Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
The medicine is dispensed with a doctor's prescription only

Mekinist® 0.5 mg, film-coated tablets
Each film-coated tablet contains trametinib (as dimethyl sulfoxide) 0.5 mg

Mekinist® 2 mg, film-coated tablets
Each film-coated tablet contains trametinib (as dimethyl sulfoxide) 2 mg

Inactive ingredients and allergens: See section 6 'Additional information' and section 2 under 'Important information about some of this medicine's ingredients'.
Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to your doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is the medicine intended for?

Mekinist is used as monotherapy or in combination with an additional medicine containing dabrafenib for the treatment of adults with a type of skin cancer called melanoma that has spread to other parts of the body or cannot be removed by surgery.
Mekinist in combination with dabrafenib is also used for the adjuvant treatment of stage III melanoma in adults, following complete removal of the lesion by surgery.
Mekinist in combination with dabrafenib is also used for the treatment of adults with an advanced stage of lung cancer called non-small cell lung cancer (NSCLC).
Mekinist in combination with dabrafenib is also intended for the treatment of a type of thyroid cancer called anaplastic thyroid cancer (ATC) that has a mutation in the BRAF gene (BRAF V600E mutation), which has spread to other parts of the body or is in one place and in advanced state, and after no satisfactory results have been obtained from local treatment options.
Mekinist in combination with dabrafenib is intended for the treatment of solid tumours in adults and children 6 years and older which cannot be removed by surgery or have spread to other areas of the body and have worsened (progressed), have no other satisfactory treatment options and carry mutation in the BRAF gene. Mekinist is not intended for the treatment of colorectal cancer.
Mekinist in combination with dabrafenib is intended for the treatment of a type of brain cancer called low-grade glioma (LGG) in children 6 years of age and older with a mutation in the BRAF gene (BRAF V600E mutation) who require systemic therapy.

Therapeutic group:
protein kinase inhibitor, antineoplastic agent.
All these types of cancer have a particular change (mutation) in a gene called BRAF at the V600 position.
This mutation in the gene may have caused the cancer to develop. The medicine targets proteins made from this mutated gene and slows down or stops the development of the cancer.

2. Before using the medicine

Mekinist should only be used to treat melanomas, non-small cell lung cancer (NSCLC), anaplastic thyroid cancer (ATC), solid tumours and low-grade glioma with the BRAF mutation. Therefore, before starting treatment, your doctor will test for this mutation.
If your doctor decides that you will receive a combined treatment of Mekinist and dabrafenib, **read the dabrafenib leaflet carefully as well as this leaflet.**
If you have any further questions on the use of this medicine, refer to your doctor.

Do not use this medicine if:

You are sensitive (allergic) to trametinib or to any of the other ingredients in this medicine (listed in section 6 of this leaflet).
Check with your doctor if you think this applies to you.

Special warnings about using this medicine
Before using Mekinist, tell your doctor if:
- you have **any liver problems**. Your doctor may perform blood tests to monitor your liver function while you are taking this medicine.
- you have or have ever had **kidney problems**.
- you have or have ever had **breathing or lung problems**.
- you have heart problems such as heart failure (which can cause shortness of breath, difficulty in breathing when lying down, swelling of the feet or legs) or problems with the way your heart beats. Your doctor should check your heart function before and during treatment.
- you have eye problems, including blockage of the vein draining the eye (retinal vein occlusion) or swelling in the eye which may be caused by fluid blockage (chorioretinopathy).

Before treatment with Mekinist in combination with dabrafenib, tell your doctor if:
- **you have had a different type of cancer other than melanoma, non-small cell lung cancer (NSCLC), anaplastic thyroid cancer (ATC) or solid tumours,** as you may be at greater risk of developing non skin cancers when taking Mekinist.

Check with your doctor if you think any of these may apply to you.

Conditions you need to look out for
Some people taking Mekinist develop other conditions which can be serious. You need to know about important symptoms to look out for.

Bleeding
Taking Mekinist or the combination of Mekinist and dabrafenib can cause serious bleeding including in the brain, the digestive system (such as stomach, rectum or intestine), lungs, and other organs, and can lead to death. Symptoms may include:
- headaches, dizziness, or feeling weak
- blood in the stools or black stools
- blood in the urine
- stomach pain
- coughing/vomiting up blood

Tell your doctor as soon as possible if you get any of these symptoms.

