Healthcare provider discussion guide

Share the following risk factors that you’ve selected with your healthcare provider:

- Prior spontaneous (unexpected) preterm delivery before 37 weeks
- African American heritage

Depending on your risk factors, Makena may or may not be appropriate for you.

When talking with your healthcare provider about your pregnancy and concerns about another preterm birth, being prepared may make the conversation easier. The following are some questions you can discuss with your healthcare provider:

- I delivered a baby unexpectedly before 37 weeks. Could this happen again?
- 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 some of the risk factors for preterm birth?
- What are the signs and symptoms of preterm labor?
- How does Makena® (hydroxyprogesterone caproate injection) work?
- Is Makena safe for me and my baby?
- Is Makena right for me?

Indication

Makena is a prescription hormone medicine (progestin) used to lower the risk of preterm birth in women who are pregnant with one baby and who have delivered one baby too early (preterm) in the past. Another study of Makena is going on to see whether Makena improves the number of babies who have serious problems shortly after birth or who die. It is not known whether Makena is safe and effective in women who have other risk factors for preterm birth.

Important Safety Information for Makena (hydroxyprogesterone caproate injection)

Makena should not be used in women with any of the following conditions: blood clots or other blood clotting problems, breast cancer or other hormone-sensitive cancers, or history of these conditions; unusual vaginal bleeding not related to your current pregnancy, yellowing of the skin due to liver problems during pregnancy, liver problems, including liver tumors, or uncontrolled high blood pressure.

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.

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).

Makena may cause serious side effects including blood clots, allergic reactions, depression, and yellowing of your skin and the whites of your eyes. The most common side effects of Makena include injection site reactions (pain, swelling, itching, bruising, or a hard bump), hives, itching, nausea, and diarrhea.

You may report an adverse event related to AMAG Pharmaceuticals’ products by calling 1-877-411-2510 or emailing amag@druginfo.com. If you prefer, you may contact the U.S. Food and Drug Administration (FDA) directly at fda.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying full Prescribing Information for Makena.
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 (≤37 weeks of gestation). 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: Makena is not intended for use in women with multiple gestations or other risk factors for preterm birth. (1)

**DOSE AND ADMINISTRATION**

- **Makena auto-injector:** Administer subcutaneously using Makena auto-injector at a dose of 275 mg (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). Dose administration for 5 mL multi-dose vial for intramuscular use contains 1250 mg of hydroxyprogesterone caproate (250 mg/mL) (3).

**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-use 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).

**ADVERSE REACTIONS**

- **Makena auto-injector:** The most common adverse reactions reported with Makena auto-injector use (and higher than with Makena intramuscular injection) were:
  - Urticaria (12%), pruritus (8%), nausea (6%), and diarrhea (2%) (6.1).

- **Makena intramuscular:** The most common adverse reactions reported with Makena intramuscular injection were:
  - 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 preeclampsia, epilepsy, cardiac or renal dysfunction (5.4).

**WARNINGS AND PRECAUTIONS**

- **Thromboembolic disorders:** Discontinue if thrombosis or thromboembolism occurs (5.1).

**ADVERSE REACTIONS**

- **Makena auto-injector:** 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:
  - In studies 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.
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 utricaria and injection site pain/swelling (1% each).

Pulmonary emboli 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 subcutaneously to 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. 2/30 (7%) of subjects who used the 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 a causal relationship to drug exposure.

• Body: as a whole: Local injection site reactions (including erythema, urticaria, rash, irritation, hyperventilation, warmth); fatigue; fever; hot flashes/flashes
• Digestive disorders: Vomiting
• Infections: Urinary tract infection
• Nervous system disorders: Headache, dizziness
• Pregnancy: puerperal and perinatal conditions: Cervical incompetence, premature rupture of membranes
• Reproductive system and breast disorders: Cervical dilation, shortened cervix
• Respiratory disorders: Dyspnea, chest discomfort
• Skin: Rash

7 DRUG INTERACTIONS

In vitro drug-drug interaction studies were conducted with Makena. Hydroxyprogesterone caproate has minimal inhibition of CYP1A2, CYP2C9, and CYP2B6 related drug-drug interactions at the clinically relevant concentrations. In vitro data indicated that therapeutic concentration of hydroxyprogesterone caproate is not likely to inhibit the activity of CYP2C9, CYP2C9, CYP2C19, CYP2D6, CYP3A4, and CYP3A4. [See Clinical Pharmacology (12.3).] No in vivo drug-drug interaction studies were conducted with Makena.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Makena is indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. Fetal, neonatal, and maternal risks are discussed throughout the labeling. Data from the placebo-controlled clinical trial and the infant follow-up safety study [see Clinical Studies (14.1)] did not show a difference in adverse developmental outcomes between children of Makena-treated women and children of control subjects. However, these data are limited and therefore cannot determine a drug-related risk of adverse developmental outcomes as none of the Makena-treated women received the drug during the first trimester of pregnancy. In animal reproduction studies, intramuscular administration of hydroxyprogesterone caproate to pregnant rats at doses of 5 times the human dose equivalent based on a 60 kg human was not associated with adverse developmental outcomes.

