Giving moms an extra layer of personalized support through Makena Care Connection®

IF YOU HAVE HAD A SINGLETON SPONTANEOUS PRETERM BIRTH (BEFORE 37 WEEKS), YOU ARE AT RISK FOR ANOTHER PRETERM DELIVERY

HELP GIVE YOUR BABY MORE TIME TO DEVELOP

EVERY WEEK COUNTS

Giving moms an extra layer of personalized support through Makena Care Connection®

Makena hydroxyprogesterone caproate injection
Makena® (hydroxyprogesterone caproate injection) helps give baby more time to develop

Makena is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. The effectiveness of Makena is based on improvement in the proportion of women who delivered <37 weeks of gestation. There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

Please see Important Safety Information on pages 8, 10, and 11 and attached full Prescribing Information.

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What is preterm birth?

The goal of a healthy pregnancy is to deliver full term (39 to 40 weeks) to give your baby the time needed to grow and develop. For example, your baby’s brain and lungs are still developing during the last weeks of pregnancy.2,3

Preterm birth is when a baby arrives too early; that’s before 37 weeks of pregnancy, or 3 weeks prior to the baby’s due date.4 Preterm birth can be unexpected or unplanned. Sometimes, a baby needs to be delivered earlier than normal in certain medical situations.5

Preterm birth can happen to any pregnant woman.

In most cases, healthcare providers don’t fully understand what actually causes preterm birth. But moms who have delivered a baby too early (before 37 weeks)—regardless of the number of weeks early they’ve delivered—in the past are at a higher risk for having another preterm birth.1,6

Every week counts—every additional week makes a difference for your baby. Talk with your healthcare provider about the risks for preterm birth and what you can do to reduce your risk

Have you delivered preterm before?

In the United States, approximately 1 in 10 babies is born prematurely each year.2 That’s nearly 400,000 babies born too early.7

Preterm birth rates vary for different racial and ethnic groups. African Americans have a 13.3% preterm birth rate, Native Americans 10.5%, Hispanics 9.1%, Caucasians 8.9%, and Asians 8.5%.8

Even if you’re healthy and do all the right things during pregnancy, such as maintaining a healthy lifestyle and eating a well-balanced diet, you still could have a premature baby. The good news is there are things you can do to decrease your risk for preterm delivery, especially if you have unexpectedly delivered a baby before 37 weeks of pregnancy in the past.

“My doctor told me that having a previous preterm birth increased my risk of having another preterm baby. My husband and I were very surprised to hear that I was at risk again.”

—Lyn, mom of a 36-week preemie

For more Makena mom stories, visit makena.com

Please see Important Safety Information on pages 8, 10, and 11 and attached full Prescribing Information.
Are you aware of the potential risk factors for preterm birth?

The below checklist includes common risk factors for preterm birth. Depending on your risk factor(s), Makena® (hydroxyprogesterone caproate injection) may or may not be right for you.

While there are many causes for preterm birth, the safety and benefits of Makena have been demonstrated only in women who’ve unexpectedly delivered their baby prior to 37 weeks of pregnancy. **Makena is not meant for use in women with multiple gestations or other risk factors for preterm birth.**

- Prior spontaneous (unexpected) preterm birth before 37 weeks
- Pregnant with twins, triplets, or other multiples
- Problems with the uterus or cervix
- African American heritage
- High blood pressure, stress, diabetes, being overweight or underweight
- Short time between pregnancies (6-18 months)
- Certain infections during pregnancy, such as an infection of the uterus, vagina, or urinary tract infection, or sexually transmitted disease
- Smoking, drinking alcohol, or using illegal drugs

**You’re not alone.** If one or more of the above applies to you, see page 17 of this brochure and talk with your healthcare provider about the risks associated with preterm birth.

What is Makena?

**Makena helps get you closer to term.**

Makena, pronounced Ma-keen-a, is a hormone medicine (progestin) prescribed to lower the risk of having another preterm baby in women:

- Who are pregnant with one baby, and
- Who’ve unexpectedly delivered one baby too early (before 37 weeks) in the past

Makena is a weekly injection (given every 7 days) by your healthcare provider either at their office or in your home.

You can start Makena between 16 weeks and 20 weeks, 6 days of your pregnancy, depending on your healthcare provider’s direction.