Fever
Taking Mekinist or the combination of Mekinist and dabrafenib may cause fever, although it is more likely if you are taking the combination treatment (see also section 4). In some cases, people with fever may develop low blood pressure, dizziness or other symptoms.
Tell your doctor immediately if you get a temperature above 38ºC or if you feel a fever coming on while you are taking this medicine.

Heart disorder
Taking Mekinist or the combination of Mekinist with dabrafenib can cause heart problems or make existing heart problems worse (*see also "Heart conditions" in section 4*).
Tell your doctor if you have a heart disorder. Your doctor will run tests to check that your heart is working properly before and during treatment with this medicine. Tell your doctor immediately if you feel like your heart is pounding, racing, or beating irregularly, or if you experience dizziness, tiredness, light headedness, shortness of breath or swelling in the legs. If necessary, your doctor may decide to interrupt your treatment or to stop it altogether.

Changes in your skin which may indicate new skin cancer
Your doctor will check your skin before you start taking this medicine and regularly while you are taking it.
Tell your doctor immediately if you notice any changes to your skin while taking this medicine or after treatment (see also section 4).

Eye problems
You should have your eyes examined by your doctor while you are taking this medicine.
Tell your doctor immediately if you get eye redness and irritation, blurred vision, eye pain or other vision changes during your treatment (see also section 4).
Mekinist can cause eye problems including blindness. Mekinist is not recommended if you have ever had blockage of the vein draining the eye (retinal vein occlusion). Tell your doctor immediately if you get the following symptoms of eye problems: blurred vision, loss of vision or other vision changes, coloured dots in your vision or halos (seeing blurred outlines around objects) during your treatment. If necessary, your doctor may decide to interrupt your treatment or to stop it altogether.

Liver problems
Mekinist or Mekinist in combination with dabrafenib can cause problems with your liver which may develop into serious conditions such as hepatitis and liver failure, which may be fatal. Your doctor will monitor you periodically. Signs that your liver may not be working properly may include:
- loss of appetite
- nausea
- vomiting
- stomach pain
- yellowing of your skin or the whites of your eyes (jaundice)
- dark-coloured urine
- itching of the skin

Tell your doctor as soon as possible if you get any of these symptoms.

Breathing or lung problems
Tell your doctor if you have any breathing or lung problems, including difficulty breathing often accompanied by a dry cough, shortness of breath and fatigue. Your doctor may conduct tests to check your lung function before you start taking your medicine.

Muscle pain
Mekinist can result in the breakdown of muscle (destruction of muscle cells - rhabdomyolysis).
Tell your doctor as soon as possible if you get any of these symptoms:
- muscle pain
- dark urine due to kidney damage

If necessary, your doctor may decide to interrupt your treatment or to stop it altogether.
➔ Read the information "Possible serious side effects" in section 4 of this leaflet.

Hole in the stomach or intestine (perforation)
Taking Mekinist or the combination of Mekinist and dabrafenib may increase the risk of developing holes in the gut wall.
Tell your doctor as soon as possible if you have severe abdominal pain.

Serious skin reactions
Serious skin reactions have been reported in people taking Mekinist in combination with dabrafenib.
Tell your doctor immediately if you notice any changes to your skin (see section 4 for symptoms to be aware of).

Inflammatory disease mainly affecting the skin, lung, eyes and lymph nodes
An inflammatory disease mainly affecting the skin, lung, eyes and lymph nodes (sarcoidosis). Common symptoms of sarcoidosis may include coughing, shortness of breath, swollen lymph nodes, visual disturbances, fever, fatigue, pain and swelling in the joints and tender bumps on your skin. Tell your doctor if you get any of these symptoms.

Immune system disorders
Mekinist in combination with dabrafenib may in rare instances cause a condition (haemophagocytic lymphohistiocytosis or HLH) in which the immune system makes too many infection fighting cells, called histiocytes and lymphocytes. Symptoms may include enlarged liver and/or spleen, skin rash, lymph node enlargement, breathing problems, easy bruising, kidney abnormalities, and heart problems. Tell your doctor immediately if you experience multiple symptoms such as fever, swollen lymph glands, bruising or skin rash, at the same time.