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

Reproduction studies of hydroxyprogesterone caproate administered to various animal species have been reported in the literature. In nonhuman primates, embryolethality was reported in rhesus monkeys administered hydroxyprogesterone caproate up to 2.4 and 24 times the human dose equivalent, but not in cynomolgus monkeys administered hydroxyprogesterone caproate at doses up to 2.4 times the human dose equivalent, every 7 days between days 20 and 146 of gestation. There were no teratogenic effects in either strain of monkey.

Reproductive studies have been performed in mice and rats at doses up to 95 and 5, respectively. Times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to hydroxyprogesterone caproate.

8.2 Lactation

Risk Summary

Low levels of progestins are present in human milk with the use of progestin-containing products, including hydroxyprogesterone caproate. Published studies have reported no adverse effects of progestins on the breastfed child or on milk production.

8.4 Pediatric Use

Makena is not indicated for use in women under 16 years of age. Safety and effectiveness in patients less than 16 years of age have not been established. A small number of women under age 16 years were studied; safety and efficacy data are not the same in women aged 16 years and above as for users 16 years and older [see Clinical Studies (14.1)].

8.5 Hepatic Impairment

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 overdose of Makena in clinical trials. In the case of overdose, 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 4-hydroxy-5-ene-3,20-dione, 17(1-oxochole) (17alpha) (11beta). It has an empirical formula of C_{23}H_{33}O_5 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:

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H
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Makena is a clear, yellow, sterile, non-pyrogenic solution for intramuscular (vials) or subcutaneous (auto-injector) injection. Each 1.1 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 preservative-free 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).
12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Hydroxyprogesterone caproate is a synthetic progestin. The mechanism by which hydroxyprogesterone caproate reduces the risk of preterm recurrent birth is not known.

12.2 Pharmacodynamics
No specific pharmacodynamic studies were conducted with Makena.

12.3 Pharmacokinetics
Absorption: Female patients with a singleton pregnancy received intramuscular doses of 250 mg hydroxyprogesterone caproate for the reduction of preterm birth starting between 16 weeks 0 days and 36 weeks 6 days. All patients had blood drawn daily for 7 days to evaluate pharmacokinetics.

Table 4 Summary of Mean (Standard Deviation) Pharmacokinetic Parameters for Hydroxyprogesterone Caproate

<table>
<thead>
<tr>
<th>Group</th>
<th>Tmax (days)</th>
<th>Cmax (ng/mL)</th>
<th>AUC0-t (µg*h/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=22)</td>
<td>7.1 (3.2)</td>
<td>5.5 (2.0)</td>
<td>1268 (530)</td>
</tr>
<tr>
<td>(N=10)</td>
<td>4.4 (1.3)</td>
<td>10.0 (3.5)</td>
<td>1774 (519.2)</td>
</tr>
</tbody>
</table>

For all three groups, peak concentration (Cmax) and area under the curve (AUC0-t) of the mono-hydroxylated metabolites were approximately 3-8-fold lower than the respective parameters for the parent drug, hydroxyprogesterone caproate. While di-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 hydroxylated 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 metabolites was 19.7 (9.2) days.

In a single-dose, open-label, randomized, parallel design bioavailability study in 120 healthy post-pubertal male subjects, hydroxyprogesterone caproate administered intramuscularly (1 mL) in the upper outer quadrant of the gluteus maximus, was rapidly absorbed. Clearance estimates range from 0.3 to 0.7 L/h/kg body weight.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Hydroxyprogesterone caproate has not been adequately evaluated for carcinogenicity. No reproductive or developmental toxicity or impaired fertility was observed in a multigenerational study in rats. Hydroxyprogesterone caproate administered intramuscularly, at gestational exposures at 10-12 weeks gestation, approximately 50% of a dose was recovered in the feces and approximately 36% recovered in the urine.

Drug Interactions
Cytochrome P450 (CYP) enzymes: In an in vitro inhibition study using human liver microsomes and CYP substrates, hydroxyprogesterone caproate demonstrated minimal inhibition of CYP1A2, CYP2A6, CYP2B6, CYP2C9, and CYP3A4. In an in vitro inhibition study using human liver microsomes, hydroxyprogesterone caproate did not inhibit or inhibit CYP1A2, CYP2A6, or CYP2B6 activity. Overall, the in vitro findings indicate that hydroxyprogesterone caproate has minimal potential for interaction with CYP enzymes.

