

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

The medicine is dispensed with a doctor's prescription only

Name of the medicine and its form:

Intelence® 100 mg, Intelence® 200 mg, Tablets

Active ingredient and its quantity in each tablet:
Etravirine 100 mg, 200 mg

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.

Intelence is intended for the treatment of adults. Intelence is not intended for treatment of patients under 18 years of age. This preparation is not usually intended for patients over 65 years of age, unless so instructed by the doctor.

1. WHAT IS THE MEDICINE INTENDED FOR?

Intelence contains the active ingredient etravirine.

Intelence is a medicine used for the treatment of HIV (Human Immunodeficiency Virus) infection. Intelence acts by reducing the level of the virus in the body, which will improve the functioning of the immune system and reduce the risk of developing illnesses associated with HIV infection.

Intelence, in combination with other anti-HIV medicines, is used to treat adult HIV carriers, who have been treated in the past with other anti-HIV medicines. Consult the doctor regarding the most suitable combination of medicines for you.

Therapeutic group: The medicine belongs to a group of anti-HIV medicines called non-nucleoside reverse transcriptase inhibitors (NNRTIs).

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

You are allergic to the active ingredient etravirine or to any of the additional ingredients contained in the medicine, listed in section 6 "Further Information".

You are taking elbasvir/grazoprevir (a medicine to treat hepatitis C infection).

Special warnings regarding use of the medicine:

Before treatment with Intelence, tell the doctor if:

(X) Intelence does not cure the HIV infection, but rather, constitutes a component of treatment intended to reduce the level of the virus in the blood. You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy.

Consult the doctor regarding precautions necessary to prevent infecting others with the virus.

(X) This preparation is not approved in Israel for patients under 18 years of age.

(X) **Elderly: Intelence has been used in a limited number of patients aged 65 and over. If you belong to this age group, you should consult the doctor regarding use of the medicine.**

(X) **Weight and increased blood lipids and glucose: During HIV therapy, there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and life style, and in certain cases of blood lipids, to the anti-HIV medicines themselves. The doctor will test for these changes.**

(X) Bone problems: Some patients, who are taking a combination of antiretroviral medicines, may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The length of combination antiretroviral therapy, use of corticosteroids, alcohol consumption, severe immunosuppression, higher body mass index, among others, may be some of the risk factors for developing this disease. Symptoms of osteonecrosis are joint stiffness, pain (mainly in the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms, inform the doctor.

Inform the doctor of the following conditions:

Check the following points and inform the doctor if they apply to you:

(X) Tell the doctor if a **rash** develops. If a rash develops, it usually appears soon after initiation of anti-HIV treatment with Intelence and usually disappears within a week or two, even with continued use of the medicine. Occasionally, during the course of treatment with Intelence, a hypersensitivity reaction may occur (an allergic reaction including rash and fever, and even swelling of the face, tongue or throat, and difficulty in breathing or swallowing), which could be life-threatening. Inform the doctor immediately if you experience a hypersensitivity reaction. The doctor will advise you on how to deal with the symptoms or whether you should stop taking the medicine. If you have stopped treatment due to a hypersensitivity reaction, do not restart therapy with Intelence.

(X) Inform the doctor if you **suffer or have suffered from liver problems**, including hepatitis B and/or C. Your doctor will assess the severity of your liver disease before deciding if you can take the medicine.

(X) Inform the doctor immediately if you notice any **symptoms of infection**. In some patients with advanced HIV infection and a history of opportunistic infections, signs and symptoms of previous infections can be manifested immediately after initiation of the treatment with the medicine. The symptoms may occur due to the improvement in the body's immune response and its ability to fight infections that may have been present in the body without any obvious symptoms.

(X) In addition to the opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissues) may also occur after beginning to take medicines for the treatment of an HIV infection. Autoimmune disorders can also occur many months after starting treatment. If you notice any symptoms of infection or symptoms such as muscle weakness, weakness beginning in the hands and feet and moving up towards the trunk of the body, palpitations, tremor or hyperactivity, inform the doctor immediately in order to receive the necessary treatment.

Children and adolescents

Intelence is not intended for treatment of patients under 18 years of age.

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:

In most cases, Intelence can be combined with other anti-HIV medicines belonging to another class. However, some combinations are not recommended, and in certain cases, increased monitoring and/or a change in the dose of the medicine are necessary. Therefore, always tell the doctor which other anti-HIV medicines you are taking and carefully follow his instructions regarding the medicines that can be combined. It is important to carefully read the patient leaflet provided with these medicines.

