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**KEEP ALL MEDICINE OUT OF THE SIGHT AND REACH OF CHILDREN**

## Hyper-CVAD chemotherapy

Hyper-CVAD is a chemotherapy treatment used to treat some types of non-Hodgkin lymphoma and acute lymphoblastic leukaemia (ALL).

## The drugs used in Hyper-CVAD

Hyper-CVAD comes from the initials of the drugs used:

- Cyclophosphamide
- Vincristine
- Doxorubicin (which is also called Adriamycin)
- Dexamethasone (a steroid).

Hyper is short for hyperfractionated. It means you have more than one treatment of the same drug given in a day.

Hyper-CVAD treatment also includes another two drugs:

- Methotrexate
- Cytarabine

## How Hyper-CVAD is given

- You have Hyper-CVAD during a short stay in hospital and at a chemotherapy day unit. A chemotherapy nurse will give it to you. During treatment, you usually see a cancer doctor, a blood specialist (haematologist), a chemotherapy nurse or a specialist nurse.
- Before or on the day of treatment, a nurse or person trained to take blood (phlebotomist) will take a blood sample from you. This is to check that it is okay for you to have chemotherapy.
- You will also see a doctor or nurse before you have chemotherapy. They will ask you about how you have been. If your blood results are alright on the day of your treatment, the pharmacist will prepare your chemotherapy. Your nurse will tell you when your treatment is likely to be ready.
- Your nurse gives you anti-sickness drugs as an injection into a vein or as tablets. They give you the drugs and chemotherapy through one of the following: a fine tube that goes under the skin of your chest and into a vein close by (central line)
- The nurse will give you chemotherapy drugs separately into your line. They run your drip through a pump, which gives you the treatment over a set time:
- cyclophosphamide is given as a drip (infusion) over two hours
- vincristine is given as a drip over 10 minutes
- doxorubicin (a red fluid) is given as a drip that takes between 2 and 48 hours (depending on the hospital)
- Dexamethasone is given as tablets or an injection into your line
- Methotrexate and cytarabine are given on a different day from the other chemotherapy drugs:
- Methotrexate is given as a drip over 24 hours
- Cytarabine is given as a drip that lasts two hours
- Sometimes both these drugs are also given by injection into the fluid around the spinal cord (intrathecally).

## When the chemotherapy is being given

Some people might have side effects while they are having the chemotherapy:

- **Allergic reaction**

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- Some of these drugs may cause an allergic reaction while they are being given. Your nurse will check you for this. If you have a reaction, they will treat it quickly. **Signs of a reaction can include:**
  - a rash
  - feeling itchy
  - flushed or short of breath
  - swelling of your face or lips
  - feeling dizzy
  - having pain in your tummy, back or chest
  - feeling unwell - Tell your nurse straight away if you have any of these symptoms.
- The drug leaks outside the vein  
If this happens when you're having chemotherapy it can damage the tissue around the vein. This is called extravasation. Tell the nurse straight away if you have any stinging, pain, redness or swelling around the vein.  
Extravasation is not common but if it happens it's important that it's dealt with quickly.  
If you get any of these symptoms after you get home, contact the doctor or nurse straight away on the number they gave you.
- **Flushes and a blocked nose**  
Some people may have hot flushes, a feeling of having a blocked nose and a strange taste when cyclophosphamide is being given.  
This doesn't last for long. But if you notice this, ask the nurse to slow down the drip, which will reduce these symptoms.
- **Facial flushing**  
You may suddenly feel warm and your face may get red while the doxorubicin is being given. This should only last a few minutes.

### **Your course of Hyper-CVAD**

You have chemotherapy as a course of several sessions (or cycles) of treatment over a few months. With Hyper-CVAD you have four cycles each of two different schedules, A and B. The two schedules alternate with each other. Each cycle of Hyper-CVAD lasts 21 days.

- **Schedule A (cycles 1, 3, 5 and 7)**
  - On the first day your nurse gives you two separate drips of cyclophosphamide 12 hours apart. They repeat this again on days two and three of treatment, so you have six doses in total. You'll be given fluids through a drip before and after the cyclophosphamide. You may also be given a drug called mesna to help prevent bladder irritation. You start a course of dexamethasone tablets on day one, which you take for four days.
  - On day four you have vincristine and doxorubicin as a drip. You can usually go home the day after it finishes.
  - On day eleven you have vincristine again, usually in the chemotherapy day unit. You also start another fourday course of dexamethasone tablets (days 11-14).
  - You then have no treatment for the next week. This completes a cycle of Hyper-CVAD. Your next cycle will be Schedule B.



