Package Leaflet: Information for the patient

Ultiva for Injection 1 mg
Ultiva for Injection 2 mg
Ultiva for Injection 5 mg

remifentanil hydrochloride

Read all of this leaflet carefully before you are given 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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1 What Ultiva is and what it is used for

Ultiva contains a medicine called remifentanil. This belongs to a group of medicines known as opioids.

Ultiva is used together with other medicines called anaesthetics

- to help put you to sleep **before** an operation
- to keep you asleep and stop you feeling pain **during** an operation
- to make you feel sleepy and stop you feeling pain while you receive treatment in an Intensive Care Unit.

2 What you need to know before you are given Ultiva

Do not have Ultiva if:

- you are allergic (hypersensitive) to remifentanil or any of the other ingredients of Ultiva (listed in section 6)
- you are allergic (hypersensitive) to any other pain-relieving medicines which are similar to fentanyl and which are related to the class of medicines known as opioids.

If you are not sure if any of the above apply to you, talk to your doctor, pharmacist or nurse before you are given Ultiva.

Warnings and precautions

Check with your doctor or pharmacist before you are given Ultiva if:

- you are allergic (hypersensitive) to any other opioid medicines, such as morphine or codeine
- you are over 65 years of age
- you are dehydrated or have lost a lot of blood
- you have been feeling weak or unwell
- if you are overweight

If you are not sure if any of the above apply to you, talk to your doctor, pharmacist or nurse before you are given Ultiva.

Other medicines and Ultiva
Please tell your doctor or pharmacist if you are taking or have recently taken or might take other medicines, including medicines obtained without a prescription. This includes herbal medicines. This is because Ultiva can work with other medicines to cause side effects.
In particular tell your doctor or pharmacist if you are taking:

- medicines for your heart or blood pressure, such as beta-blockers (these include atenolol, metoprolol, carvedilol, propanolol and bisoprolol) or calcium channel blockers (these include amlodipine, diltiazem and nifedipine).

Concomitant use of Ultiva and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible.

However if your doctor does prescribe Ultiva together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.

Please tell your doctor about all sedative medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine.

Driving and using machines
If you are only staying in hospital for the day, your doctor will tell you how long to wait before leaving the hospital or driving a car. It can be dangerous to drive too soon after having an operation.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.

- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
    - The medicine has been prescribed to treat a medical or dental problem and
    - You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
    - It was not affecting your ability to drive safely

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

3 How Ultiva is given

How your injection is given
You will never be expected to give yourself this medicine. It will always be given to you by a person who is qualified to do so.

Ultiva can be given:

- as a single injection into your vein
- as a continuous infusion into your vein. This is where the drug is slowly given to you over a longer period of time.

The way you are given the drug and the dose you receive will depend on:
- your weight
- the operation you have
- how much pain you will be in
- how sleepy the medical staff want you to be in the Intensive Care Unit.

The dose varies from one patient to another.

If you are given too much
The effects of Ultiva are carefully monitored throughout your operation and in intensive care, and appropriate action will be taken promptly if you receive too much.

After your operation
Tell your doctor or nurse if you are in pain. If you are in pain after your procedure, they will be able to give you other painkillers.

4 Possible side effects

Like all medicines, Ultiva can cause side effects, although not everybody gets them. The following side effects may happen with this medicine.

Some people can be allergic to Ultiva. **You must tell your doctor or nurse immediately if you have**:
Rare (may affect up to 1 in 1,000 people)
- sudden wheeziness and chest pain or chest tightness
- swelling of your eyelids, face, lips, mouth or tongue
- a lumpy skin rash or 'hives' anywhere on the body
- collapse.

