Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Imnovid 1 mg
Imnovid 2 mg
Imnovid 3 mg
Imnovid 4 mg

Active ingredients:
Imnovid 1 mg: Each hard capsule contains pomalidomide 1 mg
Imnovid 2 mg: Each hard capsule contains pomalidomide 2 mg
Imnovid 3 mg: Each hard capsule contains pomalidomide 3 mg
Imnovid 4 mg: Each hard capsule contains pomalidomide 4 mg

Inactive ingredients and allergens: See chapter 6 '*Additional information*'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

Imnovid is expected to cause severe harm to an unborn baby and may lead to death. Do not take this medicine if you are pregnant or anticipate becoming pregnant. You must follow the contraception advice described in this leaflet.

1. What is this medicine intended for?

Imnovid is used to treat adults with a type of cancer called 'multiple myeloma'.

Imnovid is used with:

- two other medicines - one called "bortezomib" (a type of chemotherapy medicine) and "dexamethasone" (an anti-inflammatory medicine) in adults who have had at least one other treatment - including lenalidomide.
  Or
- one other medicine called "dexamethasone" (in adults whose multiple myeloma has recurred or become worse, despite having received at least two other treatments, including lenalidomide and bortezomib) and presented progression of the disease during the last treatment.

Therapeutic group: The medicine belongs to a group of medicines which suppress the immune system.

What is multiple myeloma
Multiple myeloma is a type of cancer which affects a certain type of white blood cell (called 'plasma cells'). These cells grow out of control and accumulate in the bone marrow. This can result in damage to the bones and kidneys.

Multiple myeloma generally cannot be cured. However, if treatment is administered, it is possible to significantly reduce the signs and symptoms of the disease, and even make them disappear entirely for a period of time. When this happens, it is called 'response'.

How Imnovid works

Imnovid works in a number of different ways:

- by stopping the myeloma cells developing.
- by stimulating the immune system to attack the cancer cells.
- by stopping the formation of blood vessels in the malignant tumour.

The benefit of using Imnovid with bortezomib and dexamethasone

When Imnovid is used with bortezomib and dexamethasone, in people who have had at least one other treatment, it can stop multiple myeloma getting worse:

- On average, Imnovid when used with bortezomib and dexamethasone stops multiple myeloma from coming back for up to 11 months - compared with 7 months for patients who only used bortezomib or dexamethasone.

The benefit of using Imnovid with dexamethasone

When Imnovid is used with dexamethasone, in people who have had at least two other treatments, it can stop multiple myeloma getting worse:

- On average, Imnovid when used with dexamethasone stopped multiple myeloma from coming back for up to 4 months on average - compared with 2 months for patients who used only dexamethasone.

2. Before using this medicine

Do not use this medicine if:

Women:

- Do not use this medicine **if you are pregnant or are planning to become pregnant**. Imnovid may be dangerous for the foetus and, therefore, if you are of childbearing age - do not use the medicine without taking all the appropriate measures to prevent pregnancy (please see '**Pregnancy, contraception and breastfeeding - information for women and men**').
- After completing use of the medicine, wait at least 4 more weeks before trying to become pregnant.

Men:

- Do not use this medicine if **you cannot or are unwilling to use condoms each time you have sexual intercourse with a woman of childbearing age** (please see, '**Pregnancy, contraception and breastfeeding - information for women and men**').
- Do not donate sperm while taking this medicine, during dose interruptions of the medicine and for at least 4 weeks after discontinuation of this medicine.

All patients:

- Do not take this medicine if you are sensitive (allergic) to the active ingredient – pomalidomide or to any of the other ingredients in this medicine (see section 6: '**Additional information**').

