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

The medicine is dispensed with a doctor's prescription only

Balversa® 3 mg
Film-Coated Tablets

Balversa® 4 mg
Film-Coated Tablets

Balversa® 5 mg
Film-Coated Tablets

Active ingredient and its quantity

Each tablet of Balversa 3 mg contains:
Erdafitinib 3 mg
Each tablet of Balversa 4 mg contains:
Erdafitinib 4 mg
Each tablet of Balversa 5 mg contains:
Erdafitinib 5 mg

Inactive and allergenic ingredients in the preparation – see Section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to 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.

1. WHAT IS THE MEDICINE INTENDED FOR?

Balversa is used to treat adults with locally advanced or metastatic bladder cancer (urothelial carcinoma) and is characterized by:

- Abnormal changes in the FGFR2 or FGFR3 genes
- Disease that has progressed during or following at least one line of therapy that includes platinum-containing chemotherapeutic drugs, including within 12 months of pre-operative adjunctive therapy (neoadjuvant) that includes platinum-containing chemotherapeutic drugs, or after surgery (adjuvant) that includes platinum-containing chemotherapeutic drugs.

Therapeutic group

Kinase inhibitors

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

You are sensitive (allergic) to the active ingredient (erdafitinib) or to any of the additional ingredients contained in the medicine. For a list of additional ingredients, see Section 6 "Further Information".

Special warnings regarding use of the medicine

Before treatment with Balversa, tell the doctor about your medical condition, especially if:

- You have eye problems or vision problems.
- You are pregnant or plan to become pregnant. Balversa can harm your unborn baby. You should not become pregnant while using Balversa.
- You have high phosphate levels in the blood (hyperphosphatemia).

Children and adolescents

The medicine is not intended for children and adolescents below the age of 18.

There is no information regarding the safety and efficacy of use of the preparation in children and adolescents under the age of 18.

Tests and follow-up

The doctor will perform tests to monitor your blood phosphate levels.

In women – your doctor will request that you perform a pregnancy test before beginning treatment with Balversa.

Drug interactions

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Taking Balversa at the same time as other medicines may affect the activity of Balversa and may affect the activity of other medicines. In particular, if you are taking:

- Medicines for the treatment of fungal infections (e.g., itraconazole, fluconazole)
- Medicines to treat bacterial infections (e.g., rifampicin)
- Medicines to treat heart problems and lower blood pressure (e.g., digoxin)
- Potassium phosphate supplements
- Vitamin D supplements
- Acid-reducing medicines (antacids, histamine H2 blockers, proton pump inhibitors)
- Enema or laxatives containing phosphate
- Medicines containing phosphate as an inactive substance
- Metformin (for the treatment of diabetes)

Use of the medicine and food

Balversa can be taken with or without food.

Pregnancy, breastfeeding and fertility

Tell your doctor right away if you are pregnant or think you may be pregnant.

If you are pregnant, think you may be pregnant or are planning to have a baby, do not use Balversa as the medicine may harm your unborn baby and even pose a risk of pregnancy loss.

You should use effective birth control during treatment and for 1 month after taking the last dose. Consult the doctor about birth control methods that are right for you.

Based on findings from animal experiments, Balversa may impair fertility in women of childbearing age.

If you are breastfeeding, talk to your doctor or pharmacist before taking the medicine.

It is unknown whether Balversa passes into breast milk, has on effect on milk production or on the breastfed child. However, due to the potential for side effects in the breastfed child, your doctor will advise you not to breastfeed during treatment and up to a month after taking the last dose of Balversa.

Men

If your female partner is of childbearing age, is pregnant or may be pregnant, you should use effective birth control during treatment with Balversa and for 1 month after the last dose.

3. HOW SHOULD THE MEDICINE BE USED?

Always use according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

Take Balversa treatment once a day.

Swallow the tablet whole with or without food.

Your doctor may change your dose of Balversa, or temporarily stop or completely stop treatment if you get certain side effects.

Do not exceed the recommended dose.

There is no information regarding halving or crushing the tablet.

If you took a higher dose than recommended, or if a child has accidentally swallowed the medicine, refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine, take the regular dose as soon as possible on the same day. Return to your normal dosing regimen on the following day. Do not take more tablets than the daily dose to make up for the forgotten dose.

If you vomit after taking Balversa, do not take another tablet. Take your regular dose the next day.

Do not stop taking the medicine without consulting the doctor.

Adhere to the treatment as recommended by the doctor.