Tell your doctor **as soon as possible** if you notice any of the following:
Very common (may affect more than 1 in 10 people)
- muscle stiffness
- low blood pressure
- feeling sick or being sick

Common (may affect up to 1 in 10 people)
- slow heartbeat
- shallow breathing or temporarily stop breathing
- itching

Uncommon (may affect up to 1 in 100 people)
- problems breathing (hypoxia)
- constipation

Rare (may affect up to 1 in 1,000 people)
- allergic reactions
- heart stops beating

Not known (frequency cannot be estimated from the available data)
- physical need for Ultiva *(drug dependency)* or the need for increasing doses over time to get the same effect *(drug tolerance)*

- fits (seizures)
- a type of irregular heartbeat *(atrioventricular block)*

Other side effects that can happen when you wake up after having an anaesthetic include:
Common (may affect up to 1 in 10 people)
- shivering
- increases in blood pressure

Uncommon (may affect up to 1 in 100 people)
- aches

Rare (may affect up to 1 in 1,000 people)
- feeling very calm or drowsy (sedation)

Other side effects which occurred particularly upon abrupt cessation of Ultiva after prolonged administration of more than 3 days
- heart beating faster *(tachycardia)*
- high blood pressure *(hypertension)*
- restlessness *(agitation)*

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Ultiva

- Keep this medicine out of the sight and reach of children.
- Do not use Ultiva after the expiry date which is stated on the vial and carton after "EXP". The expiry date refers to the last day of that month.
- Do not store above 25°C.
- When Ultiva is made up it should be used straight away. Any unused solution should not be disposed of via wastewater or household waste. Your doctor or nurse will throw away any medicine that is no longer required. This will help protect the environment.
- Store in the original package with this leaflet.

6 Contents of the pack and other information

What Ultiva contains
The active substance is remifentanil hydrochloride.
The other ingredients are glycine and hydrochloric acid (for pH adjustment).

What Ultiva looks like and contents of the pack
Ultiva for injection is a sterile, non-pyrogenic, preservative-free, white to off-white, lyophilised powder and is available in the following strengths:
- 1 mg Ultiva for injection, in 3 ml glass vials
- 2 mg Ultiva for injection, in 5 ml glass vials
- 5 mg Ultiva for injection, in 10 ml glass vials

The powder will be mixed with an appropriate fluid before being injected. When mixed to form a solution, Ultiva is clear and colourless.
Each strength of Ultiva is supplied in cartons containing 5 vials.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Aspen Pharma Trading Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland
Tel: + 44 1748 828 391
Manufacturer:
GlaxoSmithKline Manufacturing S.p.A., San Polo di Torrile, Parma, Italy
or
Aspen Pharma Ireland Limited, One George's Quay Plaza, Dublin 2, Ireland

Other formats:
To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK Only)

Please be ready to give the following information:

Product name	**Ultiva for injection 1 mg** **Ultiva for injection 2 mg** **Ultiva for injection 5 mg**
Reference number	PL 39699/0095 PL 39699/0096 PL 39699/0097

This is a service provided by the Royal National Institute of Blind People.

This leaflet was last revised in February 2021.

Package Leaflet: Information for the Medical Profession

Ultiva for injection
remifentanil hydrochloride

Refer to the Summary of Product Characteristics for the complete prescribing information.

The information provided in this section are the instructions for the preparation of Ultiva prior to administration and the guidelines for infusion rates of Ultiva for manually-controlled infusion.

PREPARATION GUIDE for
Ultiva (remifentanil hydrochloride) for injection 1 mg
Ultiva (remifentanil hydrochloride) for injection 2 mg
Ultiva (remifentanil hydrochloride) for injection 5 mg

Ultiva is a sterile, non-pyrogenic, preservative-free, white to off white, lyophilised powder, to be reconstituted before use. Ultiva for injection is available in glass vials containing 1 mg, 2 mg or 5 mg of remifentanil base. The vials should be stored at or below 25°C.

When reconstituted as directed, solutions of Ultiva are clear and colourless and contain 1 mg/ml of remifentanil base as remifentanil hydrochloride. Ultiva should not be administered without further dilution after reconstitution of the lyophilised powder.

It is important that you read this guide prior to the preparation of Ultiva. This information can also be found under sections 6.4 and 6.6 of the Summary of Product Characteristics.

Reconstitution of the lyophilised powder
Ultiva should be prepared for intravenous use by adding, as appropriate 1, 2, or 5 ml of diluent (see list of diluents under "Further Dilution") to give a reconstituted solution with a concentration of 1 mg/ml remifentanil. The reconstituted solution is clear, colourless, and practically free from particulate material. After reconstitution, visually inspect the product for particulate material, discolouration or damage of container. Discard any solution where such defects are observed. Reconstituted product is for single use only. Any unused material should be discarded.