Special warnings about using this medicine
Before treatment with Imnovid, tell your doctor if:

- you have ever had blood clots - during the treatment with Imnovid you have an increased risk of getting blood clots in your veins and arteries. Your doctor may recommend you take additional medicines (such as warfarin = Coumadin) or lower the dose of Imnovid to reduce the risk of blood clots.
- you have ever had an allergic reaction after taking a similar type of medicine called: 'thalidomide' or 'lenalidomide' - such as rash, itching, swelling, dizziness or trouble breathing.
- you have heart failure, had a heart attack, have difficulty breathing, or smoke, have high blood pressure or high cholesterol levels.
- you have a large number of tumours throughout your body, including your bone marrow. This could lead to a condition where the tumours break down and as a result the quantity of the substances in the blood rises abnormally, which can lead to kidney failure. You may also experience an irregular heartbeat. This condition is called Tumour Lysis Syndrome.
- you have or have had a disease of the peripheral nervous system (neuropathy), which is expressed, for example, in tingling or pain in your hands or feet.
- you have or have had hepatitis B. Treatment with Imnovid may cause the hepatitis B virus to become active again in patients who are considered carriers, resulting in a recurrence of the infection. Your doctor should check whether you have ever had hepatitis B.
- you experience or have experienced in the past one or more of the following symptoms: rash on the face or extended rash, red skin, high fever, flu-like symptoms, enlarged lymph nodes (signs of severe skin reaction called Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) or drug hypersensitivity syndrome, Toxic Epidermal Necrolysis (TEN) or Stevens-Johnson Syndrome (SJS), see below in section 4: "Side effects").

It is important to note that patients with multiple myeloma who receive treatment with pomalidomide may develop additional types of cancer, therefore your doctor should carefully evaluate the benefit and risk when you are prescribed this medicine.

At any time during or after the treatment, tell your doctor immediately if you: experience blurred, double vision or loss of vision, difficulty speaking, weakness in an arm or a leg, a change in the way you walk and problems with your balance, persistent numbness, decreased sensation or loss of sensation, memory loss or confusion.
These symptoms may indicate a condition known as progressive multifocal leukoencephalopathy (PML). If you had these symptoms prior to beginning the medication therapy, tell your doctor.

Children and adolescents
Imnovid is not intended to treat children and young people under 18 years.

Tests and follow-up
Before and during the treatment with Imnovid, you will have regular blood tests. This is necessary because the medicine you are taking may cause a fall

in the number of blood cells that help fight infection (white blood cells) and in the number of cells that help to stop bleeding (platelets).

Your doctor will ask you to have a blood test:

- before treatment.
- every week for the first 8 weeks of treatment.
- at least once a month after that for as long as you are taking Imnovid.

According to the results of the tests, your doctor may change the dose of Imnovid you are taking or instruct you to stop the treatment. The doctor may change the dose or instruct you to stop taking the medicine because of your general health as well.

Drug interactions:

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. This is because Imnovid can affect the way other medicines work. Also, other medicines can affect the way Imnovid works. In particular, inform your doctor or pharmacist if you are taking:

- any antifungals such as ketoconazole.
- Any antibiotics, for example: ciprofloxacin, enoxacin.
- any antidepressants such as fluvoxamine.

At the end of the treatment, you should return all unused capsules to the pharmacist.

Using this medicine and food

- The capsule can be taken with or without food.

Pregnancy, contraception and breastfeeding - information for women and men

Follow the instructions below, as set out under risk management plan/pregnancy prevention programme (RMP/PPP) when taking Imnovid. Men and women taking Imnovid must avoid becoming pregnant or impregnating someone, because pomalidomide is expected to be harmful to the foetus. You and your partner should use effective means of contraception while taking this medicine.

Women

Do not take Imnovid if you are pregnant, think you may be pregnant or are planning to become pregnant, because this medicine is expected to be harmful to a foetus. Before starting the treatment, you should tell your doctor if you are able to become pregnant, even if you think this is unlikely.

If you are able to become pregnant:

- you must use effective methods of contraception for at least 4 weeks before starting the treatment, for the duration of the treatment (including dose interruptions), and until at least 4 weeks after stopping treatment. Talk to your doctor about the best method of contraception for you.
- each time your doctor writes a prescription for you, they will ensure you understand what you need to do to prevent pregnancy.