“**My doctor and I discussed the option of taking Makena to reduce my risk of another preterm birth. This gave me peace of mind knowing I was doing everything I could to help give my baby time to develop.**”

– Sarah, mom of a 34-week preemie

Please see **Important Safety Information** on pages 8, 10, and 11 and attached **full Prescribing Information**.
Makena® (hydroxyprogesterone caproate injection) therapy schedule

Makena is an injection given by a healthcare provider¹:

- In the healthcare provider’s office or
- At home during a home healthcare visit (if covered by your insurance)

With both Makena injection options, therapy starts between week 16 and week 20, 6 days of your pregnancy, depending on your healthcare provider’s direction.¹ You will receive 1 injection each week (every 7 days) until week 37 (your last injection could be as late as 36 weeks, 6 days) or until you deliver your baby, whichever happens first.¹

<table>
<thead>
<tr>
<th>Week 16</th>
<th>Your Makena Weekly Injection Calendar</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/R</td>
<td>To help make Makena part of your routine, please see pages 18 and 19 for an injection tracker.</td>
</tr>
</tbody>
</table>

Before you receive Makena, tell your healthcare provider if you have an allergy to hydroxyprogesterone caproate, castor oil, or any of the other ingredients in Makena; diabetes or prediabetes; epilepsy; migraine headaches; asthma; heart problems; kidney problems; depression; or high blood pressure.

Makena administration options

Consider choosing the Makena Auto-Injector¹:

- Designed so you never see the needle
- Given in the back of the upper arm under the surface of the skin with a shorter, thinner needle
- Full dose delivered in ~15 seconds

Another option is an intramuscular injection¹:

- Given into your hip (upper outer area of your buttocks) into the muscle with a longer needle
- Full dose delivered over one minute or longer

Whether you choose the Makena Auto-Injector or the intramuscular Makena, you can feel confident that you are getting the same therapy and the opportunity to receive personalized support throughout your pregnancy from Makena Care Connection®¹

Please see Important Safety Information on pages 8, 10, and 11 and attached full Prescribing Information.
Is Makena® (hydroxyprogesterone caproate injection) safe?

You and your healthcare provider should consider the benefits and risks of therapy with Makena prior to deciding if Makena is right for you.

Makena should not be used if you¹:

• Have now or have had a history of blood clots or other blood clotting problems
• Have now or have had a history of breast cancer or other hormone-sensitive cancers
• Have unusual vaginal bleeding not related to your current pregnancy
• Have yellowing of your skin due to liver problems during your pregnancy
• Have liver problems, including liver tumors
• Have uncontrolled high blood pressure

Before you receive Makena, tell your healthcare provider if you¹:

• Have an allergy to hydroxyprogesterone caproate, castor oil, or any of the other ingredients in Makena
• Have diabetes or prediabetes
• Have epilepsy
• Have migraine headaches
• Have asthma
• Have heart problems
• Have kidney problems
• Have depression
• Have high blood pressure

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements

What are the possible side effects?

For moms: Makena may cause serious side effects, including¹:

• Blood clots—Symptoms of a blood clot may include leg swelling, redness in your leg, a spot on your leg that is warm to touch, or leg pain that worsens when you bend your foot
• Allergic reactions—Symptoms of an allergic reaction may include hives, itching, or swelling of the face
• Depression
• Yellowing of your skin and the whites of your eyes

The most common side effects of Makena included injection site reactions (pain, swelling, itching, bruising, or a hard bump), hives, itching, nausea, and diarrhea.¹

In a clinical study, certain complications or events associated with pregnancy occurred more often in women who received Makena. These included miscarriage (pregnancy loss before 20 weeks of pregnancy), stillbirth (fetal death occurring during or after the 20th week of pregnancy), hospital admission for preterm labor, preeclampsia (high blood pressure and too much protein in your urine), gestational hypertension (high blood pressure caused by pregnancy), gestational diabetes, and oligohydramnios (low amniotic fluid levels).¹

For babies: In a follow-up study, children between the ages of 2 and 5 years old were evaluated for development in various physical, mental, and social measures. The results were comparable to children born to non-Makena-treated moms.⁹
Giving you an extra layer of support with Makena Care Connection®

When you start Makena® (hydroxyprogesterone caproate injection), you get more than the medicine. You get personalized resources that are specifically designed to help you throughout your experience with Makena. Think of us as an extra layer of support.

