

**Information for Patients**

**Folinic acid, fluorouracil  
and oxaliplatin  
(FOLFOX) for biliary  
tract cancers**

# Folinic acid, fluorouracil and oxaliplatin (FOLFOX) for biliary tract cancers

If your doctor recommended the combination of folinic acid, fluorouracil and oxaliplatin (FOLFOX) to treat your cancer, here is some important information about these medications and some aspects related to them.

You have been given this leaflet because you have been diagnosed with a biliary tract cancer. Your oncologist can discuss with you which biliary tract cancer you have and how extended it is.



Generated by Dr V Zanuso and Dr C Braconi (oncologists) based on information developed by Macmillan Cancer Support and used with permission. Revised by Ms J Milne (nurse), Ms H Morement (patient representative). This material is based upon work from the European Network for the Study of Cholangiocarcinoma and the COST Action CA22125 Precision medicine in biliary tract cancer (Precision-BTC-Network) supported by COST (European Cooperation in Science and Technology: [www.cost.eu](http://www.cost.eu)).



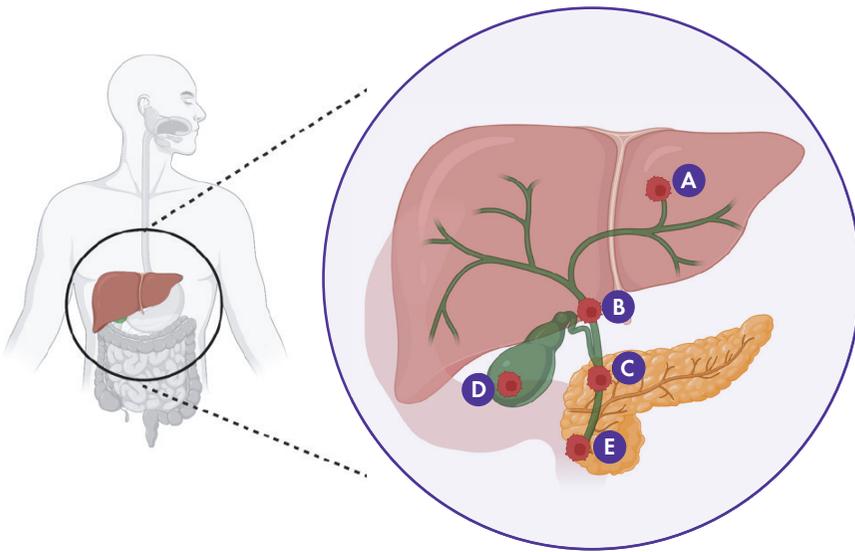
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## Biliary tract cancer

Cancers of the biliary tract develop from cells (called cholangiocytes) that normally make up the lining of the biliary system (depicted in green in the picture below). Biliary ducts are small tubes that carry the bile, which is used to digest food, from the liver and gallbladder into the small bowel.



- A** Intrahepatic cholangiocarcinoma
- B** Perihilar cholangiocarcinoma
- C** Extrahepatic cholangiocarcinoma

- D** Gallbladder cancer
- E** Ampullary cancer

Biliary tract cancers include cholangiocarcinoma, gallbladder cancer and ampullary cancer:

- **Cholangiocarcinoma** – which is also known as bile duct cancer. This cancer is categorised in three types, depending on where within the bile ducts it develops:
  - intrahepatic cholangiocarcinoma – the cancer develops in the ducts inside the liver
  - perihilar cholangiocarcinoma – it develops in the ducts just outside the liver
  - distal/extrahepatic cholangiocarcinoma – it develops in the ducts further away from the liver
- **Gallbladder cancer** – arises from the cells of the gallbladder
- **Ampullary cancer** – arises from the join between the bile ducts and the small bowel

## What is FOLFOX?

FOLFOX is a chemotherapy combination made up of folinic acid, fluorouracil and oxaliplatin. Fluorouracil and oxaliplatin are two chemotherapy drugs which kill tumour cells by interfering with the process of cell replication. However, because chemotherapy can also damage normal cells, it can cause some side effects. Folinic acid, also called leucovorin or calcium folinate, is not a chemotherapeutic drug, but it is given because it enhances fluorouracil activity.

## How is FOLFOX administered?

FOLFOX is injected intravenously (into a vein) through a PICC (*peripherally inserted central catheter*) line. The PICC line is a fine tube that goes into a vein under the skin of your arm and reaches a vein in your chest, and it will remain there during your FOLFOX treatment. The PICC will be removed at the end of your treatment.