Children and adolescents
Mekinist is not intended for children under the age of 6 years. The safety and efficacy of Mekinist in combination with dabrafenib in children below the age of 6 years are not known.
The safety and efficacy of Mekinist when used alone in children are not known.

Drug interactions
Before starting treatment, tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes non-prescription medications and dietary supplements.
Keep a list of the medicines you take, so you can show it to your doctor or pharmacist when you get a new medicine.

Using this medicine and food
It is important to take Mekinist on an empty stomach, because food affects the way the medicine is absorbed into your body *(see section 3)*.

Pregnancy, breastfeeding and fertility
Mekinist is not recommended for use during pregnancy.
- If you are pregnant, think you may be pregnant or are planning to become pregnant, consult your doctor before taking this medicine. Mekinist can harm the unborn baby.
- If you are a woman who could become pregnant, you must use reliable birth control while you are taking Mekinist and for at least 16 weeks after you stop taking it.
- Birth control using hormones (such as pills, injections or patches) may not work properly if you are taking Mekinist in combination with dabrafenib. You need to use another effective method of birth control so you do not become pregnant while you are taking this combination of medicines. Ask your doctor or pharmacist for advice.
- If you become pregnant while you are taking Mekinist, tell your doctor immediately.

Mekinist is not recommended while breastfeeding
It is not known whether the ingredients of Mekinist can pass into breast milk.
If you are breastfeeding, or planning to breastfeed, you must tell your doctor.
It is recommended that you do not breastfeed while you are taking Mekinist. You and your doctor will decide whether you will take Mekinist or breastfeed.

Fertility – in both men and women
Mekinist may impair fertility in both men and women.
Taking Mekinist with dabrafenib: Dabrafenib may permanently reduce male fertility. In addition, men who are taking dabrafenib may have a reduced sperm count, and their sperm count may not return to normal levels after they stop taking this medicine.
Prior to starting treatment with dabrafenib, talk to your doctor about options to improve your chances to have children in the future.
If you have any further questions on the effect of this medicine on fertility, ask your doctor or pharmacist.

Driving and using machines
Mekinist can have side effects that may affect your ability to drive and use machines. Avoid driving or using machines if you feel tired or weak, if you have problems with your vision or if your energy levels are low.
Descriptions of these effects can be found in other sections (see sections 2 and 4). Read all the information in this leaflet for guidance.
Consult your doctor or pharmacist if you are unsure about anything. Your disease symptoms and treatment situation may also affect your ability to drive or use machines.

Important information about some of this medicine's ingredients
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to use the medicine?

Always use this medicine according to your doctor's instructions.
Check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen of Mekinist.
The dosage and treatment regimen will be determined only by your doctor.
The standard dosage of Mekinist either used alone or in combination with dabrafenib in adults is one 2 mg tablet once a day.
The usual dosage of dabrafenib, when used in combination with Mekinist, is 150 mg twice daily.
The dosage and treatment regimen in children and adolescents will be determined only by your doctor.
Your doctor may decide to lower the dose if you get side effects.
Do not exceed the recommended dose, since this may increase the risk of side effects.

How to take the medicine
Swallow the tablet whole, with a full glass of water. Do not chew, crush or split the tablets, since they are film-coated and there is no information about their being chewed, crushed or split.
Take Mekinist once a day, on an empty stomach (at least one hour before a meal or two hours after a meal). This means that:
- after taking Mekinist, you must wait at least one hour before eating, or
- after eating, you must wait at least two hours before taking Mekinist.

Take Mekinist at about the same time each day.

If you take a higher dose of Mekinist
If you take too many tablets of Mekinist, refer to your doctor or pharmacist. If possible, show them the medication package and the leaflet.
- In case of vomiting after taking the medicine, do not take another dose. Take your next dose at the regular time.

If you forget to take the medicine
If less than 12 hours have passed since your regular dosing time, take the medicine as soon as you remember.
If more than 12 hours have passed since your regular dosing time, skip this dose and take your next dose at the usual time. Then carry on taking your tablet at regular times as usual.
Do not take a double dose to make up for a forgotten dose.
Adhere to the treatment as recommended by your doctor.

If you stop taking this medicine
Take Mekinist for as long as your doctor recommends. Do not stop unless your doctor advises you to.

