Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

FulVenir

Solution for injection in pre-filled syringe

For intramuscular injection

Composition:

Each pre-filled syringe (5 ml) contains:

fulvestrant 250 mg

For a list of inactive ingredients and allergens in this medicine, see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine.

Keep this leaflet in case you need it again. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

- FulVenir is intended to treat advanced or metastatic breast cancer expressing estrogen receptors in postmenopausal women not previously treated with endocrine therapy, or cases of disease relapse/progression with or after adjuvant endocrine therapy.
- FulVenir in combination with the medicine palbociclib is intended to treat women with HER2 negative advanced or metastatic breast cancer expressing estrogen receptors whose disease progressed after previous endocrine therapy for this disease.

  If receiving combination therapy with FulVenir and palbociclib (Ibrance) please also read the patient leaflet for palbociclib (Ibrance).

  Therapeutic group: estrogen antagonist.

  The medicine FulVenir contains the active substance fulvestrant, which belongs to the group of medicines that block estrogen activity. Estrogen is a female sex hormone which can in some cases be involved in the development of breast cancer.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to fulvestrant or to any of the other ingredients in this medicine (listed in section 6).
- you are pregnant or breastfeeding.
- you have serious liver problems.

Special warnings about using FulVenir

Before treatment with FulVenir, tell your doctor if you have:

- kidney or liver problems
- previous problems with blood clotting
- low level of platelets (which help blood clotting) or bleeding disorders
- osteoporosis (loss of bone density)
- alcohol addiction (alcoholism)
- This medicine may interfere with the results of tests measuring estradiol levels. Tell your doctor that you are taking FulVenir whenever you are referred for laboratory tests.

Children and adolescents

FulVenir is not indicated in young and adolescent girls under 18 years old.

Interactions with other medicines

If you are taking or have recently taken other medicines, including nonprescription medications, vitamins, dietary supplements, and herbal remedies, please tell your doctor or pharmacist. This is because FulVenir may affect the way some medicines work, and some medicines may affect the way FulVenir works. Particularly, if you are taking medicines for blood clotting (anticoagulants).

Pregnancy and breastfeeding

- **Pregnancy:**

Do not use FulVenir if you are pregnant. If you are of childbearing age and might become pregnant, you should use effective contraception to prevent pregnancy while being treated with FulVenir and for two years after your last dose of this therapy.

- **Breastfeeding:**

Do not breastfeed while on treatment with FulVenir.

Driving and using machines

FulVenir is not expected to affect your ability to drive or use machines. If you feel tired after treatment do not drive or use machines.

Important information about some of this medicine's ingredients:

FulVenir contains 10% w/v (weight to volume) ethanol (alcohol); for example, up to 500 mg alcohol per dose is equivalent to 10 ml beer or 4 ml wine per dose. This amount can be harmful for those suffering from alcoholism. This must be taken into account in people who are in high-risk groups such as patients with liver disease or epilepsy.

FulVenir contains 500 mg benzyl alcohol per injection which is equivalent to 100 mg/ml. Benzyl alcohol can lead to allergic reactions.

FulVenir contains 750 mg benzyl benzoate per injection which is equivalent to 150 mg/ml.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Your doctor will explain how this medicine is taken (how much and when to inject). Your doctor will decide on the strength and duration of your therapy depending on your disease.

In the absence of other instructions from your doctor, the usual dosage is:

The usual dosage is 500 mg fulvestrant (2 injections of 250 mg/5 ml) given once a month, and an additional dose of 500 mg given two weeks after the first dose.

- When fulvestrant is given in combination with Ibrance, the usual dosage of fulvestrant is 500 mg on Days 1, 15, and 29 and once a month after that. Please read the Ibrance patient leaflet.

Do not exceed the recommended dose.

Using this medicine

Your doctor or nurse will give you a FulVenir injection as a slow intramuscular injection; one injection into each of your buttocks. See instructions for using the syringes at the end of this leaflet.

If you have accidentally taken a higher dose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you**.**

Complete the therapy your doctor recommended.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

Follow the instructions for taking this medicine very carefully, and consult your doctor if you are in any doubt.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using FulVenir may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Side effects requiring special attention:

You may need urgent medical treatment if you experience any of the following side effects:

FulVenir as single therapy:

- hypersensitivity (allergic) reactions, including swelling of the face, lips, tongue and/or throat. These effects may be signs of anaphylactic reactions.
- thromboembolism (increased risk of blood clots)*
- inflammation of the liver (hepatitis)
- liver failure

FulVenir in combination with palbociclib:

- pulmonary embolism

Tell your doctor or pharmacist if you notice any of the following side effects:

Very common side effects (affect more than 1 in 10 patients):

FulVenir as single therapy:

- injection site reactions, such as pain and/or inflammation
- abnormal levels of liver enzymes (in blood tests)*
- nausea
- weakness
- tiredness*
- joint and musculoskeletal pain
- hot flushes
- skin rash

- hypersensitivity reaction (allergy), including swelling of the face, lips, tongue and/or throat

Additional side effects:
Common side effects (affect up to 1 in 10 patients):

- headache
- vomiting, diarrhea, or loss of appetite*
- urinary tract infections
- back pain*
- thromboembolism (increased risk of blood clots)*
- increase level of bilirubin (bile pigment produced by the liver)
- decreased levels of platelets (thrombocytopenia)
- vaginal bleeding
- lower back pain radiating to leg on one side (sciatica)
- sudden weakness, numbness, tingling, or loss of movement in your legs, especially on only one side of your body, sudden problems with walking or balance (peripheral neuropathy)

FulVenir in combination with palbociclib

Very common side effects (affect more than 1 in 10 patients):

