

Package leaflet: Information for the patient

Instgra Tablets Dolutegravir Tablets 50 mg

Read all of this leaflet carefully before you (or your child, if they are the patient) start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you (or your child, if they are the patient) only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Instgra is and what it is used for
2. What you need to know before you take Instgra
3. How to take Instgra
4. Possible side effects
5. How to store Instgra
6. Contents of the pack and other information

1. What Instgra is and what it is used for

Instgra contains the active ingredient dolutegravir. Dolutegravir belongs to a group of anti-retroviral medicines called *integrase inhibitors* (INIs).

Instgra is used to treat **HIV (human immunodeficiency virus) infection** in patients weighing at least 20 kg.

Instgra does not cure HIV infection; it reduces the amount of virus in your body, and keeps it at a low level. As a result of that, it also increases the CD4 cell count in your blood. CD4 cells are a type of white blood cells that are important in helping your body to fight infection.

Not everyone responds to treatment with Instgra in the same way. Your doctor will monitor the effectiveness of your treatment.

Instgra is always used in combination with other anti-retroviral medicines (*combination therapy*). To control your HIV infection, and to stop your illness from getting worse, you must keep taking all your medicines, unless your doctor tells you to stop taking any.

2. What you need to know before you take Instgra

Do not take Instgra:

- if you (or your child, if they are patient) are allergic to dolutegravir or any of the other ingredients of this medicine (listed in section 6).
 - if you (or your child) are taking another medicine called fampridine (also known as dalfampridine; used in multiple sclerosis).
- If you think any of these apply to you (or your child), tell your doctor.

Warnings and precautions

Look out for important symptoms

Some people taking medicines for HIV infection develop other conditions, which can be serious. These include:

- symptoms of infections and inflammation
- joint pain, stiffness and bone problems

You need to know about important signs and symptoms to look out for while you (or your child, if they are the patient) are taking Instgra.

→ **Read the information in Section 4 of this leaflet.**

Children

Do not give this medicine to children weighing less than 20 kg or with HIV infection that is resistant to other medicines similar to Instgra. The use of dolutegravir in children under 6 or weighing less than 14 kg has not yet been studied.

Children must **keep planned doctor's appointments** (see 'Use in children and adolescents' in Section 3 for more information).

Other medicines and Instgra

Tell your doctor if you (or your child) are taking, have recently taken or are planning to take any other medicines.

Don't take Instgra with the following medicine:

- fampridine (also known as dalfampridine), used in multiple sclerosis

Some medicines can affect how Instgra works, or make it more likely that you will have side effects.

Instgra can also affect how some other medicines work.

Tell your doctor if you (or your child) are taking any of the medicines in the following list:

- metformin, to treat **diabetes**
- medicines called **antacids**, to treat **indigestion** and **heartburn**. **Do not take an antacid** during the 6 hours before you take Instgra, or for at least 2 hours after you take it. (See also Section 3).
- calcium supplements, iron supplements and multivitamins. **Do not take a calcium supplement, iron supplement or multivitamin** during the 6 hours before you take Instgra, or for at least 2 hours after you take it (see also Section 3).
- etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir, to treat **HIV infection**
- rifampicin, to treat tuberculosis (TB) and other **bacterial infections**
- phenytoin and phenobarbital, to treat **epilepsy**
- oxcarbazepine and carbamazepine, to treat **epilepsy** or **bipolar disorder**
- **St. John's wort** (*Hypericum perforatum*), a herbal remedy to treat **depression**

→ **Tell your doctor or pharmacist** if you (or your child) are taking any of these. Your doctor may decide to adjust your dose or that you need extra check ups.

Pregnancy

If you are pregnant, think you may be pregnant, or if you are planning to have a baby:

→ **Talk to your doctor** about the risks and benefits of taking Instgra.

Taking dolutegravir at the time of becoming pregnant or during the first six weeks of pregnancy, may increase the risk of a type of birth defect, called neural tube defect, such as spina bifida (malformed spinal cord).

If you could get pregnant while receiving Instgra:

→ **Talk to your doctor** and discuss whether there is a need for contraception, such as condom or pills.