How should you take Mekinist in combination with dabrafenib
- Take Mekinist in combination with dabrafenib exactly as your doctor tells you. Do not change your dosage or stop taking Mekinist or dabrafenib unless your doctor tells you to.
- Take **Mekinist once daily** and **dabrafenib twice daily**. It may be better for you to get into the habit of taking both medicines at the same times each day. Mekinist should be taken with either the morning dose of dabrafenib **or** the evening dose of dabrafenib. The dabrafenib doses should be taken about 12 hours apart.
- Take Mekinist and dabrafenib on an empty stomach, at least one hour before or two hours after a meal. Take them whole with a full glass of water.
- Do not chew, crush or split the tablets, since they are film-coated and there is no information about their being chewed, crushed or split.

If you forget to take a dose of Mekinist or dabrafenib
- Mekinist: If there are more than 12 hours left until your next scheduled dose of Mekinist (which is taken once daily) - take the medicine as soon as you remember.
- Dabrafenib: If there are more than 6 hours left until your next scheduled dose of dabrafenib (which is taken twice daily) - take the medicine as soon as you remember.

In any other case, continue taking the next dose at the regular time. Do not compensate for forgotten doses.

If you accidentally took a higher dose
If you take too much Mekinist or dabrafenib, immediately refer to your doctor, take the medicines with you, including the package and leaflets from each of them. If a child has accidentally swallowed some medicine, immediately refer to a doctor or go to a hospital emergency room and bring the medicine package with you.
If you get side effects, your doctor may decide that you should take a lower dosage of Mekinist and dabrafenib. Take the doses of Mekinist and dabrafenib exactly as your doctor tells you.

Do not take medicines in the dark! Check the label and dose every time 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. Side effects

Like with any medicine, using Mekinist may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Possible serious side effects
Heart conditions
Mekinist can affect how well your heart pumps blood. It is more likely to affect people who have an existing heart problem. You will be checked for any heart problem while you are taking Mekinist.
Signs and symptoms of heart problems include:
- feeling like your heart is pounding, racing or beating irregularly
- dizziness
- tiredness
- feeling light-headed
- shortness of breath
- swelling in the legs

Tell your doctor as soon as possible if you get any of these symptoms, either for the first time or if they get worse.

High blood pressure
Mekinist can cause new or worsening high blood pressure (hypertension). Your doctor or nurse will check your blood pressure during treatment with Mekinist. Call your doctor or nurse right away if you develop high blood pressure, your blood pressure worsens or you have a severe headache, dizziness or lightheadedness.

Bleeding problems
Mekinist can cause serious bleeding problems, especially in your brain or stomach. Call your doctor and get medical help right away if you have any unusual signs of bleeding, including:
- headache, dizziness or weakness
- coughing up blood or coughing up blood clots
- vomit containing blood or that looks like "coffee grounds"
- red or black stools that look like tar

Eye (vision) problems
Mekinist can cause eye problems. Mekinist is not recommended if you have ever had blockage of the vein draining the eye (retinal vein occlusion). Your doctor may advise an eye examination before you take Mekinist and while you are taking it. Your doctor may ask you to stop taking Mekinist or refer you to a specialist, if you develop signs and symptoms in your vision that include:
- loss of vision
- eye redness and irritation
- coloured dots in your vision
- halo (seeing blurred outlines around objects)
- blurred vision

Changes in your skin
Serious skin reactions have been reported in people taking Mekinist in combination with dabrafenib (frequency not known). If you notice one of the following:
- reddish patches on the skin that are circular or target-shaped, with central blisters. Skin peeling. Ulcers of the mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome).
- widespread rash, fever and enlarged lymph nodes (DRESS-syndrome or drug hypersensitivity syndrome).