**Prescription Support**
Helps you get your prescription approved in a timely manner

You’re unique and so are your insurance benefits. Because getting your medicine in a timely manner is important, we’re here to lend a hand. We have a dedicated team who understands the coverage policies for Makena. Our experts can handle the details between your healthcare professional, insurance company, and pharmacy so you receive your Makena when you need it.

“It was helpful to lean on Makena Care Connection to help facilitate getting my medication. It was one less thing for me to worry about.”
– Amber, mom of a 36-week preemie

Education & Adherence
Support that helps keep you on track with weekly injections

We understand that moms receiving Makena injections may need some encouragement and support to stick to their weekly injection schedule, and we want to help. This free service offers educational and adherence support to encourage you to make Makena part of your pregnancy and take an active role in your health.

A level of personalized support you can expect:

- Injection reminders that support weekly therapy
- Educational materials to address topics during pregnancy
- Encouragement so you can take an active role in your health

“Knowing my Care Manager was just a phone call away gave me peace of mind. I appreciated feeling like I had someone supporting me every step of the way.”
– Shanise, mom of a 22-week preemie

Have Questions? Connect with us.

✉️ info@makenacareconnection.com
📞 1-800-847-3418 (M–F, 8AM–8PM ET)

Please see **Important Safety Information** on pages 8, 10, and 11 and attached **full Prescribing Information**.
Financial Assistance

Helps ensure affordable access to Makena® (hydroxyprogesterone caproate injection)

We believe that you should be able to focus on your pregnancy more than the cost of your medication. To support that, AMAG Pharmaceuticals is committed to making sure that Makena-eligible moms have affordable access to Makena. We offer eligible patients* financial assistance.

Commercially insured moms whose health plan covers Makena

- Helps lower out-of-pocket costs associated with copays, coinsurance, and deductibles*

Uninsured and commercially underinsured moms

- A free course of therapy*

“\[Image of woman with tree\]"

“I was so happy that I was approved for financial assistance. I feel very thankful that my family and I had this opportunity with the Makena Care Connection.”

– Nalleli, mom of a 36-week preemie

For more Makena mom stories, visit makena.com

Home Injections by Healthcare Professionals

Provides injection administration in the comfort of your home

We can help coordinate Makena injections through a home healthcare organization. Once you’re approved by insurance, you can choose to receive your injections by a healthcare professional in the comfort of your home or another location that’s convenient for you.

*Each patient’s eligibility is evaluated on an individual basis. To be eligible, patients must meet the FDA-approved indication (pregnant with a single baby, with a history of singleton spontaneous preterm birth <37 weeks). In compliance with federal regulations, patients insured by a government-funded program (eg, Medicaid, TRICARE, etc) are not eligible. There are no upper-level income caps.
Is Makena® (hydroxyprogesterone caproate injection) right for you?

In a clinical study, taking Makena significantly lowered the rate of preterm birth compared to moms who did not take Makena.¹

If you answer “yes” to all of the questions below, talk with your healthcare provider to see if Makena is right for you to reduce your risk of another preterm birth.

☐ Have you unexpectedly delivered a baby preterm (less than 37 weeks gestation, or more than 3 weeks too early) before?

☐ Was your preterm birth due to preterm labor or your water breaking?

☐ Are you currently pregnant with one baby?

While there are many causes for preterm birth, the safety and benefits of Makena have been demonstrated only in women who’ve unexpectedly delivered their baby prior to 37 weeks of pregnancy.

Makena is not meant for use in women with multiple gestations or other risk factors for preterm birth.

If you think you are at risk for another preterm birth due to a history of spontaneous preterm birth, ask if Makena may be right for you.

Questions to ask your healthcare provider

Here are some questions to help you start a conversation about your prior preterm birth experience and how Makena may be able to help reduce your risk of another preterm birth.

Ask your healthcare provider these questions to see if Makena is right for you:

• I delivered a baby unexpectedly before 37 weeks. Could this happen again?

• What are some of the risk factors for preterm birth?

• How can I reduce my risk and have a better chance for a full-term pregnancy?

• How early could I go into labor?

• What are the signs and symptoms of preterm labor?

• Is Makena right for me?

Make Makena a part of your weekly routine!