To ensure that it works well, your PICC line will need to be flushed once a week. This will normally be done by your nurse. Regular care of your PICC line will keep it from getting clogged or blocked. It is important that you keep your PICC clean and that you check for any signs of infection (swelling, redness or pus) while you are at home.

You will receive FOLFOX in hospital, in the chemotherapy unit, and you will also continue receiving it at home through a small pump. This small pump is connected to the PICC line and allows the fluorouracil infusion to go into the bloodstream for approximately one day (22 hours) while you are at home. After 22 hours you may come back to the hospital to remove the pump. If your nurse has explained how to remove the pump safely, and you feel confident about this, you could do it on your own. Alternatively, a district nurse can come to your house to remove it.

Your doctor will decide the exact dosage of FOLFOX you will receive based on many factors including your height, weight, age, general health and underlying conditions.

## Schedule of FOLFOX treatment

You will receive FOLFOX in cycles of treatment. The standard schedule of FOLFOX treatment follows a two-week cycle, involving one day of chemotherapy every other week.

Before each session of chemotherapy, you will have a blood test and your oncological team will check whether you are fit enough for the chemotherapy session. It is important that you report any symptom(s) and problem(s) since your last session so that the dose/schedule can be adjusted and personalised specifically for you.

The doctor may ask you to have the bloods taken at your GP practice the day before your chemotherapy appointment.

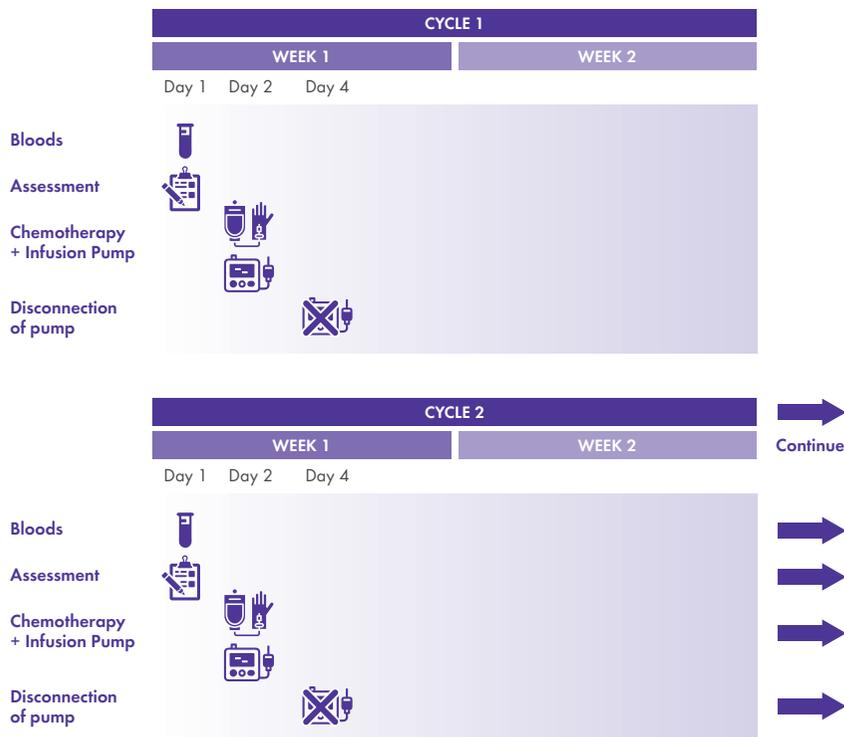
On DAY 1 of the first week of each cycle of chemotherapy, you will come to hospital to see the oncology team to be assessed and have a blood test. You will come back 1 or 2 days later to receive the chemotherapy. On this occasion you will not meet the doctor unless you have developed some issues. The chemotherapy session will last for 2 to 3 hours. At the end of the session the nurse will attach the small pump to your PICC line, which will release the drug continuously for 22 hours. You will go home with this pump. Once the treatment is finished, on DAY 2 you could be asked to come back to hospital to take the pump off. If your nurse has explained how to remove the pump safely, and you feel confident about this, you could do it on your own.

You will not need to stay in hospital overnight.

## Duration of FOLFOX treatment

The doctor will discuss the duration of your treatment with you. Each FOLFOX cycle will last for 2 weeks. If the treatment is well tolerated, it can be repeated for 12 cycles. You will receive at least 3 months of chemotherapy before your doctor will advise a repeat scan to understand if the chemotherapy is working. If the first 3 months scan shows your cancer is stable or shrinking, your doctor may advise continuing the chemotherapy for another 3 months. After the first 6 months of treatment your doctor will discuss with you whether you should take a break from chemotherapy or you should continue.