14 CLINICAL STUDIES

14.1 Clinical Trial to Evaluate Reduction of Risk of Preterm Birth
In a double-center, randomized, double-blind, vehicle (placebo)-controlled clinical trial, the safety and effectiveness of Makena for the reduction of the risk of spontaneous preterm birth was studied in 1,338 women with singleton pregnancies at 20 to 32 weeks gestation who had a documented history of a spontaneous preterm birth (defined as delivery at least 37 weeks of gestation following spontaneous preterm labor or premature rupture of membranes). At the time of randomization (between 16 weeks, 0 days and 36 weeks, 6 days), the patients were participating in pregnancy care, and included: 59.0% Black, 25.5% Caucasian, 13.9% Hispanic and 0.6% Asian. The mean body mass index was 26.9 kg/m2.

The demographic and baseline characteristics of the Makena-treated women were similar to those in the control group. Makena-treated women were similar to control subjects in terms of age, gravidity, parity, gestational age at study entry, and prior spontaneous preterm birth.

Compared to controls, treatment with Makena reduced the proportion of women who delivered preterm at < 35 weeks and < 32 weeks and was also lower among women treated with Makena. The upper bounds of the confidence intervals for the treatment difference at < 35 and < 32 weeks were close to zero. Inclusion of zero in a confidence interval would indicate the treatment difference is not statistically significant. Compared to the other gestational ages evaluated, the number of preterm births at < 32 weeks was limited.

The rates of fetal losses and neonatal deaths in each treatment arm are displayed in Table 4. Due to the higher rate of miscarriages in the Makena arm, there was no overall survival difference demonstrated in this clinical trial.

Table 4 Fetal Losses and Neonatal Deaths

<table>
<thead>
<tr>
<th>Complication</th>
<th>Makena (N=306)</th>
<th>Control (N=153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriages ≥20 weeks gestation</td>
<td>5 (2.4)</td>
<td>6 (3.9)</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>6 (2.0)</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Antepartum stillbirth</td>
<td>5 (1.6)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Intrapartum stillbirth</td>
<td>0 (0.0)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>8 (2.6)</td>
<td>9 (5.9)</td>
</tr>
</tbody>
</table>

15 HOW SUPPLIED/STORAGE AND HANDLING

Makena auto-injector (for subcutaneous injection)
Makena auto-injector (NDC 64011-301-03) is supplied as 1.1 mL of a clear yellow sterile preservative-free solution in an auto-injector containing a pre-filled syringe. Each 1.1 mL auto-injector contains hydroxyprogesterone caproate USP, 250 mg/mL (25% w/v), in castor oil USP, benzyl alcohol USP, and benzyl benzoate USP (46% v/v) with the preservative benzyl alcohol NF (2% v/v).

Table 5 Proportion of Subjects Delivering at < 35 weeks and < 32 weeks Gestational Age (ITT Population)

<table>
<thead>
<tr>
<th>Delivery Outcome</th>
<th>Makena (N=310)</th>
<th>Control (N=153)</th>
<th>Treatment difference and 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 weeks</td>
<td>37.1 (54.4)</td>
<td>54.9 (28.0)</td>
<td>-17.8% [-28.0%, -7.4%]</td>
</tr>
<tr>
<td>&lt;32 weeks</td>
<td>32.1 (49.4)</td>
<td>49.7 (25.6)</td>
<td>-14.6% [-25.8%, -3.4%]</td>
</tr>
</tbody>
</table>

Four Makena-treated subjects were lost to follow-up. They were counted as failures at their gestational ages at time of last contact (18.2, 22.3, 34 and 36 weeks).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Informed consent is necessary. The patient should be aware that the study medication may cause changes in behavior or mood. The patient should be counseled to report any changes in behavior, mood, anxiety, or depression to their healthcare provider. The patient should be advised to avoid driving or engaging in hazardous activities until the effects of the study medication are fully understood.

The patient should be advised to use two forms of birth control during and for at least 30 days following discontinuation of the study medication.

For all patients, the patient should be counseled to avoid hormone-containing products such as oral contraceptives, hormone replacement therapy, and hormone replacement therapy with progestins.

18 ADVERSE REACTIONS

See international labeling for complete adverse events information.

The most common adverse events during the study were injection site reactions such as pain, tenderness, redness, swelling, and induration. These events were usually mild to moderate in severity and did not require treatment. The injection site reactions were more common in the Makena arm, with a higher frequency of injection site reactions in the Makena arm compared to the control arm.

The most common adverse events in the Makena arm were injection site reactions (pain, tenderness, redness, swelling, and induration) and decreased fetal movement. These adverse events were reported with an incidence of 3% to 4% in the Makena arm and 0% to 1% in the control arm.

The rates of fetal losses and neonatal deaths in each treatment arm are displayed in Table 6. Due to the higher rate of miscarriages in the Makena arm, there was no overall survival difference demonstrated in this clinical trial.

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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 (progestin) 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 an 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.

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

- 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 benzy alcohol. 5 mL multi-dose vials also contain benzy 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

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