Use this calendar as a resource to track your weekly injections

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**SECOND TRIMESTER**

<table>
<thead>
<tr>
<th>Week 16</th>
<th>Week 17</th>
<th>Week 18</th>
<th>Week 19</th>
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**THIRD TRIMESTER**

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<th>Week 35</th>
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A Makena is administered once weekly (every 7 days) by your healthcare provider, between 16 weeks and 20 weeks, 6 days, continuing until 37 weeks (your last injection could be as late as 36 weeks, 6 days) or until you deliver your baby, whichever happens first.¹

B Each week you receive your injection, your healthcare provider will rotate the injection site from the previous side.¹ You’ll be able to keep track of this on the calendar too!

C Set a day to make your Makena injections part of your weekly routine.

Please note that your results and duration of therapy may vary.

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Please see **Important Safety Information** on pages 8, 10 and 11 and attached **full Prescribing Information**.

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Weeks 37-38
This is early term, and baby is still growing³

Weeks 39-40
This is full term—the goal of a healthy pregnancy³
Every week counts when you’re pregnant

Your baby keeps growing and developing every week of pregnancy until your due date. Together, you and your healthcare provider can take an important step to help give your baby more time to develop. Ask your healthcare provider about the importance of having a full-term delivery.

Have Questions? Connect with us.
1-800-847-3418 (M–F, 8AM–8PM ET)

Full Prescribing Information attached here.
If missing, please visit http://www.makena.com/pi

Please see Important Safety Information on pages 8, 10, and 11 and attached full Prescribing Information.
HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MAKENA safely and effectively. See full prescribing information for MAKENA.

MAKENA® (hydroxyprogesterone caproate injection) for intramuscular or subcutaneous use.

Initial U.S. Approval: 1956

RECENT MAJOR CHANGES

Dosage and Administration, Dosing (2.1) 02/2018
Dosage and Administration, Preparation & Administration (2.2) 02/2018

INDICATIONS AND USAGE

MAKENA is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth (1).

The effectiveness of MAKENA is based on improvement in the proportion of women who delivered < 37 weeks of gestation (14). There are no controlled trials demonstrating a direct clinical benefit, such as improvement in neonatal mortality and morbidity.

Limitation of Use: MAKENA is not intended for use in women with multiple gestations or other risk factors for preterm birth. (1)

DOSAGE AND ADMINISTRATION

• MAKENA auto-injector: Administer subcutaneously using MAKENA auto-injector at a dose of 275 mg (1.1 mL) once weekly, in the back of either upper arm (2.1)
• MAKENA (single- and multi-dose vials): Administer intramuscularly at a dose of 250 mg (1 mL) once weekly in the upper outer quadrant of the gluteus maximus (2.1)
• Begin treatment between 16 weeks, 0 days and 20 weeks, 6 days of gestation (2.1)
• Continue administration once weekly until week 37 (through 36 weeks, 6 days) of gestation or delivery, whichever occurs first (2.1)

DOSAGE FORMS AND STRENGTHS

1.1 mL single-use auto-injector for subcutaneous use contains 275 mg of hydroxyprogesterone caproate (250 mg/mL) (3)
1 mL single-dose vial for intramuscular use contains 250 mg of hydroxyprogesterone caproate (3)
5 mL multi-dose vial for intramuscular use contains 1250 mg of hydroxyprogesterone caproate (250 mg/mL) (3)

WARNINGS AND PRECAUTIONS

• Current or history of thrombosis or thromboembolic disorders (4)
• Known or suspected breast cancer, other hormone-sensitive cancer, or history of these conditions (4)
• Undiagnosed abnormal vaginal bleeding unrelated to pregnancy (4)
• Cholestatic jaundice of pregnancy (4)
• Liver tumors, benign or malignant, or active liver disease (4)
• Uncontrolled hypertension (4)

ADVERSE REACTIONS

• Thromboembolic disorders: Discontinue if thrombosis or thromboembolism occurs (5.1)
• Allergic reactions: Consider discontinuing if allergic reactions occur (5.2)
• Decreased glucose tolerance: Monitor prediabetic and diabetic women receiving MAKENA (5.3)
• Fluid retention: Monitor women with conditions that may be affected by fluid retention, such as pre eclampsia, eclampsia, cardiac or renal dysfunction (5.4)
• Depression: Monitor women with a history of clinical depression; discontinue MAKENA if depression recurs (5.5)