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- **Schedule B (cycles 2, 4, 6 and 8)**
  - On the first day your nurse gives you methotrexate as a drip. The next day you usually start having a drug called folinic acid (Leucovorin) as a drip to reduce the side effects of methotrexate. You have it regularly with fluids until the methotrexate is out of your system.
  - On the second day and on the third day you have cytarabine as a drip given twice - 12 hours apart. You can usually go home after this if you are well enough and your methotrexate levels are okay. You then have no treatment for the next 18 days. This completes another cycle of Hyper-CVAD. Your next cycle will be Schedule A again.
  - If you are having cytarabine and methotrexate by injection into the spinal fluid, your doctor or nurse will explain more about this. You usually have these on different days from the rest of your chemotherapy treatment.

### **Chemotherapy by injection into the spinal fluid**

- Methotrexate and cytarabine can be given into the spinal fluid to allow the drug to reach the spinal cord and brain. This is called intrathecal chemotherapy.
- The doctor numbs an area of skin over your spine with local anaesthetic. They gently insert a needle between two of the spinal bones. This is called a lumbar puncture. They inject the chemotherapy drug through this needle into the spinal fluid. Your cancer doctor and nurse will explain everything in advance so you know what to expect. You may get a headache after a lumbar puncture. To help prevent this, you need to lie flat for a few hours afterwards and drink plenty of fluids.

### **Going home**

Before you go home the nurse or pharmacist will give you anti-sickness drugs to take. You may also be given other drugs to take, for example, to help reduce your risk of getting an infection. Take all your tablets exactly as they have explained to you.

### **Possible side effects of Hyper-CVAD**

We explain the most common side effects of Hyper-CVAD here. But we don't include all the rare ones that are unlikely to affect you.

You may get some of the side effects we mention but you are very unlikely to get all of them. If you are having other chemotherapy drugs as well, you may have some side effects that we don't list here. Always tell your doctor or nurse about the side effects you have.

Your doctor can prescribe drugs to help control some side effects. It is very important to take them exactly as your nurse or pharmacist has explained. This means they will be more likely to work better for you. Your nurse will give you advice about managing your side effects. After your treatment is over, the side effects will start to improve.

### **Risk of infection**

Hyper-CVAD reduces the number of white blood cells in your blood. This will make you more likely to get an infection. When the number of white blood cells is low, it's called neutropenia. Your nurse may give you injections of a drug called GCSF under the skin. It encourages the bone marrow (where blood cells are made) to make more white blood cells.

### **Contact the hospital straight away on the contact number you've been given if:**

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- **Your temperature goes over 38°C.**
- You suddenly feel unwell, even with a normal temperature
- You have symptoms of an infection – this can include feeling shaky, a sore throat, a cough, diarrhoea
- Needing to pass urine a lot.

The number of white blood cells usually increases steadily and return to normal before your next treatment.

You will have a blood test before having more chemotherapy. If your white blood cells are still low, your doctor may delay your treatment for a short time.

### **Bruising and bleeding**

Hyper-CVAD reduces the number of platelets in your blood. Platelets are cells that help the blood to clot. Tell your doctor if you have any bruising or bleeding you can't explain. This includes nosebleeds, bleeding gums, blood spots or rashes on the skin. Some people may need a drip to give them extra platelets.

### **Anaemia (low number of red blood cells)**

Hyper-CVAD reduces the number of red blood cells in your blood. These cells carry oxygen around the body.

If the number of red blood cells is low, you may be tired and breathless. Tell your doctor or nurse if you feel like this. If you are very anaemic, you may need a drip to give you extra red blood cells (blood transfusion).

### **Feeling sick**

This may happen in the first few days after chemotherapy. Your doctor will prescribe anti-sickness (antiemetic) drugs to help prevent or control sickness. Take the drugs exactly as your nurse or pharmacist explains to you. It's easier to prevent sickness than to treat it after it has started.

If you still feel sick or are vomiting, contact the hospital as soon as possible. They can give you advice and change the anti-sickness drug to one that works better for you.

### **Tiredness**

Feeling very tired is a common side effect. It's often worse towards the end of treatment and for some weeks after it's finished. Try to pace yourself and get as much rest as you need. It helps to balance this with some gentle exercise, such as short walks. If you feel sleepy, don't drive or operate machinery.

### **Hair loss**

You usually lose all the hair on your head. Your eyelashes, eyebrows and other body hair may also thin or fall out. This usually starts after your first or second cycle of chemotherapy. It is almost always temporary and your hair will grow back after chemotherapy ends. It is important to cover your head to protect your scalp when you are out in the sun until your hair grows back. Your nurse can give you advice about coping with hair loss.

### **Sore mouth**

Your mouth may become sore and you may get ulcers. This can make you more likely to get an infection in your mouth. Gently clean your teeth and/or dentures morning and night and after meals. Use a soft-bristled or children's toothbrush. Your nurse might ask you to rinse your mouth regularly or use mouthwashes. It's important to follow any advice you are given and to drink plenty of fluids.