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

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

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

Balversa may cause serious side effects, including:

Eye problems – Eye problems are common during treatment with Balversa but can be serious. Eye problems include dry or inflamed eyes, inflamed cornea (front part of the eye) and disorders of the retina (the internal part of the eye). Tell your doctor right away if you develop blurred vision, loss of vision or other visual changes. You should use artificial tear substitutes, hydrating or lubricating eye gels or ointments at least every 2 hours during waking hours to help prevent dry eyes. During treatment with Balversa, your doctor will send you to see an eye specialist.

High phosphate levels in the blood (hyperphosphatemia) – Hyperphosphatemia is common with treatment with Balversa but can be serious. Your doctor will check your blood phosphate level between 14 and 21 days after starting treatment with Balversa, and then monthly, and may change your dose if needed.

The most common side effects of Balversa include:

- mouth sores
- feeling tired
- change in kidney function
- diarrhea
- dry mouth
- nails separate from the bed or poor formation of the nail
- change in liver function
- low sodium levels
- poor appetite
- change in sense of taste
- low red blood cells (anemia)
- dry skin
- dry eyes
- hair loss
- redness, swelling, peeling or tenderness, mainly on the hands or feet ('hand-foot syndrome')
- constipation
- abdominal pain
- nausea
- muscle pain

Tell your doctor right away if you develop any skin or nail problems including nails separating from the nail bed, nail pain, nail bleeding, breaking of the nails, color or texture changes in your nails, inflamed skin around the nail, an itchy skin rash, dry skin, or cracks in the skin.

Balversa may affect fertility in women of childbearing age. Consult with your doctor if this is a concern for you.

The table below shows side effects by body systems:

Body System	*Side effect*
Gastrointestinal disorders	Stomatitis Vomiting
General disorders and administration site conditions	Pyrexia
Skin and subcutaneous disorders	Onycholysis Alopecia Nail discoloration
Eye disorders	Blurred vision Lacrimation increased
Nervous system disorders	Dysgeusia
Infections and infestations	Paronychia Urinary tract infection Conjunctivitis
Respiratory and thoracic disorders	Lower pharyngeal pain Dyspnea
Renal and urinary tract disorders	Hematuria (blood in the urine)
Musculoskeletal and connective tissue disorders	Musculoskeletal pain Joint pain
Investigations	Weight decreased
Laboratory abnormalities	<u>Hematology</u>: Hemoglobin decreased Platelets decreased Leukocytes decreased Neutrophils decreased <u>Chemistry</u>: Phosphate level increased/decreased Creatinine increased Sodium decreased Increase in an enzyme called alanine aminotransferase Increase in an enzyme called alkaline phosphatase Albumin decreased Increase in an enzyme called aspartate aminotransferase Magnesium decreased Calcium increased Potassium increased Fasting glucose levels increased

If a side effect occurs, or if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. Date) appearing on the package. The expiry date refers to the last day of that month.

Do not store above 25°C.

After first opening the package, use within 12 months and no later than the expiry date of the preparation.

Store the tablets in their original package.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Microcrystalline cellulose
Mannitol
Croscarmellose sodium
Magnesium stearate
Meglumine

Opadry amb II 88A120003 Yellow (3 mg):
Polyvinyl alcohol-partially hydrolyzed
Talc
Titanium dioxide
Iron oxide yellow
Glycerol monocaprylocaprate Type 1
Sodium lauryl sulfate

Opadry amb II 88A130001 Orange (4 mg):
Polyvinyl alcohol-partially hydrolyzed
Talc
Titanium dioxide
Iron oxide yellow
Glycerol monocaprylocaprate Type 1
Sodium lauryl sulfate
Iron oxide red

Opadry amb II 88A165000 Brown (5 mg):
Polyvinyl alcohol-partially hydrolyzed
Talc
Titanium dioxide
Iron oxide red
Glycerol monocaprylocaprate Type 1
Sodium lauryl sulfate
Iron oxide yellow
Iron oxide black/ferrosoferric oxide

What does the medicine look like and what are the contents of the package:

Balversa 3 mg is a yellow, round, biconvex, film-coated tablet, debossed with "3" on one side and "EF" on the other side.

Balversa 4 mg is an orange, round, biconvex, film-coated tablet, debossed with "4" on one side and "EF" on the other side.

Balversa 5 mg is a brown, round, biconvex, film-coated tablet, debossed with "5" on one side and "EF" on the other side.

Balversa 3 mg is supplied in a plastic bottle containing 56 or 84 tablets.

Balversa 4 mg is supplied in a plastic bottle containing 28 or 56 tablets.

Balversa 5 mg is supplied in a plastic bottle containing 28 tablets.

Importer and Registration Holder and Address: J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Balversa 3 mg: 165-77-36132-00
Balversa 4 mg: 165-78-36133-00
Balversa 5 mg: 165-79-36134-00

Approved in 11/20