ADVERSE REACTIONS

In a study where the MAKENA intramuscular injection was compared with placebo, the most common adverse reactions reported with MAKENA intramuscular injection (reported incidence in ≥ 2% of subjects and higher than in the control group) were:

Injection site reactions (pain, swelling, induration, bruising, itching, redness, and tenderness) were reported in 10% of subjects (4)

In a study where the MAKENA subcutaneous injection using auto-injector was compared with MAKENA intramuscular injection, the most common adverse reaction reported with MAKENA auto-injector use (and higher than with MAKENA intramuscular injection) was injection site pain (10% in one study and 34% in another). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AMAG Pharmaceuticals at 1-877-411-2510 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised 02/2018

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4 CONTRAINDICATIONS
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Because MAKENA auto-injector is preservative-free, once the cap is removed the device should be used immediately or discarded.

Rotate the injection site to the alternate arm from the previous week. Do not use areas where the skin is tender, bruised, red, scaly, raised, thick, or hard. Avoid areas with scars, tattoos, or stretch marks.

The solution is viscous and oily. The auto-injector takes approximately 15 seconds to deliver the dose; when the viewing window is fully blocked (completely orange), the full dose has been administered. The "Instructions for Use" contains detailed steps for administering the subcutaneous injection using the auto-injector [see Dosage and Administration (2.3)]. Read the "Instructions for Use" carefully before administering MAKENA auto-injector.

2.3 Instructions for Use (MAKENA Auto-injector)

Specific instructions for administration by dosage form:

MAKENA single-dose or multi-dose vials (intramuscular use only)

MAKENA single-dose or multi-dose vials are only for intramuscular use with a syringe into the upper outer quadrant of the gluteus maximus, rotating the injection site to the alternate side from the previous week, using the following preparation and administration procedure:

1. Clean the vial top with an alcohol swab before use.
2. Draw up 1 mL of drug into a 3 mL syringe with an 18 gauge needle.
3. Change the needle to a 21 gauge 1½ inch needle.
4. After preparing the skin, inject in the upper outer quadrant of the gluteus maximus. The solution is viscous and oily. Slow injection (over one minute or longer) is recommended.
5. Applying pressure to the injection site may minimize bruising and swelling.
6. If the 5 mL multi-dose vial is used, discard any unused product 5 weeks after first use.

For subcutaneous injection, single use, multi-dose vials or auto-injector:

1. Defrost the subcutaneous injection site at room temperature for a minimum of 30 minutes prior to injection.
2. Hold the auto-injector in a perpendicular position over the injection site (Figures 3A and 3B). Do not use if the injection site is red, hot, or tender.
3. After preparing the skin, inject in the upper outer quadrant of the gluteus maximus. The solution is viscous and oily. Slow injection (over one minute or longer) is recommended.
4. Applying pressure to the injection site may minimize bruising and swelling.
5. If the 5 mL multi-dose vial is used, discard any unused product 5 weeks after first use.

MAKENA auto-injector (subcutaneous use only)

MAKENA auto-injector is a single-use, pre-filled, disposable device containing a 27 gauge, 0.5 inch needle that delivers one dose subcutaneously in the back of the upper arm.
In the clinical trial using intramuscular injection, 2.2% of subjects receiving Makena were reported as discontinuing therapy due to adverse reactions compared to 2.6% of control subjects. The most common adverse reactions that led to discontinuation in both groups were uterine and injection site pain/swelling (1% each).

Pulmonary embolism in one subject and injection site cellulitis in another subject were reported as serious adverse reactions in Makena-treated subjects.

Two clinical studies were conducted in healthy post-menopausal women, comparing Makena administered via subcutaneous auto-injector to Makena administered as an intramuscular injection. In the first study, injection site pain occurred in 3/30 (10%) of subjects who used the subcutaneous auto-injector vs. 2/20 (10%) of subjects who received intramuscular injection. In the second study, injection site pain occurred in 20/39 (52%) of subjects who used the subcutaneous auto-injector vs. 5/61 (8%) of subjects receiving intramuscular injection.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of Makena. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish their causal relationship to the drug.