- your doctor will arrange performance of pregnancy tests before treatment begins, every 4 weeks during treatment (including dose interruptions), and 4 weeks after the treatment has finished.

If you become pregnant despite the prevention measures you took:
- you must stop the treatment immediately and talk to your doctor urgently.

Breastfeeding:
It is not known if Imnovid passes into breast milk. Tell your doctor if you are breastfeeding or planning to breastfeed. A decision must be made on whether you should stop breastfeeding or stop treatment.

Men
Imnovid passes into human semen.
- If your partner is pregnant or able to become pregnant, you must use condoms for the whole time you are taking treatment, during dose interruptions and for at least 4 weeks after the end of treatment.
- If your partner becomes pregnant while you are taking Imnovid or in the 4 weeks after the end of treatment, tell your doctor straight away. Your partner should also tell her doctor straight away.
- Do not donate sperm during treatment (including during dose interruptions) and for at least 4 weeks after the end of treatment.

Blood donation and blood tests
You may not donate blood during treatment (including dose interruptions) and for 4 weeks after the end of treatment.

Driving and using machines
Imnovid may cause fatigue, dizziness, reduced level of consciousness or fainting.
If you have these symptoms, do not drive or operate tools or machinery.

Imnovid contains sodium
This medicine contains less than 1 millimole sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to use this medicine?

Only a doctor with experience in treating multiple myeloma can instruct you to take Imnovid. Imnovid is taken with another medicine called dexamethasone or in combination with dexamethasone and bortezomib. See the leaflet that comes with dexamethasone and bortezomib for further information on its use and effects.

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
Your doctor will determine your dose and how you should take the medicine.

When to take Imnovid with other medicines

Imnovid with bortezomib and dexamethasone

- See the leaflets that come with bortezomib and dexamethasone for further information on their use and effects.
- Imnovid, bortezomib and dexamethasone are taken in 'treatment cycles'. Each treatment cycle lasts 21 days (3 weeks).
- Look at the table below to see what to take on each day of the 3-week cycle:
  - Each day, look at the chart and find the correct day to see which medicines to take.
  - Some days, you take all 3 medicines, some days just 2 or 1 medicines, and some days none at all.

IMN: Imnovid, **BOR:** Bortizomib, **DEX:** Dexamethasone

Treatment cycle 1 to 8

	Medicine name		
Day	**IMN**	**BOR**	**DEX**
1	√	√	√
2	√		√
3	√		
4	√	√	√
5	√		√
6	√		
7	√		
8	√	√	√
9	√		√
10	√		
11	√	√	√
12	√		√
13	√		
14	√		
15			
16			
17			
18			
19			
20			
21			

Treatment cycle 9 and onwards

	Medicine name		
Day	**IMN**	**BOR**	**DEX**
1	√	√	√
2	√		√
3	√		
4	√		
5	√		
6	√		
7	√		
8	√	√	√
9	√		√
10	√		
11	√		
12	√		
13	√		
14	√		
15			
16			
17			
18			
19			
20			
21			

- After completing each 3-week cycle, start a new one.

Imnovid with dexamethasone only

- See the leaflet that comes with dexamethasone for further information on its use and effects.
- Imnovid and dexamethasone are taken in 'treatment cycles'. Each treatment cycle lasts 28 days (4 weeks).
- Look at the table below to see what to take on each day of the 4-week cycle:
  - Each day, look at the chart and find the correct day to see which medicines to take.
  - Some days, you take both medicines, some days just one medicine, and some days none at all.

IMN: Imnovid, **DEX:** Dexamethasone

	Medicine name	
Day	**IMN**	**DEX**
1	√	√
2	√	
3	√	
4	√	
5	√	
6	√	
7	√	
8	√	√
9	√	
10	√	
11	√	
12	√	
13	√	
14	√	
15	√	√
16	√	
17	√	
18	√	
19	√	
20	√	
21	√	
22		√
23		
24		
25		
26		

27		
28		

- After completing each 4-week cycle, start a new one.

