PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Xospata 40 mg

Composition:
Each film-coated tablet contains 40 mg gilteritinib (as fumarate).

Inactive ingredients and allergens - see section 6 "Further information".

Read all of this leaflet carefully before you start taking this medicine.
This leaflet contains concise information about the medicine. If you have further questions, consult the doctor or pharmacist.
This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

Patient information card:
This card contains important safety information which you should know prior to beginning treatment with Xospata and during the treatment with Xospata.
The card contains information intended for both the patient and the healthcare staff.
It provides guidance for the patients on how to minimize the risk of differentiation syndrome.
In addition, the card contains personal details of the patient and information regarding Xospata for the healthcare staff.
Present this card to any healthcare professional involved in your treatment.

1. What is this medicine used for?

What Xospata is used for
Xospata is indicated as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation.

Therapeutic group
Xospata belongs to a group of cancer medicines called protein kinase inhibitors.

How Xospata works
In AML, patients develop large numbers of abnormal white blood cells. Gilteritinib blocks the action of certain enzymes (kinases) needed for the abnormal cells to multiply and grow, thus preventing the growth of the cancer.

2. Before using this medicine

Do not use Xospata if:
- you are allergic to gilteritinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to you doctor, pharmacist or nurse straight away:
- if you have any of the following symptoms: fever, trouble breathing, rash, dizziness or lightheadedness, rapid weight gain, swelling of your arms or legs. These may be signs of a condition called differentiation syndrome (see section 4 –Side effects). Differentiation syndrome can happen any time during the first 3 months of Xospata treatment from as early as 1 day after starting treatment. If it occurs, your doctor will monitor you and may give you a medicine to treat your condition. Your doctor may also pause Xospata treatment until symptoms are reduced.
- if you have a seizure or quickly worsening symptoms such as headache, decreased alertness, confusion, blurred vision or other problems with seeing. These may be signs of a condition

called PRES (see section 4. –Side effects). Your doctor may do a test to check if you have developed PRES and will stop Xospata treatment if it is confirmed that you have PRES.

Talk to your doctor, pharmacist or nurse before taking Xospata:
- if you have a heart rhythm disorder, such as an irregular heartbeat or a condition called QT prolongation (see section 4. –Side effects).
- if you have a history of low levels of the salts potassium or magnesium in your blood, as this may increase the risk of an abnormal heart rhythm.
- if you have severe pain in the upper abdomen and back, nausea and vomiting. These may be signs of an inflammation of the pancreas (pancreatitis).

Tests and follow-up
Your doctor will carry out regular blood tests before and during treatment with Xospata. Your doctor will also regularly check your heart function before and during treatment.

Children and adolescents
This medicine is not intended for children and adolescents under the age of 18.
There is no information regarding the safety and efficacy of use of this medicine in children and adolescents under the age of 18.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
In particular, if you are taking:
- medicines to treat certain types of cancer such as mitoxantrone or methotrexate;
- medicines used to treat tuberculosis, such as rifampicin;
- medicines used to treat epilepsy, such as phenytoin;
- medicines used to treat fungal infections such as voriconazole, posaconazole or itraconazole;
- medicines used to treat bacterial infections such as erythromycin, clarithromycin or azithromycin;
- medicines used to treat high blood pressure (hypertension) such as captopril or carvedilol;
- medicines used to treat high blood sugar (hyperglycemia) such as metformin;
- medicines used to reduce cholesterol levels such as rosuvastatin;
- medicines used to treat infections with the human immunodeficiency virus (HIV) such as ritonavir;
- medicines used to treat depression such as escitalopram, fluoxetine or sertraline;
- medicines used to treat heart problems, such as digoxin;
- medicines used to prevent blood clots, such as dabigatran etexilate;
- St. John’s wort (also known as Hypericum perforatum), a herbal medicine used to treat depression.

Xospata may affect the way these medicines work, or these medicines may affect how Xospata works.

If you normally take any of these medicines, your doctor might change it and prescribe a different medicine for you during your treatment with Xospata.

Pregnancy and breast-feeding
Xospata may harm your unborn baby and should not be used during pregnancy. Women taking Xospata who are able to become pregnant should use an effective method of contraception during treatment with Xospata and for at least 6 months after stopping Xospata. If you use a hormonal contraceptive, you must also use a barrier method, such as a condom or a diaphragm. Men taking Xospata whose partners are able to become pregnant should use an effective method of contraception during treatment with Xospata and for at least 4 months after stopping the treatment.

It is not known if Xospata passes into your breast milk and could harm your baby. You should not breast-feed during treatment with Xospata and for at least 2 months after stopping the treatment.

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before taking this medicine.

Driving and using machines
You may feel dizzy after taking Xospata. If this happens, do not drive or use machines.

3. How should you use the medicine?

Always use according to the doctor's instructions.