1. N = Total number of subjects enrolled prior to 20 weeks 0 days
2. Stillbirth (%)
3. Pregnancy Complication Makena Control

<table>
<thead>
<tr>
<th>Pregnancy Complication</th>
<th>Makena N=153</th>
<th>Control N=153</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligohydramnios (&lt; 20 weeks)</td>
<td>5/209</td>
<td>0/107</td>
</tr>
<tr>
<td>Stillbirth (&lt; 20 weeks)</td>
<td>5/209</td>
<td>0/107</td>
</tr>
<tr>
<td>Miscarriage (≥ 20 weeks)</td>
<td>8/209</td>
<td>6/107</td>
</tr>
</tbody>
</table>

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data
Animal Data

No studies have been conducted to examine the pharmacokinetics of Makena in patients with hepatic impairment. Makena is extensively metabolized and hepatic impairment may reduce the elimination of Makena.

10. OVERDOSAGE

There have been no reports of adverse events associated with overdosage of Makena in clinical trials. In the case of overdosage, the patient should be treated symptomatically.

11. DESCRIPTION

The active pharmaceutical ingredient in Makena is hydroxyprogesterone caproate, a progestin. The chemical name for hydroxyprogesterone caproate is [17α-hydroxy-4-oxo-androst-17-en-17βyl][3-(3-hydroxypropyl)] caproate. It has an empirical formula of C_{27}H_{40}O_{4} and a molecular weight of 428.60. Hydroxyprogesterone caproate exists as white to practically white crystals or powder with a melting point of 120°-124°C. The structural formula is:

\[ \text{C}_{27}\text{H}_{40}\text{O}_{4} \]

Makena is a clear, yellow, sterile, non-pyrogenic solution for intramuscular (vials) or subcutaneous (auto-injector) injection. Each 1 mL Makena auto-injector for subcutaneous use and each 1 mL single-dose vial for intramuscular use contains hydroxyprogesterone caproate USP, 250 mg/mL (25% w/v), in a preserved solution containing castor oil USP (30.6% v/v) and benzyl benzoate USP (46% v/v) with the preservative benzyl alcohol NF (2% v/v).
For all three groups, peak concentration (C max) and area under the curve (AUC(1-7 days)) of the hydroxyprogesterone caproate were approximately 3-8 fold lower than the respective parameters for the 12 mg daily subcutaneous injection. While de-hydroxylated and tri-hydroxylated metabolites were also detected in human plasma to a lesser extent, no meaningful quantitative results were derived due to the absence of reference standards for these multiple metabolites. The relative activity and significance of these metabolites are not known.

The elimination half-life of hydroxyprogesterone caproate, as evaluated from 4 patients in the study who reached full-term in their pregnancies, was 16.4 (±3.6) days. The elimination half-life of the mono-hydroxylated metabolite was 19.7 (±9.2) days.

In a single-dose, open-label, randomized, parallel design bioavailability study in 120 healthy postmenopausal women, comparable systemic exposure of hydroxyprogesterone caproate was seen when Makena was administered subcutaneously with the auto-injector (1 mL) in the back of the upper arm and when Makena was dosed intramuscularly (1 mL) in the upper outer quadrant of the gluteus maximus.
PATIENT INFORMATION

MAKENA (mah-KEE-na) (hydroxyprogesterone caproate injection) auto-injector for subcutaneous use

MAKENA (mah-KEE-na) (hydroxyprogesterone caproate injection) vial for intramuscular use

Read this Patient Information leaflet before you receive MAKENA. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

What is MAKENA?

MAKENA is a prescription hormone medicine (progesterin) used in women who are pregnant and who have delivered a baby too early (preterm) in the past. MAKENA is used in these women to help lower the risk of having a preterm baby again. It is not known if MAKENA reduces the number of babies who are born with serious medical conditions or die shortly after birth. MAKENA is for women who:

- Are pregnant with one baby.
- Have had a preterm delivery of one baby in the past.

MAKENA is not intended for use to stop active preterm labor. It is not known if MAKENA is safe and effective in women who have other risk factors for preterm birth.

MAKENA is not for use in women under 16 years of age.

Who should not receive MAKENA?

MAKENA should not be used if you have:

- blood clots or other blood clotting problems now or in the past
- breast cancer or other hormone-sensitive cancers now or in the past
- unusual vaginal bleeding not related to your current pregnancy
- yellowing of your skin due to liver problems during your pregnancy
- liver problems, including liver tumors
- high blood pressure that is not controlled

What should I tell my healthcare provider before receiving MAKENA?

