CHAPTER IV: COMBINED INJECTABLE CONTRACEPTIVES

WHAT ARE COMBINED INJECTABLE CONTRACEPTIVES?

Combined injectable contraceptives (CICs) are monthly injectable preparations that contain a short-acting natural estrogen and a long-acting progestogen. Once given intramuscularly, these hormones are slowly released for 28 to 30 days. CICs come in the following preparations:

- 25 mg depot-medroxyprogesterone acetate and 5 mg estradiol cypionate (Cyclofem) intramuscularly injected once a month.
- 50 mg norethindrone enanthate and 5 mg estradiol valerate (Mesigyna) intramuscularly injected once a month. This preparation is available in the Philippines as Norifam.

HOW EFFECTIVE ARE CICs?

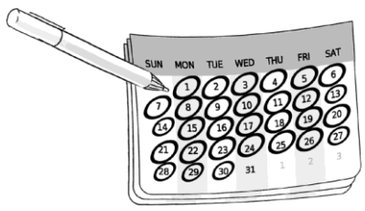
CICs are 99.9% effective in preventing pregnancy when used properly. With typical use, the effectiveness rate is lower at 97.0%.

WHAT ARE THE ADVANTAGES OF USING CICs?

- Immediate effectiveness
- Pelvic examination not required prior to use
- Does not interfere with intercourse
- Few side effects
- Can be provided by a trained nurse or midwife
- Contributes to decreased menstrual flow (lighter, shorter periods)
- Reduces menstrual cramps
- May improve anemia as menses are reduced
- Reduces the risk of ectopic pregnancy
- Protects against some causes of pelvic inflammatory disease (PID)

WHAT ARE THE DISADVANTAGES OF USING CICs?

- Some nausea, dizziness, mild breast tenderness, headaches, and spotting (minimal bleeding) caused by the estrogen component of CICs but to a lower degree than those caused by COCs. These side effects disappear within two or three injections because the “natural” estrogen approximates the physiologic dose.
- Effectiveness may be lowered by rifampicin and most anticonvulsants.
- CICs can delay return to fertility by a few weeks from the last injection.
- CICs can cause serious side effects, such as cardiovascular disease, but such cases are rare.
- CICs do not protect against STIs, such as the human papillomavirus and HIV/ AIDS.
- CICs cause changes in the menstrual bleeding pattern (irregular bleeding/ spotting) of some women.
- Users of CICs must return for injection every 30 days.



WHO CAN USE CICs?

- This method is useful for women who want a highly effective contraceptive method but have problems adhering to other CHC regimens.
- This method is also suitable for women who want the convenience of an injectable contraceptive without the bleeding irregularities associated with progesterone-only injectables.

Table 8. MEC categories for CICs

Category 1: Use the method without restriction.

- Menarche to 40 years old
- Women who may or may not have given birth
- More than 42 days postpartum
- Any time post-abortion
- Past ectopic pregnancy
- History of pelvic surgery
- Minor surgery without immobilization
- Varicose veins
- Epilepsy
- Depressive disorders
- Women with irregular vaginal bleeding patterns
- Diagnosed with benign ovarian tumor, endometriosis, severe dysmenorrhea
- Cervical ectropion
- Benign breast disease, or family history of cancer
- Women with gestational trophoblastic disease, endometrial cancer, or ovarian cancer
- Among women with uterine anatomical abnormalities (e.g., fibroids)
- Current or history of PID or STIs such as HIV/AIDS
- Schistosomiasis
- Tuberculosis
- Malaria
- History of gestational diabetes
- Any thyroid disorder
- Chronic or carrier viral hepatitis
- Mild liver cirrhosis
- Thalassemia or iron-deficiency anemia
- Current use of nucleoside reverse transcriptase inhibitors, broad-spectrum antibiotics, antifungal, or antiparasitics

Category 2: Generally use the method but with more than the usual follow-up.

- Women more than 40 years old
- Breastfeeding women, more than six months after childbirth
- Non-breastfeeding women, 21 to 42 days postpartum
- Women who smoke and are less than 35 years old
- Women who smoke less than 15 cigarettes/day and are more than 35 years old
- Body mass index of more than or equal to 30 kg/m^2
- History of high blood pressure during pregnancy
- Family history of DVT/PE
- Major surgery WITHOUT prolonged immobilization
- Superficial thrombophlebitis

- Known hyperlipidemia
- Uncomplicated valvular heart disease
- Systemic lupus erythematosus with negative antiphospholipid antibodies
- Continued use in women with non-migrainous headache
- Initiation of method in women with migraine, without aura, aged less than 35 years
- Unexplained vaginal bleeding prior to evaluation
- Women diagnosed with cervical intraepithelial neoplasia or cervical cancer prior to treatment
- Undiagnosed breast mass
- Diabetes, without vascular disease
- Asymptomatic or symptomatic gall bladder disease treated with cholecystectomy
- Symptomatic gall bladder disease
- History of COC or pregnancy-related cholestasis
- Benign liver tumors such as focal nodular hyperplasia
- Sickle cell disease
- Current use of non-nucleoside reverse transcriptase inhibitors, some anticonvulsant therapies, or rifampicin/rifabutin therapy

WHO CANNOT USE CICs?