➔ Stop using the medicine and seek medical attention immediately.
Up to 3 in 100 people taking Mekinist in combination with dabrafenib may develop a different type of skin cancer called *cutaneous squamous cell carcinoma (cuSCC)*. Others may develop a type of skin cancer called *basal cell carcinoma (BCC)*. Usually, these skin changes remain local and can be removed with surgery, and treatment with Mekinist and dabrafenib can be continued without interruption.
Some people taking Mekinist in combination with dabrafenib may also notice that new melanomas have appeared. These melanomas are usually removed by surgery and treatment with Mekinist and dabrafenib can be continued without interruption.
Your doctor will check your skin before you start taking dabrafenib, then check it again every month while you are taking dabrafenib and for 6 months after you stop taking it. This is to look for any new skin cancers.
Your doctor will also check your head, neck, mouth and lymph glands, and you will have scans of your chest and stomach area (called CT scans) regularly. You may also have blood tests. These checks are to detect if any other cancer, including cutaneous squamous cell carcinoma, develops inside your body. Pelvic examinations (for women) and anal examinations are also recommended before and at the end of your treatment.
Mekinist as monotherapy or in combination with dabrafenib can cause rash or acne-like rash. Follow your doctor's instructions for what to do to help prevent rash. Tell your doctor as soon as possible if you get any of these symptoms for the first time or if they get worse.
Refer to your doctor immediately if you get a severe skin rash with any of the following symptoms: blisters on your skin, blisters or sores in your mouth, peeling of your skin, fever, redness or swelling of your face or your feet.
Tell your doctor as soon as possible if you get any skin rash, or if you have a rash that gets worse.

Muscle pain
Mekinist can result in the breakdown of muscle (destruction of muscle cells - rhabdomyolysis). Tell your doctor if you have any new or worsening symptoms, including:
- muscle pain
- dark urine due to kidney damage

Breathing or Lung problems
Mekinist can cause inflammation of the lung (pneumonitis or interstitial lung disease). Tell your doctor if you have any new or worsening symptoms of lung or breathing problems, including:
- shortness of breath
- cough
- fatigue

Immune system disorders
If you experience multiple symptoms such as fever, swollen lymph glands, bruising or skin rash, at the same time, tell your doctor immediately. It may be a sign of a condition where the immune system makes too many infection-fighting cells called histiocytes and lymphocytes that may cause various symptoms (a condition called haemophagocytic lymphohistiocytosis), see section 2 (frequency rare).

Possible side effects in patients taking Mekinist alone
Side effects that you may experience when you take Mekinist alone are as follows:
Very common side effects (may appear in more than one in 10 users):
- High blood pressure
- Bleeding at various sites in the body, which may be mild or serious
- Cough
- Shortness of breath
- Diarrhoea
- Nausea, vomiting
- Constipation
- Stomach ache
- Dry mouth
- Skin rash, acne-like rash, redness of the face, dry or itching skin (see also "Changes in your skin" at the beginning of section 4)
- Unusual hair loss or thinning
- Lack of energy or feeling weak or tired
- Swelling of the hands or feet (oedema peripheral)
- Fever

Very common side effects that may show up in your blood tests
- Abnormal blood test results related to the liver

Common side effects (may appear in 1-10 in 100 users):
- Inflammation of hair follicles in the skin
- Nail disorders such as nail bed changes, nail pain, infection and swelling of the cuticles
- Infection of the skin (cellulitis)
- Skin rash with pus-filled blisters (*see also "Changes in your skin" at the beginning of section 4*)
- Allergic reaction (hypersensitivity)
- Dehydration (low levels of water or fluids)
- Blurred vision
- Swelling around the eyes
- Eyesight problems (*see also "Eye (vision) problems" at the beginning of section 4*)
- Changes in how the heart pumps blood (left ventricular dysfunction) (*see also "Heart conditions" at the beginning of section 4*)
- Heart rate that is lower than the normal range and/or a decrease in heart rate
- Localised tissue swelling
- Inflammation of the lung (pneumonitis or interstitial lung disease)
- Sore mouth or mouth ulcers, inflammation of mucous membranes
- Redness, chapping or cracking of the skin
- Red and painful hands and feet
- Swelling of the face
- Inflammation of the mucosa
- Feeling weak
- Damage to the nerves that can produce pain, loss of sensation or tingling in hands and feet and/or muscle weakness (peripheral neuropathy)

Common side effects that may show up in your blood tests
- Decreased red blood cells (anaemia), abnormal results of creatine phosphokinase values (an enzyme found mainly in heart, brain, and skeletal muscles).