(X) It is not recommended to take Intelence together with the following medicines:

(X) Tipranavir/ritonavir, efavirenz, nevirapine, rilpivirine, indinavir, nelfinavir, atazanavir/cobicistat, darunavir/cobicistat (medicines to treat HIV infection)

(X) Carbamazepine, phenobarbital and phenytoin (for treatment of seizures)

(X) Rifampicin because it is contraindicated with protease inhibitors (boosted protease inhibitors), and rifapentine (for treatment of infections such as tuberculosis)

(X) Preparations that contain St. John's Wort (Hypericum perforatum) (a herbal product for treatment of depression).

(X) Daclatasvir, simeprevir (medicines to treat hepatitis C infection)

Consult the doctor if you are taking any of these medicines.

(X) If you are taking any of the following medicines together with Intelence, their action or that of Intelence may be affected. The dosage of some medicines might need to be changed since their therapeutic effect or side effects may be influenced when combined with Intelence. Tell the doctor if you are taking any of the following medicines:

(X) Dolutegravir, maraviroc, amprenavir/ritonavir and fosamprenavir/ritonavir (anti-HIV medicines).

(X) Amiodarone, bepridil, digoxin, disopyramide, flecainide, lidocaine, mexiletine, propafenone and quinidine (for treatment of heart problems, such as abnormal heart beat).

(X) Warfarin (to reduce blood clotting); your doctor will instruct you to have blood tests performed.

(X) Fluconazole, itraconazole, ketoconazole, posaconazole or voriconazole (to treat fungal infections)

(X) Clarithromycin, rifabutin (antibiotics)

(X) Artemether/lumefantrine (a medicine for treatment of malaria)

(X) Diazepam (to treat sleep disturbances and/or anxiety)

(X) Dexamethasone (a corticosteroid to treat a variety of conditions, such as inflammation and allergic reactions)

(X) Boceprevir (a medicine to treat hepatitis C infection)

(X) Atorvastatin, fluvastatin, lovastatin, rosuvastatin or simvastatin (to lower blood cholesterol levels).

(X) Cyclosporine, sirolimus or tacrolimus (immunosuppressants)

(X) Sildenafil, vardenafil or tadalafil (to treat erectile dysfunction and/or pulmonary arterial hypertension)

(X) Clopidogrel (a medicine to prevent formation of blood clots)

Use of the medicine and food:

It is very important to take the medicine after a meal. Taking the medicine on an empty stomach impairs its absorption and reduces the amount that is absorbed by half. For further information, see section 3 "How should you use the medicine?".

Pregnancy, breastfeeding and fertility:

Inform your doctor immediately if you are pregnant.

Do not take this medicine if you are pregnant, unless explicitly instructed to do so by the doctor.

HIV infected mothers must not breastfeed, as there is a chance of infecting the baby with the virus.

Driving and operating machinery:

Do not drive or operate machinery if you feel drowsy or dizzy after taking the medicine.

Important information about some of the ingredients in this medicine:

Intelence 100 mg tablet contains lactose. Each tablet contains 160 mg lactose monohydrate.

If you have been told by your doctor that you suffer from an intolerance to some sugars such as lactose, consult the doctor before starting to use the medicine.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen for the medicine.

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

The usual dosage is generally: 200 mg, twice a day.

If you are taking 100 mg tablets:

In the morning, take 2 Intelence 100 mg tablets after a meal and in the evening, take 2 Intelence 100 mg tablets after a meal.

If you are taking 200 mg tablets:

In the morning, take one Intelence 200 mg tablet after a meal and in the evening, take one Intelence 200 mg tablet after a meal.

It is very important to take the medicine after a meal. Taking the medicine on an empty stomach impairs its absorption and reduces the amount that is absorbed by half. Consult the doctor regarding the type of food that is suitable.

Swallow the tablet whole with a full glass of water. Do not chew the tablet. The tablet can be halved.

If you are unable to swallow the tablet whole, please follow the following instructions:

- Place the tablet in 5 ml (a teaspoon) of water, or at least in an amount of fluid sufficient to cover the tablet.

- Mix well until the water looks milky.

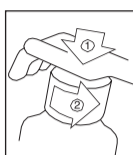
- More water may be added, or, alternatively, orange juice or milk (do not place the tablet directly in orange juice or milk).

- Drink immediately.

- Rinse the glass several times with water, orange juice or milk and drink all of it each time to ensure that the entire dose is taken.

- Do not use hot water (40 degrees and above) or carbonated drinks when taking Intelence.

(X) Instructions for opening the bottle: The bottle has a safety cap which prevents inadvertent opening by children.



Open the bottle by pressing down on the cap while turning counterclockwise, and remove the cap.

Do not exceed the recommended dose.

(X) If you accidentally took a higher dosage, refer to the doctor or pharmacist immediately. The most common side effects of Intelence are rash, diarrhea, nausea, and headache (see section 4 "Side effects").

(X) If you forgot to take this medicine at the scheduled time and remember within 6 hours of the scheduled time, take a dose as soon as you remember, and always following a meal, and continue taking the next dose as usual. If more than 6 hours have elapsed since the time you should have taken the medicine, skip the forgotten dose and continue to take the next dose as usual.