How much Imnovid to take with other medicines

Imnovid with bortezomib and dexamethasone

- The recommended starting dose of Imnovid is 4 mg per day.
- The recommended starting dose of bortezomib will be calculated by your doctor and based on your height and weight (1.3 mg/m^2 body surface area).
- The recommended starting dose of dexamethasone is 20 mg per day. However, if you are over the age of 75, the recommended starting dose is 10 mg per day.

Imnovid with dexamethasone only

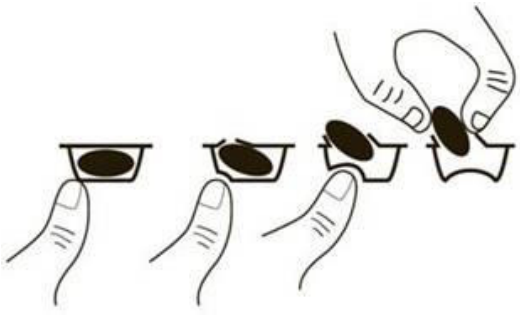
- The recommended starting dose of Imnovid is 4 mg per day.
- The recommended starting dose of dexamethasone is 40 mg per day. However, if you are over the age of 75, the recommended starting dose is 20 mg per day.

Your doctor may reduce the dose of Imnovid, bortezomib or dexamethasone or stop one or more of these medicines based on the results of your blood tests, your general condition, other medicines you may be taking (e.g. ciprofloxacin, enoxacin and fluvoxamine) and side effects (especially rash or swelling) from treatment, if any appear. If you suffer from liver or kidney problems, your doctor will check your condition very carefully during treatment with this medicine.

How to take Imnovid

- Do not break, open or chew the capsules. If powder from a broken capsule makes contact with the skin, wash the skin immediately and thoroughly with soap and water.
- Healthcare professionals, caregivers and family members should wear disposable gloves when handling the blister or capsule. Gloves should then be removed carefully to prevent skin exposure, placed in a sealable plastic bag and disposed of in accordance with the instructions. Hands should then be washed thoroughly with soap and water. Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule.
- Swallow the capsule whole - preferably with water.
- The capsule can be taken with or without food.
- Take your capsules at about the same time each day.

To remove the capsule from the blister, press only one end of the capsule out to push it through the foil. Do not apply pressure on the centre of the capsule as this can cause it to break.



Your doctor will instruct you on how and when to take Imnovid if you have kidney problems and are receiving dialysis treatment.

Duration of the treatment with Imnovid
You should continue the cycles of treatment until your doctor instructs you to stop.

Do not exceed the recommended dose.

If you have accidentally taken a higher dose
If you have taken an overdose or if a child has accidentally swallowed some medicine, refer immediately to a doctor or go to a hospital emergency room and bring the medicine package with you. Do not induce vomiting unless explicitly instructed to do so by a doctor.

If you forget to take Imnovid
If you forget to take Imnovid at the scheduled time, do not take a double dose. Take the next dose at the regular time the next day.

Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.
Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

If you stop taking this medicine
Do not stop using this medicine without consulting your doctor.

4. <u>Side effects</u>

Like with all medicines, using Imnovid may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Stop taking Imnovid and contact a doctor straight away if you notice any of the following serious side effects – you may need urgent medical treatment:
- Fever, chills, sore throat, cough, mouth ulcers or any other signs of infection (due to a drop in the number of white blood cells, which fight infection).
- Bleeding or bruising without a cause, including nosebleeds and bleeding from the bowels or stomach (due to effects on blood cells called ‘platelets’).
- Rapid breathing, rapid pulse, fever and chills, passing very little to no urine, nausea and vomiting, confusion, unconsciousness (due to infection of blood called sepsis or septic shock).
- Severe, persistent or bloody diarrhoea (possibly with stomach pain or fever) caused by bacteria called Clostridium difficile.
- Chest pain, leg pain and swelling, especially in your lower leg or calf (caused by blood clots).