Before you receive MAKENA, tell your healthcare provider about all of your medical conditions, including if you have:

- a history of allergic reaction to hydroxyprogesterone caproate, castor oil, or any of the other ingredients in MAKENA. See the end of this Patient Information leaflet for a complete list of ingredients in MAKENA.
- diabetes or pre-diabetes.
- epilepsy (seizures).
- migraine headaches.
- asthma.
- heart problems.
- kidney problems.
- depression.
- high blood pressure.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

MAKENA may affect the way other medicines work, and other medicines may affect how MAKENA works.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I receive MAKENA?

- Do not give yourself MAKENA injections. A healthcare provider will give you the MAKENA injection 1 time each week (every 7 days) either:
  - in the back of your upper arm as an injection under the skin (subcutaneous), or
  - in the upper outer area of the buttocks as an injection into the muscle (intramuscular).
- You will start receiving MAKENA injections anytime from 16 weeks and 0 days of your pregnancy, up to 20 weeks and 6 days of your pregnancy.
- You will continue to receive MAKENA injections 1 time each week until week 37 (through 36 weeks and 6 days) of your pregnancy or when your baby is delivered, whichever comes first.

What are the possible side effects of MAKENA?

MAKENA may cause serious side effects, including:

- Blood clots. Symptoms of a blood clot may include:
  - leg swelling
  - redness in your leg
  - a spot on your leg that is warm to the touch
  - leg pain that gets worse when you bend your foot

Call your healthcare provider right away if you get any of the symptoms above during treatment with MAKENA.

- Allergic reactions. Symptoms of an allergic reaction may include:
  - hives
  - itching
  - swelling of the face

Call your healthcare provider right away if you get any of the symptoms above during treatment with MAKENA.

- Decrease in glucose (blood sugar) tolerance. Your healthcare provider will need to monitor your blood sugar while taking MAKENA if you have diabetes or pre-diabetes.
- Your body may hold too much fluid (fluid retention).
- Depression.
- Yellowing of your skin and the whites of your eyes (jaundice).
- High blood pressure.

The most common side effects of MAKENA include:

- pain, swelling, itching or a hard bump at the injection site
- hives
- itching
- nausea
- diarrhea

Call your healthcare provider if you have the following at your injection site:

- increased pain over time
- oozing of blood or fluid
- swelling

Other side effects that may happen more often in women who receive MAKENA include:

- Miscarriage (pregnancy loss before 20 weeks of pregnancy)
- Stillbirth (fetal death occurring during or after the 20th week of pregnancy)
- Hospital admission for preterm labor
- Preeclampsia (high blood pressure and too much protein in your urine)
- Gestational hypertension (high blood pressure caused by pregnancy)
- Gestational diabetes
- Oligohydramnios (low amniotic fluid levels)

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of MAKENA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store MAKENA?

- MAKENA auto-injector for subcutaneous use:
  - Store the auto-injector at room temperature between 68°F to 77°F (20°C to 25°C).
  - Do not refrigerate or freeze.
  - Protect the auto-injector from light.
  - Store the auto-injector in its box.

- MAKENA vial for intramuscular use:
  - Store the vial at room temperature between 68°F to 77°F (20°C to 25°C).
  - Do not refrigerate or freeze.
  - Protect the vial from light.
  - Store the vial in its box in an upright position.

Keep MAKENA and all medicines out of the reach of children.

General information about the safe and effective use of MAKENA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use MAKENA for a condition for which it was not prescribed. Do not give MAKENA to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about MAKENA. If you would like more information, talk with your healthcare provider.

You can ask your healthcare provider or pharmacist for information about MAKENA that is written for health professionals.

What are the ingredients in MAKENA?

Active ingredient: hydroxyprogesterone caproate

Inactive ingredients: castor oil and benzyl benzoate. 5 mL multi-dose vials also contain benzyl alcohol (a preservative).

Distributed by: AMAG Pharmaceuticals, Inc. Makena is a registered trademark of AMAG Pharmaceuticals, Inc. For more information, go to www.MAKENA.com or call AMAG Pharmaceuticals Customer Service at the toll-free number 1-877-411-2510.

This Patient Information has been approved by the U.S. Food and Drug Administration Revised: 02/2018