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Tell your nurse or doctor if you have any problems with your mouth. They can prescribe medicines to prevent or treat mouth infections and reduce any soreness.

### **Diarrhoea**

Your doctor can prescribe drugs to control diarrhoea. Let them know if it is severe or if it doesn't get better.

Make sure you drink at least two litres (three and a half pints) of fluids every day if you have diarrhoea.

### **Constipation**

Hyper-CVAD may make you constipated and cause tummy pain. Drinking at least two litres of fluids every day will help. Try to eat more foods that contain fibre (such as fruit, vegetables and wholemeal bread) and take some regular gentle exercise.

### **Discoloured urine**

Your urine may be a pink-red colour for up to 48 hours after you've had your treatment. This is due to the colour of doxorubicin.

### **Bladder irritation**

Cyclophosphamide may irritate your bladder and cause discomfort when you pass urine. Drink plenty of fluids - at least two litres (three and a half pints) during the 24 hours following chemotherapy. It is also important to empty your bladder regularly and to try to pass urine as soon as you feel the need to go.

You will be given fluids through a drip (infusion) and the drug mesna (Uromitexan) as a drip.

This helps to prevent bladder irritation.

Tell your nurse or doctor straight away if you feel any discomfort or stinging when you pass urine, or if you notice any blood in it.

### **Tummy pain and/or indigestion**

Steroids can irritate the stomach lining. Let your nurse or doctor know if you have pain in your tummy or indigestion. They can prescribe drugs to help reduce stomach irritation.

Take your tablets with food to help protect your stomach.

### **Raised blood sugar levels**

Steroids can raise your blood sugar levels. Your nurse will check your blood regularly for this. They may also test your urine for sugar. Symptoms of raised blood sugar include feeling thirsty, needing to pass urine more often and feeling tired. Tell your doctor or nurse if you have these symptoms.

If you have diabetes, your blood sugar levels may be higher than usual. Your doctor will talk to you about how to manage this. You may need to adjust your insulin or tablet dose.

### **Increased appetite**

Steroids can make you feel much hungrier than usual and you may gain weight. Your appetite will go back to normal when you stop taking them. If you're worried about gaining weight, talk to your doctor or nurse.

### **Skin changes**

Chemotherapy may affect your skin. Your doctor or nurse can tell you what to expect. If your skin feels dry, try using an unperfumed moisturising cream every day. During treatment and for several months afterwards, you'll be more sensitive to the sun and your skin may burn more easily than usual. You can still



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go out in the sun, but use a suncream with a sun protection factor (SPF) of at least 30, and cover up with clothing and a hat.

Your skin may darken. It will return to its normal colour after you finish treatment. If you've had radiotherapy (either recently or in the past), the area that was treated may become red or sore. Always tell your doctor or nurse about any skin changes. They can give you advice and may prescribe creams or medicines to help. Any changes to your skin are usually temporary and improve when treatment finishes.

### **Soreness and redness of palms of hands and soles of feet**

This is called palmar-plantar or hand-foot syndrome. It gets better when treatment ends. Your doctor or nurse may prescribe creams to improve the symptoms. It can help to keep your hands and feet cool and to avoid tight-fitting socks, shoes and gloves.

### **Nail changes**

Your nails may become brittle and break easily. They may get darker or discoloured, and you may get lines or ridges on them. These changes grow out after treatment finishes. Wearing gloves when washing dishes or using detergents will help protect your nails during treatment.

### **Numb or tingling hands or feet**

These symptoms are caused by the effect of vincristine on nerves. It's called peripheral neuropathy. You may also find it hard to fasten buttons or do other fiddly tasks.

Tell your doctor if you have these symptoms. They sometimes need to lower the dose of the drug. The symptoms usually improve slowly after treatment finishes but in some people they may never go away. Talk to your doctor if you are worried about this.

### **Build-up of fluid**

You may put on weight or your ankles and legs may swell because of fluid building up. This is caused by dexamethasone and is more common if you are taking it for a long time. Tell your doctor or nurse if fluid builds up. If your ankles and legs swell it can help to put your legs up on a foot stool or cushion. The swelling gets better after your treatment ends.

### **Eye problems**

This treatment may make your eyes feel sore, red and itchy (conjunctivitis). Your doctor will prescribe steroid eye drops to prevent this. It's important to use these as instructed.

The drugs may also make your eyes more sensitive to light and cause blurry vision or eye pain. Always tell your doctor or nurse if you have pain or notice any change in your vision.