### FOLFOX cycle: 1 week on, 1 week off



## Side effects of the FOLFOX treatment?

There are known side effects with this treatment, but you may not experience any of them. This does not mean that the treatment is not working; there is no relationship between the presence or severity of side effects and the efficacy of the medication.

You may get some of the side effects, but you are unlikely to get them all. Remember that side effects are often predictable in terms of their onset, duration and severity; they are almost always reversible and, except for those related to oxaliplatin, should completely go away after treatment.

As with many other chemotherapy drugs, fluorouracil and oxaliplatin kill cancer cells because of their ability to stop cell division and proliferation. Unfortunately, chemotherapy drugs are not able to recognise the difference between the cancerous cells and normal cells. So chemotherapy will also kill normal cells that are rapidly dividing, like blood cells, cells in the mouth, stomach, bowel and elsewhere, which is what causes some of the different side effects. Once treatment ends, those normal cells will grow back and be healthy.

There are many medications available that can be taken during chemotherapy to control and minimise the impact of any side effects you may have.

## Some of the most common side effects related to FOLFOX



**Hematotoxicity:** side effects on your blood cells including:

- **Low number of white blood cells and risk of infection:**

Chemotherapy often reduces the number of white blood cells, which help you fight against infections. If your white blood cell count is too low (this is called neutropenia) you may be at risk of infections. At this time, it is important to be careful to avoid situations that could increase this risk of infections, such as being in crowded places or near with people with colds.

As the number of your white cells is most likely to be at its lowest between day 9 and day 14 of each of the cycles of your chemotherapy, during these days it is especially important to avoid risk of infection.

Reduction in white cells is one of the important blood checks your doctor will make before you receive your next dose of chemotherapy to ensure that the number of white blood cells is enough to protect you from infection while you receive chemotherapy.

The number of white cells will usually return to normal before your next treatment. Sometimes it may happen they are too low to allow you receive the scheduled treatment and your doctor will delay your treatment for a short time until the cell count returns to normal.

It is important you are aware of the signs and symptoms of infection, and you must contact the helpline at your institution if you develop any of the following:

- Your body temperature rises above 38 °C (100.4 °F), despite using paracetamol
- You suddenly feel shivery or unwell
- You develop a sore throat, a cough, diarrhoea, increased frequency of urination

- **Low number of red blood cells:** Chemotherapy can reduce the number of red blood cells. The most important role of red blood cells is carrying oxygen to every part of your body. If the number of red blood cells is too low (this is called *anaemia*) you can feel tired and breathless. If your *anaemia* is severe, you will need a blood transfusion.

- **Low number of platelets and risk of bruising or bleeding:** Chemotherapy can reduce the number of platelets. Platelets are useful to help the blood clotting. If your number of platelets is too low (this is called *thrombocytopenia*) you cannot receive chemotherapy and your doctor will delay your treatment for a short time until the platelet count improves.

If you have any bruising or bleeding, such as nosebleeds, bleeding gums, tiny red or purple spots on the skin, please inform your doctor.



- **Numbness or tingling in fingers and toes (peripheral neuropathy):** Oxaliplatin-based chemotherapy can affect nerves by causing numbness, tingling or pain in the hands or feet.

Numbness or tingling in fingers and toes can make it difficult to do fiddly things such as tying your shoelaces or doing up buttons. This might start within a few days or weeks and last for a few months. Rarely, the numbness may be permanent. You can find specific tips below to help to reduce these symptoms, if they occur.



**Diarrhoea:** You need to get in touch with your team if you have 4 or more loose poos (stools) in 24 hours. Your doctor will give you anti-diarrhoea drug. Remember to drink plenty of water to replace fluids lost. You should eat low-fibre food and avoid raw fruits, fruit juice, cereals and vegetables. It can help to also avoid alcohol, caffeine, dairy products and high-fat-foods.



**Nausea:** Sometimes accompanied by vomiting but is usually well controlled by anti-sickness drugs. You can experience it from a few hours to a few days after treatment. It is important to take antisickness medicines even if you don't feel sick, because it is easier to prevent sickness rather than treat it once it has started. Contact your doctor or nurse straight away if you've been feeling sick more than once in a day.



**Mouth sores and ulcers:** you should always brush your teeth after eating to avoid germs growing. To prevent or to help treat mouth sores use a soft toothbrush and rinse three times a day with 1/2 to 1 teaspoon of baking soda mixed in water. It's better to avoid acidic foods such as oranges, lemons and grapefruits. Tell your doctor or nurse if you have ulcers, as they can help to prevent or to treat mouth sores.



