD.

<b>System Organ Class</b>	<b>MedDRA term</b>
Cardiac disorders	Bradycardia (1,2,4)
Gastrointestinal disorders	Abdominal pain (3)
General disorders and administration site conditions	Complication of device insertion Complication of device removal Device breakage Embedded IUD (Partial) device expulsion (5)
Infections and infestations	Genital infection Sepsis Urinary tract infection
Injury, poisoning and procedural complications	Uterine perforation (5)
Musculoskeletal and connective tissue disorders	Back pain Pain in extremity
Nervous system disorders	Syncope vasovagal (1,2,4)
Pregnancy, puerperium and perinatal conditions	Abortion spontaneous Ectopic pregnancy
Reproductive system and breast disorders	Dysmenorrhoea Dyspareunia Menorrhagia (6) Metrorrhagia (6) Vaginal discharge
Skin and subcutaneous tissue disorders	Dermatitis allergic Urticaria

(1): during or immediately after insertion of IUD

(2): during or immediately after removal of IUD

(3): after insertion of IUD

(4): particularly in nulliparous women

(5): uterine perforation and IUD displacement into the abdomen have been followed by peritonitis, abdominal adhesions, intestinal penetration, intestinal obstruction and cystic masses in the pelvis.

(6): mainly during first cycle(s) after insertion of IUD

\*: The most appropriate MedDRA term (version 13.0) to describe a certain adverse reaction is listed. Synonyms or related conditions are not listed, but should be taken into account as well.

### **Interactions**

- The foreign body reaction is crucial in the contraceptive activity of IUDs. Since this is a sterile inflammatory reaction of the endometrium, treatments that may interfere with this inflammatory process may reduce the contraceptive efficacy of IUDs. Accordingly, women needing long-lasting intensive treatment with corticosteroids, non-steroidal anti-inflammatory agents, or immunosuppressive therapy, preferably should opt for another contraceptive method. In case of occasional intensive treatment with anti-inflammatory or immunosuppressive agents, the IUD user should be advised to take additional contraceptive measures during these periods.
- It has been suggested that tetracyclines may reduce the contraceptive efficacy of copper-containing IUDs.
- Since the occurrence of pelvic inflammatory disease seems to be most strongly related to the background risk of sexually transmissible disease, multiple sexual partners is included as a relative contraindication.
- It has been suggested that medical diathermy (short-wave and microwave) of the abdominal and sacral areas might induce heat injuries because of the presence of metallic copper on the IUD. However, in situ measurements indicate that diathermic treatment of women with copper-bearing IUDs can be regarded to be safe when using dose intensities within the normal therapeutic range.

- The energetic status of copper will not be changed by Magnetic Resonance Imaging (MRI). Therefore, an effect on the IUD induced by MRI can be neglected. Furthermore, based on the non-ferro characteristics of copper the scan obtained with Magnetic Resonance Imaging (MRI) is considered not to be impaired by the presence of the IUD.

### **Overdosage**

Not applicable.

### **Pharmaceutical Precautions**

#### **Incompatibilities**

No relevant incompatibilities are known.

#### **Shelf-Life**

The shelf-life of MULTILOAD, under the given storage conditions, is 5 years. MULTILOAD may be inserted until the expiration date indicated on the package.

### **Special Precautions for Storage**

The intact package has to be stored dry and below 25°C in the original carton box.

### **Medicine Classification**

Prescription Medicine.

### **Package Quantities**

Packed as single items in sterile containers (pouches).

### **Further Information**

#### **Adverse Event Reporting**

Details of any adverse event noticed, or reported, by a user should be reported immediately to the Medical Assessor, Medicines Adverse Reactions Committee, P.O. Box 913, Dunedin, on the standard ADR form (H1574).

### **Customer Services**

In order to maintain the high quality of this product Merck Sharp & Dohme is very interested in all complaints or remarks with respect to MULTILOAD. These can be reported to the local Merck Sharp & Dohme distributor (for address details see below). In case of complaints, it is important also to report the Lot number of the MULTILOAD.

### **Qualitative and Quantitative Composition**

MULTILOAD Cu375/375 SL are intrauterine devices with flexible side-arms, made of a mixture of high density polyethylene, ethylene vinyl acetate copolymer and barium sulphate in a weight ratio of 44/36/20. A copper wire is wound around the stem, giving a total copper surface area of 375mm<sup>2</sup>. A monofilament nylon thread is attached to the stem. The stem length of the MULTILOAD Cu375 standard device is 35mm; the stem of MULTILOAD Cu375 SL is 30mm. Except for stem length, these devices have identical dimensions.

The introducer tube consists of:

- Tube made of polypropylene;
- Cervical stop consist of a 44/36/20 mixture of high density polyethylene, ethylene vinyl acetate copolymer and barium sulphate, or high density polyethylene only.

### **Nature and Contents of Container**

MULTILOAD radio-opaque intrauterine devices (IUD) are packed individually in a transparent 3-sided sealed sachet, made of a laminated film comprising polyethylene terephthalate (polyester) and low density polyethylene. A paper ruler is inserted and the sachet is sealed on the fourth side.

### **Preclinical Safety Date**

No particulars.

### **Name And Address**

Merck Sharp & Dohme (NZ) Ltd  
P O Box 99 851  
Newmarket

Auckland 1149

Tel: 0800 500 673

**Date Of Preparation**

24 March 2011

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