- Shortness of breath (due to serious chest infection, inflammation of the lung, heart failure or blood clot).
- Swelling of face, lips, tongue and throat, which may cause difficulty breathing (due to serious types of allergic reaction called angioedema and anaphylactic reaction).
- Certain types of skin cancer (squamous cell carcinoma and basal cell carcinoma), which can cause changes in the appearance of your skin or growths on your skin. If you notice any changes to your skin whilst being treated with Imnovid, tell your doctor as soon as possible.
- Recurrence of hepatitis B infection, which can cause yellowing of the skin and eyes, dark brown-coloured urine, right-sided abdominal pain, fever and feeling nauseous or being sick. Tell your doctor straightaway if you notice one of these symptoms.
- Widespread rash, high body temperature, enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome, Toxic Epidermal Necrolysis or Stevens-Johnson Syndrome). Stop using Imnovid if you develop these symptoms and contact your doctor or seek medical attention immediately.

Stop taking Imnovid and see a doctor straight away if you notice any of the serious side effects listed above – you may need urgent medical treatment.

Other side effects

Very common (may appear in more than 1 in 10 patients):
- Shortness of breath (dyspnoea).
- Infections of the lungs (pneumonia and bronchitis).
- Infections of the nose, sinuses and throat, caused by bacteria or viruses.
- Flu-like symptoms (influenza).
- Low red blood cells, which may cause anaemia leading to tiredness and weakness.
- Low blood levels of potassium (hypokalaemia), which may cause weakness, muscle cramps, muscle aches, palpitations, tingling or numbness, dyspnoea, mood changes.
- High blood levels of sugar.
- A fast and irregular heartbeat (atrial fibrillation).
- Loss of appetite.
- Constipation, diarrhoea or nausea.
- Being sick (vomiting)
- Abdominal pain
- Lack of energy.
- Difficulty in falling asleep or staying asleep.
- Dizziness, tremor.
- Muscle spasm, muscle weakness.
- Bone pain, back pain.
- Numbness, tingling or burning sensation to the skin, pain in hands or feet (peripheral sensory neuropathy).
- Swelling of the body, including swelling of the arms or legs.
- Rashes

- Urinary tract infection, which may cause a burning sensation when passing urine, or a need to pass urine more often.

Common (may appear in up to 1 in 10 patients):

- Fall.
- Bleeding within the skull.
- Decreased ability to move or feel (sensation) in your hands, arms, feet and legs because of nerve damage (peripheral sensorimotor neuropathy).
- Numbness, itching, and a feeling of pins and needles on your skin (paraesthesia).
- A spinning feeling in your head, making it difficult to stand up and move normally.
- Swelling caused by fluid.
- Hives (urticaria).
- Itchy skin.
- Shingles.
- Heart attack (chest pain spreading to the arms, neck, jaw, feeling sweaty and breathless, feeling sick or vomiting).
- Chest pain, chest infection.
- Increased blood pressure.
- A fall in the number of red and white blood cells and platelets at the same time (pancytopenia), which will make you more prone to bleeding and bruising. You may feel tired and weak, and short of breath and you are also more likely to get infections.
- Decreased number of lymphocytes (one type of white blood cells) often caused by infection (lymphopenia).
- Low blood levels of magnesium (hypomagnesaemia), which may cause tiredness, generalised weakness, muscle cramps, irritability and may result in low blood levels of calcium (hypocalcaemia), which may cause numbness and/or tingling of hands, feet, or lips, muscle cramps, muscle weakness, light-headedness, confusion.
- High blood levels of calcium (hypercalcaemia), which may cause slowing reflexes and skeletal muscle weakness.
- High blood levels of potassium, which may cause abnormal heart rhythm.
- Low blood levels of sodium, which may cause tiredness and confusion, muscle twitching, fits (epileptic seizures) or coma.
- High blood levels of uric acid, which may cause a form of arthritis called gout.
- Low blood pressure, which may cause dizziness or fainting.
- Sore or dry mouth.
- Low blood levels of phosphate (hypophosphataemia), which may cause muscle weakness and irritability or confusion.
- Changes in the way things taste.
- Swollen abdomen.
- Feeling confused.
- Feeling down (depressed mood).
- Loss of consciousness, fainting.
- Clouding of the eye (cataract).
- Damage to the kidney.
- Inability to pass urine.
- Abnormal liver test
- Pain in the pelvis.