Uncommon side effects (may appear in 1-10 in 1,000 users):
- Swelling in the eye caused by fluid leakage (*chorioretinopathy*) *(see also "Eye (vision) problems" at the beginning of section 4*)
- Swelling of nerves at the back of the eye (optic nerve head oedema - papilloedema) (*see also "Eye (vision) problems" at the beginning of section 4*)
- Separation of the light-sensitive membrane in the back of the eye (the retina) from its supporting layers (retinal detachment) (*see also "Eye (vision) problems" at the beginning of section 4*).
- Blockage of the vein draining the eye (retinal vein occlusion) (*see also "Eye (vision) problems" at the beginning of section 4*)
- Heart pumping less efficiently, causing shortness of breath, extreme tiredness and swelling in ankles and legs (heart failure)
- A hole (perforation) in the stomach or intestines
- Inflammation of the intestines (colitis)
- Breakdown of muscle which can cause muscle pain and kidney damage (destruction of the muscle cells - rhabdomyolysis)

Side effects of unknown frequency (the frequency of these effects has not been established):
- Irregular heartbeat (atrioventricular block)

If you experience any side effects, refer to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

Side effects when Mekinist and dabrafenib are taken together
When you take Mekinist and dabrafenib together, you may experience any of the side effects given in the lists above, although their frequency may change (increase or decrease).
You may also suffer from **additional side effects due to taking dabrafenib** together with Mekinist that appear in the list below.
Tell your doctor as soon as possible if you get any of these symptoms, either for the first time or if they get worse.
Please read the dabrafenib Package Leaflet for details of the side effects you may get when taking this medicine.

The side effects that you may notice when you take Mekinist in combination with dabrafenib:
Very common side effects (may appear in more than one in 10 users):
- Nasal and throat inflammation
- Decreased appetite
- Headache
- Dizziness
- High blood pressure
- Bleeding, at various sites in the body, which may be mild or serious (haemorrhage)
- Cough
- Stomach ache
- Constipation
- Diarrhoea
- Nausea, vomiting
- Rash, dry skin, itching, skin reddening
- Joint pain, muscle pain or pain in the hands or feet
- Muscle spasms
- Feeling weak, lack of energy
- Chills
- Swelling of the hands or feet (oedema peripheral)
- Fever
- Flu-like illness

Very common side effects that may show up in your blood tests:
- Abnormal blood test results related to the liver

Common side effects (may appear in 1-10 in 100 users):
- Infection of the urinary system
- Skin effects including infection of the skin (cellulitis), inflammation of hair follicles in the skin, nail disorders such as nail bed changes, nail pain, infection and swelling of the cuticles, skin rash with pus-filled blisters, cutaneous squamous cell carcinoma (a type of skin cancer), papilloma (a type of skin tumour which is usually not harmful), wart-like growths, increased sensitivity of the skin to sun (see also "Changes in your skin" at the beginning of section 4)
- Dehydration (low levels of water or fluids)
- Blurred vision, eyesight problems, inflammation of the eye (uveitis)
- Heart pumping less efficiently
- Low blood pressure
- Localised tissue swelling
- Shortness of breath
- Dry mouth
- Sore mouth or mouth ulcers, inflammation of mucous membranes
- Acne-like problems
- Thickening of the outer layer of the skin (hyperkeratosis), patches of thick, scaly, or crusty skin (actinic keratosis), chapping or cracking of the skin
- Increased sweating, night sweats
- Unusual hair loss or thinning
- Red and painful hands and feet
- Inflammation of the fatty layer under the skin (panniculitis)
- Inflammation of the mucosa
- Swelling of the face
- Damage to the nerves that can produce pain, loss of sensation or tingling in hands and feet and/or muscle weakness (peripheral neuropathy)

Common side effects that may show up in your blood tests:
- Low levels of white blood cells
- Decrease in number of red blood cells (anaemia), blood platelets (cells that help blood to clot), and a type of white blood cells (leukopenia)
- Low levels of sodium (hyponatraemia) or phosphate (hypophosphataemia) in the blood
- Increase in blood sugar level
- Increase in creatine phosphokinase, an enzyme found mainly in heart, brain, and skeletal muscles
- Increase in enzymes produced by the liver