The medical conditions classified under MEC 3 and MEC 4 for CHCs and CICs are almost the same. However, for certain conditions such as those enumerated below, MEC for CICs differ:

- Smoking > 15 cigarettes/ day (MEC 3)
- Rifampicin or rifabutin therapy (MEC 2)

Category 3: Do not use the method unless no other appropriate method is available under close supervision.

- Breastfeeding women, six weeks to six months after childbirth
- Non-breastfeeding women, less than 21 days postpartum, without other risk factors for VTE
- Women who smoke more than 15 cigarettes/day, aged more than 35 years
- Multiple risk factors for arterial cardiovascular disease such as older age, smoking, diabetes, and hypertension
- History of hypertension, in which blood pressure CANNOT be evaluated
- Adequately controlled hypertension, in which blood pressure CAN be evaluated
- Have increased blood pressure (systolic of 140 mm Hg to 159 mm Hg or diastolic of 90 mm Hg to 99 mm Hg)
- Initiation of method in women with migraine, without aura, aged more than 35 years
- History of breast cancer with no evidence of disease in the last 5 years
- Diabetes with nephropathy, retinopathy, neuropathy, or other vascular diseases
- Severe liver cirrhosis
- Benign liver tumors such hepatocellular adenoma and hepatoma
- Initiation of method in women with acute or flare viral hepatitis
- Current use of ritonavir-boosted protease inhibitors and lamotrigine

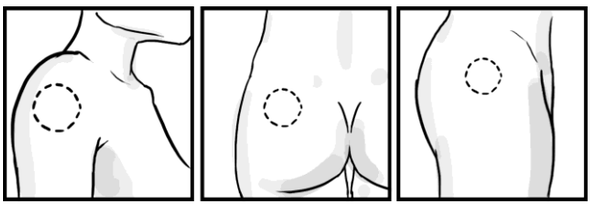
Category 4: Do NOT use the method.

- Breastfeeding women, less than six months after childbirth
- Have high blood pressure (systolic of more than or equal to 160 mm Hg or diastolic of more than or equal to 100 mm Hg)
- Hypertension with vascular disease
- History or currently diagnosed with DVT/PE on anticoagulant therapy
- Major surgery with prolonged immobilization
- Known thrombogenic mutations
- Current or history of ischemic heart disease or stroke
- Complicated valvular heart disease
- Women diagnosed with systemic lupus erythematosus and with positive (or unknown) antiphospholipid antibodies

- Migraine with aura at any age
- Diagnosed with breast cancer

HOW ARE CICs USED?

A woman using CICs must be injected with one vial of the drug monthly. The drug may be injected into the muscles of the upper arm, thigh, or buttocks. Infection prevention principles must be observed in giving the injection and disposing of the needles and syringes.



WHEN SHOULD USE OF CICs BEGIN?

- Any time as long as the client is not pregnant.
- Between day 1 and day 7 of the menstrual cycle, preferably on day 1.
- If the client is reasonably sure that she is not pregnant, she may start using CICs even after the first seven days of her menstrual cycle. However, she will need to abstain from sex or use a backup for the next seven days after the injection.
- Among postpartum women:
  - Later than six months for breastfeeding women because CICs may affect the quantity of breast milk;
  - At three to six weeks after childbirth for non-breastfeeding women.
- Immediately or within seven days for clients who just had an abortion.

WHEN CAN THE NEXT INJECTION BE PROVIDED?

The best time to provide the next injection is on the same date each month (a four- week schedule is practical). This information must be emphasized when counseling clients because it indicates the duration of drug effectiveness.

WHAT SHOULD BE DONE IF THE NEXT INJECTION IS DELAYED?

- Instruct the client to return to the clinic after 30 days for the next injection. She should comply with the scheduled date.
- If, for some reason, the next injection was not given after 30 days, the client should

abstain from sexual intercourse or make her partner use a condom until she gets the next injection.

- Instruct the client to come back to the clinic regardless of how late the next injection is as long as she is reasonably certain that she is not pregnant.
- The grace period of CICs is seven days without the need for extra contraceptive protection.
- A client who comes in after seven days of the due date can have the injection provided that she is definitely not pregnant. She also needs to abstain from sex or use a backup contraceptive method for the next seven days.

WHAT ARE THE IMMEDIATE AND LASTING EFFECTS OF USING CICs?