- Weight loss.

Uncommon (may appear in up to 1 in 100 patients):
- Stroke.
- Inflammation of the liver (hepatitis) which can cause itchy skin, yellowing of the skin and the whites of the eyes (jaundice), pale coloured stools, dark coloured urine and abdominal pain.
- The breakdown of cancer cells resulting in the release of toxic compounds into the bloodstream (Tumour Lysis Syndrome). This can result in kidney problems.
- Underactive thyroid gland, which may cause symptoms such as tiredness, lethargy, muscle weakness, slow heart rate, weight gain.

Unknown frequency (the frequency of these effects has not been established yet):
- Rejection of solid organ transplant (such as heart or liver).

If you experience any side effect, if any side effect gets worse, or if you experience 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 following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:
https://sideeffects.health.gov.il
And by e-mail to the registration holder's Patient Safety Unit:
drugsafety@neopharmgroup.com

5. How to store the medicine?

- Prevent poisoning! Keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants and by doing so prevent poisoning.
- Do not use this medicine after the expiry date that appears on the blister and the package after EXP. The expiry date refers to the last day of that month.

Storage conditions
- Store the medicine at a temperature below 25˚C. Store in the original package to protect from light.
- Do not use Imnovid if you notice any damage.
- Do not throw the medicine in the toilet or in the household trashcan. Any unused medicinal product should be returned to the pharmacy at the end of treatment. This helps protect the environment.

6. Additional information

In addition to the active ingredients, this medicine also contains:
pregelatinised starch, mannitol, sodium stearyl fumarate.

White ink -
shellac, titanium dioxide (E171), Isopropyl Alcohol, ammonium hydroxide (E527), propylene glycol (E1520), N-butyl Alcohol and simethicone.
Black ink -
shellac, iron oxide black (E172), N-butyl Alcohol, Purified Water, propylene glycol (E1520), Dehydrated Ethanol, Isopropyl Alcohol and ammonium hydroxide (E527).

A hard capsule of Imnovid 1 mg also contains:

- The capsule shell contains:
white and black ink-
gelatin, titanium dioxide (E171), indigotine (E132) and yellow iron oxide (E172)

A hard capsule of Imnovid 2 mg also contains:

- The capsule shell contains:
White ink -
gelatin, titanium dioxide (E171), indigotine (E132), erythrosin (E127), yellow iron oxide (E172)

A hard capsule of Imnovid 3 mg also contains:

- The capsule shell contains:
White ink -
gelatin, titanium dioxide (E171), indigotine (E132) and yellow iron oxide (E172)

A hard capsule of Imnovid 4 mg also contains:

- The capsule shell contains:
White ink -
gelatin, titanium dioxide (E171), indigotine (E132), brilliant blue FCF (E133)

What the medicine looks like and contents of the pack
Imnovid 1 mg hard capsules: Dark blue opaque cap and yellow opaque body, with “POML 1 mg” written on them.
Imnovid 2 mg hard capsules: Dark blue opaque cap and orange opaque body, with “POML 2 mg” written on them.
Imnovid 3 mg hard capsules: Dark blue opaque cap and green opaque body, with “POML 3 mg” written on them.
Imnovid 4 mg hard capsules: Dark blue opaque cap and blue opaque body, with “POML 4 mg” written on them.

Each carton contains 21 hard capsules.

Registration holder: Neopharm Scientific Ltd., P.O. Box 7063, Petach Tikva 4917001.

Manufacturer: Celgene International Sarl, Boudry, Switzerland

Revised in February 2024.

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

Imnovid 1 mg: 152-02-33954

Imnovid 2 mg: 152-03-33955

Imnovid 3 mg: 152-04-33956
Imnovid 4 mg: 152-05-33957

Imnovid cap PIL vr 01A