**Fatigue:** A very common side effect, which may increase during the treatment course.



**Poor appetite:** Don't worry if you don't eat much for a day or two.



**Blood clotting:** Contact the helpline if your legs are swollen, red and sore or if you develop breathlessness.

## Some less common side effects related to FOLFOX



**Flu-like symptoms:** You may experience these during treatment or shortly after:

- Feeling hot, cold or shivery
- Fever
- Headache
- Muscle pain
- Fatigue



**Allergic reaction:** Sometimes this happens while treatment is given. Tell your doctor or nurse immediately if you have any of these sudden symptoms:

- rash
- shortness of breath
- redness or swelling of the face
- feeling hot
- dizziness
- need to pass urine



**Extravasation (leakage) of infusional treatment:** While it is being administered, chemotherapy and immunotherapy can sometimes leak outside the vein and damage the tissue around. Tell your nurse immediately if you have any stinging, pain, redness, or swelling around the vein.



**Constipation:** Eating high-fibre foods (vegetables, fruit, wholemeal bread) and drinking at least 2 litres of water can help you. You may need laxatives if it lasts for longer than two/three days.



**Drowsiness:** Chemotherapy may cause you to feel very sleepy (drowsy) and tired. If you feel very sleepy, do not drive or operate machinery.



**Headache:** If this happens, you may take painkillers like paracetamol.



**Difficulty of sleeping:** You can take sleeping tablets if you need them.



**Skin changes:** Your skin may be drier or develop a rash. It is important to protect your skin with a sun cream with a high protection factor.



**Build-up of fluid:** You may put on weight and your face or your ankles or legs may swell. It can help to put your legs up on a cushion. The swelling will get better after your treatment ends.



**Hair loss:** Your hair may get thinner, but it is unlikely that you will lose your hair.

## Medication to help control side effects

Make sure to let your doctor know of any side effects; there are useful medications to control the symptoms.

## Should I continue to take my usual medications?

Yes, you have to keep taking all your usual medications.

Please report to your oncology team all the medications you are taking, so that they can advise.

## Can I have the flu and COVID vaccination?

Yes, it is advised you have the flu and COVID vaccination before you start your treatment. If you have already started your treatment, please ask your doctor who can advise on the best timing to have the vaccination.

## When to contact the hospital?

If your symptoms are severe or do not improve after 24 hours, do not hesitate to contact the hospital.

## Tips during treatment

- Drink plenty of fluids (at least 2 litres per day) and protect your kidneys.
- Maintain good nutrition. Eating small frequent meals may help to reduce nausea. You should avoid fatty or fried foods. You can take anti-sickness drugs if you need.
- Avoid sun exposure. Wear SPF 15 (or higher) sunblock and protective clothing.
- Get plenty of rest.
- To prevent or minimize numbness and tingling:
  - Avoid exposing your hands or feet to sudden changes of temperature. You can be helped by using gloves when you go for a walk in winter or by avoiding touching frozen food/drink.
  - Use oven gloves when cooking and protective gloves when gardening.
  - Keep your hands and feet warm, and wear well fitting, protective shoes.
  - Take care when using hot water as you may not be able to feel how hot it is and could burn yourself.
  - Take care when cutting your nails.
  - Moisturise your skin at least a couple of times a day.

- Keep at home the medications you may need to help control the symptoms.
- You may experience drowsiness or dizziness; avoid driving or engaging in tasks that require alertness until your response to chemotherapy is known.
- Use an electric razor when shaving and a soft toothbrush to minimize bleeding.
- Before starting chemotherapy, tell your doctor about any medication you are taking. Sometimes side effects may be related to your medicines and not to chemotherapy.
- If your symptoms are severe or do not improve after 24 hours, do not hesitate to contact the hospital.
- Pay attention to symptoms of a blood clot: pain, redness, swelling of an arm or a leg, breathlessness or chest pain. If you have any of these symptoms contact your doctor.
- Do not receive any kind of vaccination without your doctor's approval while taking chemotherapy.
- If you are a woman of childbearing age:
  - inform your doctor if you are pregnant or may be pregnant prior to starting this treatment.
  - avoid getting pregnant during chemotherapy
  - do not breast feed during chemotherapy



## Where can I get more information?

If you want to get more information in this field you can visit *ESMO website for Biliary tract cancer: Guide for Patients* and on the *AMMF The Cholangiocarcinoma Charity website*.

You can find the related links below:

[www.esmo.org/for-patients/patient-guides/  
biliary-tract-cancer-a-guide-for-patients](http://www.esmo.org/for-patients/patient-guides/biliary-tract-cancer-a-guide-for-patients)

[www.ammf.org.uk](http://www.ammf.org.uk)



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