- CICs may reduce menstrual flow and regulate menstrual pattern, thereby reducing the incidence of anemia and dysmenorrhea.
- The effects produced by COCs are presumably present in CIC users. However, CICs are relatively new; thus, epidemiologic data on their long-term effects are lacking.

WHAT ARE THE COMMON SIDE EFFECTS OF CIC USE?

- Vaginal bleeding/spotting.
  - Changes in bleeding patterns with CIC use are fewer than those with use of progestin-only injectables because of the estrogenic effect on cycle control.
  - Irregular bleeding may occur in 30% of women users during the first three months, but the majority of these women have normal cycles at the end of the first year.
  - Amenorrhea (absence of any bleeding) for at least three consecutive months is uncommon.

- Other side effects may include weight gain, dizziness, and mild headaches. These effects are not dangerous and are transitory.
- Certain drugs (rifampicin and most anticonvulsants) may reduce the effectiveness of CICs. Clients must inform their providers if they are taking any medications.

WHAT ARE THE POTENTIAL COMPLICATIONS AND ADVERSE SIDE EFFECTS OF CIC USE?

- The estrogens in CICs have a shorter life span and are less potent than those in COCs.
  - Consequently, the estrogen-related side effects associated with CIC use are assumed to be less than those associated with COCs.
- CICs have minimal effect on blood pressure, blood coagulation, lipid metabolism, and liver function (no first-pass effect) compared with COCs.
- Unlike the contraceptive hormone components of COCs, those of CICs remain in a woman's system for several weeks after discontinued use.
- However, the WHO MEC recommends the use of COCs and CICs for almost the same conditions.

WHAT ARE THE DRUG INTERACTIONS OF CICs?

- Drug interactions of CICs are the same as those of CHCs.
- The effectiveness of CICs is not affected by most broad-spectrum antibiotics.
- Similar to the effectiveness of other CHCs, that of CICs can be diminished by some medications:
  - Certain antimicrobials (rifampicin)
  - Certain anticonvulsants, such as phenytoin (Dilantin), carbamazepine, barbiturates (such as Phenobarbital), primidone, topiramate, and oxcarbazepine
  - Some ARVs, such as non-nucleoside reverse transcriptase inhibitors and ritonavir-

boosted protease inhibitors. ARVs can increase or decrease the bioavailability of steroid hormones in CHCs; thus, consistent condom use must be recommended to prevent STI and HIV transmission and to compensate for any possible reduction in contraceptive effectiveness.

WHEN CAN A WOMAN SWITCH AND DISCONTINUE CICs?

- The client may switch any time without finishing her current cycle on CICs.
  - A woman who wants to prevent pregnancy but wants to stop CICs should consider starting another contraceptive method before discontinuing CICs.
  - A woman switching to a certain contraceptive method may need a backup method until the effectivity of the new method.

WHAT HAPPENS WHEN CLIENTS STOP USING CICs?

- The return to fertility after the client's last injection has no significant delay. More than 50% of women become pregnant within six months of discontinuing CICs and 80% within one year.
- Women who discontinue CICs are likely to experience temporary spotting or bleeding.

IS A REFERRAL NEEDED? HOW AND WHEN?

Only a few life-threatening complications can be attributed to CIC use. These complications can be reduced by the proper initial screening of the client.

The following signs and symptoms require medical attention:

- Jaundice
- Abdominal pain (severe constant pain)
- Chest pain (severe constant pain) or shortness of breath
- Headaches (intense pain that starts or becomes worse after every injection)
- Eye problems (brief loss of vision, seeing flashes of light or zigzag lines)
- Severe arm or leg pain (difficulty in moving)

When these symptoms occur, clients are instructed to return to the clinic or go directly to referral facilities.

HOW IS CIC SUPPLY MANAGED?

- Clients must be informed about where to go for reinjection or purchase of the CIC.
- Clients are advised to use the same preparation unless otherwise advised by the provider.

IS FOLLOW-UP NEEDED? HOW AND WHEN?

- Clients should be advised to return to the clinic a month after their first injection. Remind them to comply with the scheduled date of the next injection or to return no matter how late they are.
- Clients should return to the clinic at any time for any problems or questions that may arise.
- During the annual follow-up, a physical and pelvic examination may be performed as part of good medical practice. Cervical and breast cancer screening procedures are usually undertaken.

WHAT COUNSELING TIPS SHOULD BE PROVIDED TO THE CLIENT?

The following points must be emphasized:

- Timing of injection: when to receive the first injection and date of succeeding injections.
- Signs and symptoms that require consultation with a health provider.
- The fact that CHCs do not protect the client against STIs, including HIV, and that use of condoms is necessary.
- Smoking increases the risk of serious circulatory disorders. Women who intend to use CHCs should be advised to quit smoking.