### **Changes in the way the kidneys work**

Methotrexate can affect how your kidneys work. You will have blood tests before and during treatment to check this. Your nurse will ask you to drink plenty of fluid. Tell them if there are any changes in how much urine you are producing. You may be given sodium bicarbonate as a drip or as tablets during treatment. This is to reduce the risk of kidney problems. The nurses will also test your urine regularly.

### **Changes in the way the liver works**

Hyper-CVAD may affect how your liver works. This is usually mild and goes back to normal after treatment. You will have blood tests to check how well your liver is working.



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### **Raised levels of uric acid in the blood**

Hyper-CVAD may cause the cancer/leukaemia cells to break down quickly. This releases uric acid (a waste product) into the blood. Too much uric acid can cause swelling and pain in the joints, which is called gout. Your doctor may give you tablets called allopurinol to help prevent this. Drinking at least two litres of fluid a day will also help. You will have regular blood tests to check the uric acid levels.

### **Mood and behaviour changes**

Steroids can affect your mood. You may feel anxious or restless, or have mood swings or problems sleeping.

Taking your steroids in the morning may help you sleep better.

Tell your doctor or nurse if you have any of these side effects. They may make some changes to your treatment if the side effects become a problem.

### **Less common side effects of Hyper-CVAD**

#### **Reaction to cytarabine**

Cytarabine may cause a reaction 6-12 hours after it's been given. Signs of a reaction can include:

- a high temperature or chills,
- a rash;
- pain in the eyes, bones, tummy or chest.

Tell your nurse straight away if you have any of these symptoms.

#### **Effects on the lungs**

Treatment can cause changes to the lungs. Always tell your doctor if you develop wheezing, a cough, or a fever, or feel breathless. You should also let them know if any existing breathing problems get worse. If necessary, they can arrange for you to have tests to check your lungs.

#### **Changes in the way the heart works**

Doxorubicin and cyclophosphamide can affect the way the heart works. You may have tests to see how well your heart is working before, during and sometimes after treatment.

If you have pain or tightness in your chest or feel breathless or notice changes to your heartbeat at any time during or after treatment, tell a doctor straight away. These symptoms can be caused by other conditions but it's important to get them checked by a doctor.

#### **Effects on the nervous system**

Rarely Hyper-CVAD can affect the nervous system. You may feel drowsy or confused, dizzy or unsteady.

Tell your doctor or nurse straight away if you notice any of these symptoms. It's important not to drive or operate machinery if you notice these effects.

Rarely, it can cause seizures (fits). Your doctor or nurse will explain more about this.

#### **Intrathecal chemotherapy**

The side effects may be different from those mentioned here. Your doctor or nurse will talk to you about this.

When methotrexate is given this way it can cause headaches, dizziness, tiredness, blurred vision and loss of balance for a few hours. Tell your nurse or doctor straightaway if you have any of these.



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It's important to tell your doctor or nurse straight away if you feel ill or have severe side effects. This includes any we don't mention here.

### **Other information about Hyper-CVAD**

#### **Blood clot risk**

Cancer increases the chance of a blood clot (thrombosis) and chemotherapy can add to this. A clot can cause symptoms such as pain, redness and swelling in a leg, breathlessness and chest pain. Contact your doctor straight away if you have any of these symptoms. A blood clot is serious but your doctor can treat it with drugs that thin the blood. Your doctor or nurse can give you more information.

#### **Other medicines**

Some medicines can interact with chemotherapy or be harmful when you are having chemotherapy. This includes medicines you can buy in a shop or chemist. Tell your doctor about any medicines you are taking, including over-the-counter drugs, complementary therapies and herbal drugs.

#### **Fertility**

Hyper-CVAD may affect your fertility (being able to get pregnant or father a child). If you are worried about this, you can talk to your doctor or nurse before treatment starts.

#### **Contraception**

Your doctor will advise you not to become pregnant or to father a child during treatment. This is because the drugs may harm a developing baby. It's important to use effective contraception during and for a few months after chemotherapy. You can talk to your doctor or nurse about this.

#### **Sex**

If you have sex within the first couple of days of having chemotherapy you need to use a condom. This is to protect your partner in case there is any chemotherapy in semen or vaginal fluid.

#### **Changes to your periods**

Chemotherapy can sometimes stop the ovaries working. You may not get a period every month and they may eventually stop. In some women, this is temporary, but for others it is permanent and they start the menopause.

#### **Breastfeeding**

Women are advised not to breastfeed during treatment and for a few months after. This is in case there is chemotherapy in their breast milk.

#### **Medical and dental treatment**

If you need to go into hospital for any reason other than cancer, always tell the doctors and nurses that you are having chemotherapy. Give them contact details for your cancer doctor.

Talk to your cancer doctor or nurse if you think you need dental treatment. Always tell your dentist you are having chemotherapy.