- reduced number of white blood cells (neutropenia, leucopenia)
- infections
- tiredness
- nausea, vomiting
- anemia
- inflammation in the mouth (stomatitis)
- headache
- diarrhea
- reduced number of platelets (thrombocytopenia)
- constipation
- alopecia rash
- reduced appetite
- fever

Additional side effects:

- weakness

FulVenir as single therapy

Uncommon side effects (affect up to 1 in 100 patients):

- thick, whitish vaginal discharge and fungal infection
- bruising, bleeding at the site of injection
- increased level of liver enzymes called gamma GT (in blood tests)

- inflammation of the liver (hepatitis)
- liver failure
- tingling, numbness, and pain
- anaphylactic (allergic) reaction

* Includes side effects for which the effect of FulVenir is unclear due to the underlying disease.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants.
- Do not induce vomiting unless explicitly instructed to do so by the doctor!
- Store at 2°C-8°C (in a refrigerator).
- Keep FulVenir in its original package to protect from light.
- Do not use the medicine after the expiry date (Exp. date) which is stated on the package. The expiry date refers to the last day of that month. If you are in any doubt, consult the pharmacist who supplied you with the medicine.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Benzyl benzoate, Benzyl alcohol, Alcohol, Castor oil.

What the medicine looks like and contents of the pack:

- FulVenir is a clear, colorless to yellow, viscous solution for injection in a pre-filled syringe with safety cap.
- Packs contain two glass pre-filled syringes, and safety needles (BD SafetyGlide™) for connecting to each syringe.

Manufacturer's name and address:

Chia Tai Tianqing Pharmaceutical Group CO. Ltd., China

Lianyungang, Jiangsu Province 222062, China.

Importer and registration holder's name: BioAvenir Ltd., 1 David Hamelech St., Herzlia Pituach.

Registration number of the medicine in the Ministry of Health's National Drug Registry:

168-64-36677-99

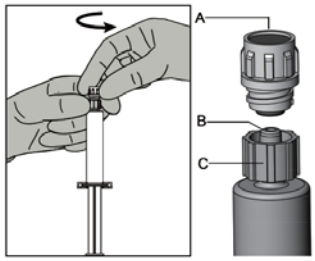
Revised in December 2021 according to MOH guidelines.

Instructions for using the syringes:

For each single-dose prefilled syringe:

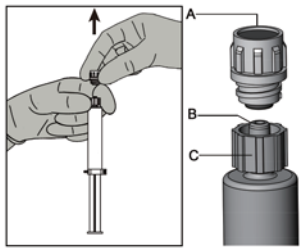
1. Remove glass syringe barrel from tray and check that it is not damaged.
2. Inspect drug product in glass syringe for any visible particulate matter or discoloration prior to use. Discard if particulate matter or discoloration is present.
3. Peel open the safety needle (SafetyGlide™) outer packaging.
4. Hold the syringe upright on the ribbed part (C). With the other hand, take hold of the cap (A) and carefully twist the cap counter-clockwise until the cap disconnects for removal (see Figure 1).

Figure 1



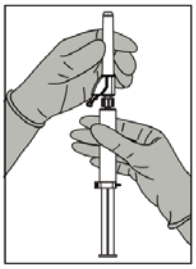
5. Pull the cap (A) off in a straight upward direction. DO NOT TOUCH THE STERILE SYRINGE TIP (Luer-Lok) (B) (see Figure 2).

Figure 2



6. Attach the safety needle to the syringe tip (Luer-Lok). Twist needle until firmly seated (see Figure 3). Confirm that the needle is locked to the Luer connector before moving or tilting the syringe out of the vertical plane to avoid spillage of syringe contents.

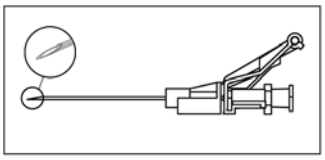
Figure 3



For Administration:

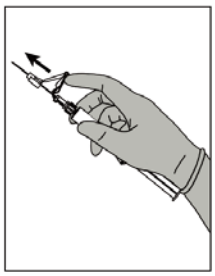
7. Pull shield straight off needle to avoid damaging needle point.
8. Remove needle sheath.
9. Expel excess gas from the syringe (a small gas bubble may remain).
10. Administer intramuscularly slowly (1-2 minutes/injection) into the buttock (gluteal area). For user convenience, the needle 'bevel up' position is orientated to the lever arm, as shown in Figure 4.

Figure 4



11. After injection, immediately activate the lever arm to deploy the needle shielding by applying a single-finger stroke to the activation assisted lever arm to push the lever arm completely forward. Listen for a click. Confirm that the needle shielding has completely covered the needle (see Figure 5).
    NOTE: Activate away from self and others.

Figure 5



12. Discard the empty syringe into an approved sharps collector in accordance with applicable regulations and institutional policy.
13. Repeat steps 1 through 12 for second syringe.

How To Use Fulvestrant Injection

For the 2 x 5 mL syringe package, the contents of both syringes must be injected to receive the 500 mg recommended dose.

SAFETYGLIDE™ INSTRUCTIONS FROM BECTON DICKINSON

SafetyGlide™ is a trademark of Becton Dickinson and Company.

Important Administration Information

To help avoid HIV (AIDS), HBV (Hepatitis), and other infectious diseases due to accidental needlesticks, contaminated needles should not be recapped or removed, unless there is no alternative or that such action is required by a specific medical procedure. Hands must remain behind the needle at all times during use and disposal.

Do not autoclave SafetyGlide™ Needle before use.

Becton Dickinson guarantees the contents of their unopened or undamaged packages to be sterile, non-toxic and non-pyrogenic.