Further Dilution
After reconstitution, Ultiva should not be administered by manually-controlled infusion without further dilution to concentrations of 20 to 250 micrograms/ml (50 micrograms/ml is the recommended dilution for adults and 20 to 25 micrograms/ml for paediatric patients aged 1 year and over when used in maintenance of anaesthesia). Use of Ultiva in paediatric patients aged under 18 is not recommended for provision of analgesia in mechanically ventilated intensive care patients.

After reconstitution, Ultiva should not be administered by Target Controlled Infusion (TCI) without further dilution (20 to 50 micrograms/ml is the recommended dilution for TCI).

The dilution is dependent upon the technical capability of the infusion device and the anticipated requirements of the patient.

One of the following IV fluids listed below should be used for dilution:

- Water for Injections
- Glucose 5% solution for injection
- Glucose 5% and Sodium Chloride 0.9% solution for injection
- Sodium Chloride 0.9% solution for injection
- Sodium Chloride 0.45% solution for injection

After dilution, visually inspect the product to ensure it is clear, colourless, practically free from particulate matter and the container is undamaged. Discard any solution where such defects are observed.

The reconstituted and further diluted solution of Ultiva is chemically and physically stable for 24 hours at room temperature (25°C). However, Ultiva does not contain an antimicrobial preservative and thus care must be taken to assure the sterility of prepared solutions, reconstituted product should be used promptly, and any unused material discarded.

Ultiva has been shown to be compatible with the following intravenous fluids *when administered into a running IV catheter*:
Lactated Ringer's solution for injection
Lactated Ringer's and Glucose 5% solution for injection

Ultiva has been shown to be compatible with propofol *when administered into a running IV catheter*.

GUIDELINES FOR INFUSION RATES
The tables below give guidelines for infusion rates of Ultiva for manually-controlled infusion:

Table 1. Ultiva for injection Infusion Rates (ml/kg/h)

Drug Delivery Rate (micrograms/kg/min)	Infusion Delivery Rate (ml/kg/h) for Solution Concentrations of			
	20 micrograms/ml 1 mg/50 ml	25 micrograms/ml 1 mg/40 ml	50 micrograms/ml 1 mg/20 ml	250 micrograms/ml 10 mg/40 ml
0.0125	0.038	0.03	0.015	Not recommended
0.025	0.075	0.06	0.03	Not recommended
0.05	0.15	0.12	0.06	0.012
0.075	0.23	0.18	0.09	0.018
0.1	0.3	0.24	0.12	0.024
0.15	0.45	0.36	0.18	0.036
0.2	0.6	0.48	0.24	0.048
0.25	0.75	0.6	0.3	0.06
0.5	1.5	1.2	0.6	0.12
0.75	2.25	1.8	0.9	0.18
1.0	3.0	2.4	1.2	0.24
1.25	3.75	3.0	1.5	0.3
1.5	4.5	3.6	1.8	0.36
1.75	5.25	4.2	2.1	0.42
2.0	6.0	4.8	2.4	0.48

Table 2. Ultiva for injection Infusion Rates (ml/h) for a 20 micrograms/ml Solution

Infusion Rate (micrograms/kg/min)	Patient Weight (kg)						
	5	10	20	30	40	50	60
0.0125	0.188	0.375	0.75	1.125	1.5	1.875	2.25
0.025	0.375	0.75	1.5	2.25	3.0	3.75	4.5
0.05	0.75	1.5	3.0	4.5	6.0	7.5	9.0
0.075	1.125	2.25	4.5	6.75	9.0	11.25	13.5
0.1	1.5	3.0	6.0	9.0	12.0	15.0	18.0
0.15	2.25	4.5	9.0	13.5	18.0	22.5	27.0
0.2	3.0	6.0	12.0	18.0	24.0	30.0	36.0
0.25	3.75	7.5	15.0	22.5	30.0	37.5	45.0
0.3	4.5	9.0	18.0	27.0	36.0	45.0	54.0
0.35	5.25	10.5	21.0	31.5	42.0	52.5	63.0
0.4	6.0	12.0	24.0	36.0	48.0	60.0	72.0