Check with your doctor or pharmacist if you are not sure.

Xospata is taken by mouth as tablets.

Your doctor will tell you what dose of Xospata to take. The recommended dose is 120 mg (three tablets) once a day. Your doctor may decide to increase or lower your dose or temporarily interrupt treatment. Continue treatment at the dose prescribed by your doctor.

Do not exceed the recommended dose.

Directions for use
- Take Xospata once a day at the same time each day.
- Swallow the tablets whole with water.
- Do not break or crush the tablets.
- Xospata can be taken with or without food.
- Continue taking Xospata for as long as your doctor tells you.

If you take accidentally higher dose than you should
If you take more tablets than you should, stop taking Xospata and contact your doctor.
If a child accidentally swallowed the medicine, immediately contact a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take Xospata
If you forget to take Xospata at the usual time, take your usual dose as soon as you remember on the same day and take your next dose at the usual time on the following day. Do not take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by the doctor.
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

If you stop taking Xospata
Do not stop taking this medicine unless your doctor tells you to. Response may be delayed; therefore, continue taking Xospata for as long as your doctor tells you.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine.
Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult a doctor or pharmacist.

4. Side effects

As with any medicine, use of Xospata may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Some possible side effects may be serious:
- **Differentiation syndrome.** Contact your doctor straight away if you have any of the following symptoms: fever, trouble breathing, rash, dizziness or lightheadedness, rapid weight gain,

swelling of your arms or legs. These may be signs of a condition called differentiation syndrome (may affect up to 1 in 10 people).
- **Posterior reversible encephalopathy syndrome (PRES).** Contact your doctor straight away if you have a seizure, quickly worsening headache, confusion, or other vision problems.There have been uncommon reports of a condition involving the brain, in patients treated with Xospata, called PRES (may affect up to 1 in 100 people).
- **Heart rhythm problems (QT prolongation).** Contact your doctor straight away if you have a change in your heartbeat, or if you feel dizzy, lightheaded, or faint. Xospata may cause a heart problem called QT prolongation (may affect up to 1 in 10 people).

Other possible side effects

Very common (may affect more than 1 in 10 people):
- diarrhoea
- nausea
- constipation
- tiredness
- swelling due to fluid retention (oedema)
- loss of energy, weakness (asthenia)
- abnormal blood test results: high levels of blood creatine phosphokinase (indicative of muscle or heart function), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and/or blood alkaline phosphatase (indicative of liver function)
- pain in limbs
- joint pain (arthralgia)
- muscle pain (myalgia)
- cough
- shortness of breath (dyspnoea)
- dizziness
- low blood pressure (hypotension)

Common (may affect up to 1 in 10 people):
- collection of fluid around the heart, which, if severe, can decrease the heart's ability to pump blood (pericardial effusion)
- a vague feeling of discomfort, feeling unwell (malaise)
- a severe life-threatening allergic reaction, e.g., swelling in the mouth, tongue, face and throat, itching, hives (anaphylactic reaction)
- muscle stiffness
- passing less urine, swelling in the legs (signs of sudden kidney injury)
- inflammation of the heart (pericarditis)
- heart failure

If you get any side effects, if any of the side effects worsen, or if you are suffering from a side effect not mentioned in the leaflet, consult a doctor.

Side effects can be reported to the Ministry of Health through a link "report of side effects due to medicine treatment" located in the home page of the Ministry of Health website (www.health.gov.il) refers to online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. How should the medicine be stored?

There are no special storage conditions. It is recommended to keep at room temperature.
Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach of children and/or infants in order to avoid poisoning.
Do not induce vomiting without an explicit instruction from the doctor.

Do not use this medicine after the expiry date (exp. Date) which is stated on the carton and the blister. The expiry date refers to the last day of that month.

Store in the original package in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Further information

In addition to the active ingredient, the medicine also contains:
mannitol, low-substituted hydroxypropylcellulose, hydroxypropylcellulose, OPARDY 03F42203 magnesium stearate, hypromellose, macrogol, talc, titanium dioxide, iron oxide yellow.

What Xospata looks like and contents of the pack
Xospata 40 mg film-coated tablets (tablets) are round, light yellow film-coated tablets with the company logo and '235' debossed on one side of the tablet.

The tablets are provided in blisters and are available in packs containing 84 film-coated tablets (4-blisters of 21 film-coated tablets).

License holder and address:
Astellas Pharma International B.V., 21 Ha'melacha Street, Rosh Ha'ayin, 4809157.

Manufacturer and address:
Astellas Pharma Europe B.V.
Sylviusweg 62, 2333 BE Leiden, The Netherlands.

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Registration number of the medicine in the National Drug Registry of the Ministry of Health:
165-30-36203-00

For simplicity and ease of reading, this leaflet was drafted in male language, though this medication is intended for both genders.