Tell your doctor immediately if you become pregnant or are planning to become pregnant. Your doctor will review your treatment. Do not stop taking Instgra without consulting your doctor, as this may harm you and your unborn child.

Breast-feeding

Breast-feeding is **not recommended** in women living with HIV because HIV infection can be passed on to the baby in breast milk.

A small amount of the ingredient in dolutegravir can pass into your breast milk.

If you are breast-feeding, or thinking about breast-feeding, you should discuss it with your doctor as soon as possible.

Driving and using machines

Dolutegravir can make you dizzy and have other side effects that make you less alert.

→ **Don't drive or operate machinery** unless you are sure you're not affected.

3. How to take Instgra

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

- **The usual dose** is 50 mg **once a day**;
 - if you are taking **certain other medicines**, the dose is 50 mg **twice a day**
- For HIV that is resistant** to other medicines similar to Instgra, the usual dose is 50 mg tablet, **twice a day**.

Your doctor will decide on the correct dose of Instgra for you.

Swallow the tablet (s) with some liquid.

Instgra can be taken **with or without food**. When Instgra is taken twice a day, your doctor may advise you to take with food.

Use in children and adolescents

Children's dose of dolutegravir needs to be adjusted as they get older or gain weight.

→ It is important therefore that children **keep planned doctor's appointments**.

- Children and adolescents weighing at least 20 kg can take the adult dose of 50 mg. Your doctor will decide how dolutegravir should be given.
- To reduce the risk of choking, children **must not swallow more than one tablet at a time**.
- Dolutegravir should **not** be used in children and adolescents with **HIV infection that is resistant** to other medicines similar to dolutegravir.

Antacid medicines

Antacids, to treat **indigestion** and **heartburn**, can stop dolutegravir being absorbed into your body and make it less effective.

Do not take an antacid during the 6 hours before you take dolutegravir, or for at least 2 hours after you take it.

Other acid-lowering medicines like ranitidine and omeprazole can be taken at the same time as dolutegravir.

→ Talk to your doctor for further advice on taking acid-lowering medicines with Instgra.

Calcium supplements, iron supplements or multivitamins

Calcium supplements, iron supplements or multivitamins can stop dolutegravir being absorbed into your body and make it less effective.

Do not take a calcium supplement, iron supplement or multivitamin during the 6 hours before you take dolutegravir, or for at least 2 hours after you take it.

→ Talk to your doctor for further advice on taking calcium supplements, iron supplements or multivitamins with dolutegravir.

If you take more Instgra than you should

If you (or your child) take too many tablets of Instgra, **contact your doctor or pharmacist for advice**. If possible, show them the Instgra pack.

If you forget to take Instgra

If you (or your child) miss a dose, take it as soon as you remember. But if your next dose is due within 4 hours, skip the dose you missed and take the next one at the usual time. Then continue your treatment as before.

→ **Don't take a double dose** to make up for a missed dose.

Do not stop taking Instgra without advice from your doctor

Take Instgra for as long as your doctor recommends. Don't stop unless your doctor advises you to.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Allergic reactions

These are uncommon in people taking dolutegravir. Signs include:

- skin rash
- a high temperature (*fever*)
- lack of energy (*fatigue*)
- swelling, sometimes of the face or mouth (*angioedema*), causing difficulty in breathing
- muscle or joint aches.

→ **See a doctor straight away**. Your doctor may decide to carry out tests on your liver, kidneys or blood, and may tell you to stop taking Instgra.

Very common side effects

These may affect **more than 1 in 10 people**:

- headache

- diarrhoea
- feeling sick (*nausea*).