Table 3. Ultiva for injection Infusion Rates (ml/h) for a 25 micrograms/ml Solution

Infusion Rate (micrograms/kg/min)	Patient Weight (kg)									
	10	20	30	40	50	60	70	80	90	100

0.0125	0.3	0.6	0.9	1.2	1.5	1.8	2.1	2.4	2.7	3.0
0.025	0.6	1.2	1.8	2.4	3.0	3.6	4.2	4.8	5.4	6.0
0.05	1.2	2.4	3.6	4.8	6.0	7.2	8.4	9.6	10.8	12.0
0.075	1.8	3.6	5.4	7.2	9.0	10.8	12.6	14.4	16.2	18.0
0.1	2.4	4.8	7.2	9.6	12.0	14.4	16.8	19.2	21.6	24.0
0.15	3.6	7.2	10.8	14.4	18.0	21.6	25.2	28.8	32.4	36.0
0.2	4.8	9.6	14.4	19.2	24.0	28.8	33.6	38.4	43.2	48.0

Table 4. Ultiva for injection Infusion Rates (ml/h) for a 50 micrograms/ml Solution

Infusion Rate (micrograms/kg/min)	**Patient Weight (kg)**							
	30	**40**	**50**	**60**	**70**	**80**	**90**	**100**
0.025	0.9	1.2	1.5	1.8	2.1	2.4	2.7	3.0
0.05	1.8	2.4	3.0	3.6	4.2	4.8	5.4	6.0
0.075	2.7	3.6	4.5	5.4	6.3	7.2	8.1	9.0
0.1	3.6	4.8	6.0	7.2	8.4	9.6	10.8	12.0
0.15	5.4	7.2	9.0	10.8	12.6	14.4	16.2	18.0
0.2	7.2	9.6	12.0	14.4	16.8	19.2	21.6	24.0
0.25	9.0	12.0	15.0	18.0	21.0	24.0	27.0	30.0
0.5	18.0	24.0	30.0	36.0	42.0	48.0	54.0	60.0
0.75	27.0	36.0	45.0	54.0	63.0	72.0	81.0	90.0
1.0	36.0	48.0	60.0	72.0	84.0	96.0	108.0	120.0
1.25	45.0	60.0	75.0	90.0	105.0	120.0	135.0	150.0
1.5	54.0	72.0	90.0	108.0	126.0	144.0	162.0	180.0
1.75	63.0	84.0	105.0	126.0	147.0	168.0	189.0	210.0
2.0	72.0	96.0	120.0	144.0	168.0	192.0	216.0	240.0

Table 5. Ultiva for injection Infusion Rates (ml/h) for a 250 micrograms/ml Solution

Infusion Rate (micrograms/kg/min)	**Patient Weight (kg)**							
	30	**40**	**50**	**60**	**70**	**80**	**90**	**100**
0.1	0.72	0.96	1.20	1.44	1.68	1.92	2.16	2.40

0.15	1.08	1.44	1.80	2.16	2.52	2.88	3.24	3.60
0.2	1.44	1.92	2.40	2.88	3.36	3.84	4.32	4.80
0.25	1.80	2.40	3.00	3.60	4.20	4.80	5.40	6.00
0.5	3.60	4.80	6.00	7.20	8.40	9.60	10.80	12.00
0.75	5.40	7.20	9.00	10.80	12.60	14.40	16.20	18.00
1.0	7.20	9.60	12.00	14.40	16.80	19.20	21.60	24.00
1.25	9.00	12.00	15.00	18.00	21.00	24.00	27.00	30.00
1.5	10.80	14.40	18.00	21.60	25.20	28.80	32.40	36.00
1.75	12.60	16.80	21.00	25.20	29.40	33.60	37.80	42.00
2.0	14.40	19.20	24.00	28.80	33.60	38.40	43.20	48.00

This leaflet was last revised in February 2021.