Uncommon side effects (may appear in 1-10 in 1,000 users):
- Appearance of new skin cancer (melanoma)
- Skin tags
- Allergic reactions (hypersensitivity)
- Eye changes including swelling in the eye caused by fluid leakage (chorioretinopathy), separation of the light-sensitive membrane in the back of the eye (the retina) from its supporting layers (retinal detachment) and swelling around the eyes
- Heart rate that is lower than the normal range and/or a decrease in heart rate
- Inflammation of the lung (pneumonitis)
- Inflammation of the pancreas
- Inflammation of the intestines (colitis)
- Kidney failure
- Inflammation of the kidneys
- Inflammatory disease mainly affecting the skin, lung, eyes and lymph nodes (sarcoidosis)
- Irregular heartbeat (atrioventricular block)

Rare side effects (may appear in 1-10 in 10,000 users):
- A hole (perforation) in the stomach or intestines

Side effects of unknown frequency (the frequency of these effects has not yet been established):
- Inflammation of the heart muscle (myocarditis) which can result in breathlessness, fever, palpitations and chest pain
- Inflamed, flaky skin (exfoliative dermatitis)

Very common side effects in children when Mekinist and dabrafenib are taken together:
- Fever
- Rash
- Vomiting
- Fatigue
- Dry skin
- Cough
- Diarrhoea
- Acne
- Headache
- Stomach ache
- Nausea
- Bleeding
- Constipation
- Inflammation of the cuticles in the hands or feet
- Musculoskeletal pain
- Dizziness
- Upper respiratory infection
- Weight increased
- Ulcers of the mouth
- Sore throat

Additional side effects in children when Mekinist and dabrafenib are taken together:
- Peripheral neuropathy
- Balding
- Pain in jaw
- Decreased appetite
- Anxiety

Abnormalities that may show up in blood tests in children when Mekinist and dabrafenib are taken together:
Chemistry:
- High blood sugar level
- Low level of albumin
- Low level of calcium
- Decrease in phosphate level
- Decrease in magnesium level
- Increase in magnesium level
- High level of sodium
- Decrease in sodium level
- Low level of potassium
- High level of potassium

Liver:
- Increase in aspartate aminotransferase
- Increase in alanine aminotransferase
- Increase in alkaline phosphatase
- Increase in bilirubin

Haematology:
- Decrease in haemoglobin level
- Anaemia
- Decrease in blood platelets
- Decrease in level of white blood cells
- Increase in level of white blood cells (lymphocytes)

If a side effect appears, if any side effect gets worse, or if you suffer from 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 clicking the link 'Reporting Side Effects of Drug Treatment' found on the Ministry of Health home page (www.health.gov.il) which directs you to the online form for reporting side effects, or by using the link: https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, this medicine, and all other medicines should be kept 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.
Do not use the medicine after the expiry date (exp. date) which appears on the package. The expiry date refers to the last day of that month.
Storage conditions: Store in a refrigerator (2°C to 8°C).
Store in the original package in order to protect from light and moisture.
Keep the bottle tightly closed with the desiccant inside (small cylinder-shaped container).
After first opening of the bottle: It should be kept below 30°C and used within 30 days.
Do not throw away medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines which are no longer in use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, the medicine also contains:
Tablet core
Mannitol (E421)
Microcrystalline cellulose (E460)
Hypromellose (E464)
Croscarmellose sodium (E468)
Magnesium stearate (E470b)
Sodium lauryl sulfate
Colloidal silicon dioxide (E551)
Film coating of 0.5 mg tablet
Hypromellose (E464)
Titanium dioxide (E171)
Polyethylene glycol
Iron oxide yellow (E172)
Film coating of 2 mg tablet
Hypromellose (E464)
Titanium dioxide (E171)
Polyethylene glycol
Polysorbate 80 (E433)
Iron oxide red (E172)

What the medicine looks like and contents of the pack:
The Mekinist 0.5 mg film-coated tablets are yellow, modified oval, biconvex, with "GS" debossed on one side and "TFC" on the opposing side.
The Mekinist 2 mg film-coated tablets are pink, round, biconvex, with "GS" debossed on one side and "HMJ" on the opposing side.
The film coated tablets are supplied in opaque white plastic bottles with plastic closures.
One bottle contains 30 tablets.
The bottles also include a silica gel desiccant in a small cylinder-shaped container. The desiccant must be kept inside the bottle and must not be swallowed.
Registration holder and importer's name and address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Revised in April 2024.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Mekinist 0.5 mg: 154 95 34309
Mekinist 2 mg: 154 96 34322