Common side effects

These may affect **up to 1 in 10 people**:

- rash
- itching (*pruritus*)
- being sick (*vomiting*)
- stomach pain (*abdominal pain*)
- stomach (*abdominal*) discomfort
- weight gain
- insomnia
- dizziness
- abnormal dreams
- depression (feelings of deep sadness and unworthiness)
- anxiety
- lack of energy (*fatigue*)
- wind (*flatulence*)
- increase in the level of liver enzymes
- increase in the level of enzymes produced in the muscles (*creatine phosphokinase*)

Uncommon side effects

These may affect **up to 1 in 100 people**:

- inflammation of the liver (*hepatitis*)
- suicide attempt*
- suicidal thoughts*
- panic attack
- joint pain
- muscle pain

**particularly in patients who have had depression or mental health problems before.*

Rare side effects

These may affect **up to 1 in 1000 people**:

- liver failure (signs may include yellowing of the skin and the whites of the eyes or unusually dark urine)
- increase in bilirubin (a test of liver function) in your blood.
- suicide (particularly in patients who have had depression or mental health problems before)

→ **Tell your doctor immediately** if you experience any mental health problems (see also other mental health problems above).

Symptoms of infection and inflammation

People with advanced HIV infection (AIDS) have weak immune systems, and are more likely to develop serious infections (*opportunistic infections*). Such infections may have been “silent” and not detected by the weak immune system before treatment was started. After starting treatment, the immune system becomes stronger, and may attack the infections, which can cause symptoms of infection or inflammation. Symptoms usually include **fever**, plus some of the following:

- headache

- stomach ache
- difficulty breathing

In rare cases, as the immune system becomes stronger, it can also attack healthy body tissue (*autoimmune disorders*). The symptoms of autoimmune disorders may develop many months after you start taking medicine to treat your HIV infection. Symptoms may include:

- palpitations (rapid or irregular heartbeat) or tremor
- hyperactivity (excessive restlessness and movement)
- weakness beginning in the hands and feet and moving up towards the trunk of the body.

If you (or your child) get any symptoms of infection and inflammation or if you notice any of the symptoms above:

→ **Tell your doctor immediately.** Don't take other medicines for the infection without your doctor's advice.

Joint pain, stiffness and bone problems

Some people taking combination therapy for HIV develop a condition called *osteonecrosis*. With this

condition, parts of the bone tissue die because of reduced blood supply to the bone. People may be more likely to get this condition:

- if they have been taking combination therapy for a long time
- if they are also taking anti-inflammatory medicines called corticosteroids
- if they drink alcohol
- if their immune systems are very weak
- if they are overweight.

Signs of osteonecrosis include:

- stiffness in the joints
- aches and pains in the joints (especially in the hip, knee or shoulder)
- difficulty moving.

If you notice any of these symptoms:

→ **Tell your doctor.**

Weight, blood lipid and blood glucose effects

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 lifestyle, and in the case of blood lipids sometimes to the HIV medicines themselves. Your doctor will test for these changes.

5. How to store Instgra

Store in a cool and dry place , below 30 °C.

6. Contents of the pack and other information

What Instgra contains?

- The active substance is dolutegravir. Each tablet contains dolutegravir sodium equivalent to 50 mg dolutegravir.
- The other ingredients are:
 1. Mannitol (Pearlitol 25C)
 2. Microcrystalline cellulose (Avicel PH 101)
 3. Sodium Starch glycolate (Primogel Type A)
 4. Povidone (Kollidon 12PF)
 5. Sodium Stearyl Fumarate (PRUV JRS)
 6. Film coating agent
 1. Polyvinyl alcohol-part.hydrolyzed

2. Titanium dioxide
3. Talc
4. FD&C blue #2/ Indigo
5. Carmine Aluminum lake
6. FD&C blue #2 Indigo Carmine Aluminum lake

What Instgra looks like and contents of the pack?

30 Tablets are packed in 60 cc white opaque HDPE (High Density polyethylene) container sealed with 33 mm white opaque child resistant closure. Each such container is packed in a carton along with leaflet.

90 Tablets are packed in 60 cc white opaque HDPE (High Density polyethylene) container sealed with 33 mm white opaque child resistant closure. Each such container is packed in a carton along with leaflet.

180 Tablets are packed in 100 cc white opaque HDPE (High Density polyethylene) container sealed with 38 mm white opaque child resistant closure. Each such container is packed in a carton along with leaflet.

Marketing Authorisation Holder and Manufacturer:

Marketing Authorisation Holder

Emcure Pharmaceuticals Limited

Manufacturer

Emcure Pharmaceuticals Limited