Never take two doses together to make up for a forgotten dose!

If you vomit less than 4 hours after taking Intelence, take another tablet following a meal. If you vomit more than 4 hours after taking Intelence, there is no need to take another dose until the next time you have to take the medicine.

How can you contribute to the success of the treatment?

(X) Adhere to the treatment regimen as recommended by the doctor. Do not stop using Intelence before the doctor gives his approval.

(X) It is possible that the treatment may cause you to feel better. Even if there is an improvement in the condition of your health, do not stop treatment with the medicine or with other anti-HIV medicines without consulting the doctor. Stopping treatment without the doctor's approval may increase the risk of the virus developing resistance.

Do not take medicines in the dark! Check the label and the dose each time 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 Intelence 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.

Very common side effects (effects which occur in more than one in ten users):

(X) Skin rash, usually of a mild or moderate degree. In rare cases, serious rash has been reported, which could be life-threatening. It is therefore important to tell the doctor immediately if a rash develops, so that he can advise you how to treat it and whether treatment with the medicine should be discontinued.

(X) Headache

(X) Diarrhea, nausea

Common side effects (effects which occur in 1-10 in 100 users):

(X) Allergic reaction (hypersensitivity)

(X) Diabetes, decreased appetite

(X) Anxiety, sleepiness, sleeplessness, sleep disorders.

(X) Tingling or pain in hands or feet, numbness, loss of skin sensibility, loss of memory, tiredness.

(X) Blurred vision

(X) Kidney failure, high blood pressure, heart attack, shortness of breath when exercising.

(X) Vomiting, heartburn, abdominal pain, distension of the abdomen, inflammation of the stomach, flatulence, constipation, mouth inflammation, dry mouth.

(X) Night sweats, itching, dry skin.

(X) Changes in blood and urine test values. The doctor will explain these to you. For example: low red blood cells.

Uncommon side effects (effects which occur in 1-10 in 1,000 users):

(X) Decreased number of white blood cells

(X) Symptoms of infection (for example, enlarged lymph nodes and fever)

(X) Abnormal dreams, confusion, disorientation, nervousness, nightmares.

(X) Drowsiness, trembling, fainting, seizures, attention disturbances.

(X) Dizziness, sluggishness

(X) Angina, irregular heart rhythm

(X) Difficulty breathing

(X) Retching, inflammation of the pancreas, vomiting blood.

(X) Liver problems, such as hepatitis, enlarged liver.

(X) Excessive sweating, swelling of the face and/or throat.

(X) Swelling of breasts in men

Rare side effects (effects which occur in 1-10 in 10,000 users):

(X) Stroke

Side effects of unknown frequency (effects whose frequency has not yet been determined):

(X) Severe hypersensitivity reactions characterized by rash accompanied by fever and inflammation of any organ, such as hepatitis.

If a side effect occurs, 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.

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) that appears on the outer package/bottle label. The expiry date refers to the last day of that month.

(X) Do not store above 30°C. Store the tablets in the original bottle. Keep the bottle tightly closed in order to protect from moisture. The bottle contains 3 small pouches which contain a desiccant, thereby keeping the tablets dry. Leave the pouches in the bottle at all times. The pouches are not to be eaten.

After first opening the bottle, do not use this medicine for more than 2 months.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains: Intelence 100 mg: hypromellose; microcrystalline cellulose; croscarmellose sodium; magnesium stearate; colloidal anhydrous silica

and in addition: lactose monohydrate 160.0 mg

Intelence 200 mg: hypromellose; silicified microcrystalline cellulose; microcrystalline cellulose; croscarmellose sodium; magnesium stearate; colloidal anhydrous silica

What the medicine looks like and the contents of the package:

Intelence 100 mg is an oval-shaped, white-beige tablet with T125 imprinted on one side and 100 imprinted on the other side.

Each box contains one plastic bottle containing 120 Intelence 100 mg tablets. In addition, inside the bottle, there are 3 pouches that contain a desiccant, which keep the tablets dry. Leave the pouches in the bottle at all times.

Intelence 200 mg is an elongated, biconvex, white-beige tablet, with T200 imprinted on one side.

The plastic bottle contains 60 Intelence 200 mg tablets. In addition, inside the bottle, there are 3 pouches that contain a desiccant, which keep the tablets dry. Leave the pouches in the bottle at all times.

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

Manufacturer: Janssen-Cilag, Via C Janssen 04100, Borgo San Michele, Latina, Italy.

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved by the Ministry of Health on 03/03/2016, and was updated, in accordance with the Ministry of Health guidelines, on 07/01/2019.

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

Intelence 100 mg: 141293178900

Intelence 200 mg: 149613366600