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Cancer Pain

What is Cancer Pain?

Let us answer some of your questions.

ESMO Patient Guide Series

based on the ESMO Clinical Practice Guidelines

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Cancer pain
An ESMO guide for patients

Patient information based on ESMO Clinical Practice Guidelines

This guide has been prepared to help you, as well as your friends, family and caregivers, better understand cancer pain and its treatment. It contains up-to-date guidance on the types of treatments that may be available and any possible side effects of treatment.

The medical information described in this document is based on the ESMO Clinical Practice Guideline for cancer pain in adults, which is designed to help clinicians with the management of cancer pain. All ESMO Clinical Practice Guidelines are prepared and reviewed by leading experts using evidence gained from the latest clinical trials, research and expert opinion.

The information included in this guide is not intended as a replacement for your doctor's advice. Your doctor knows your full medical history and will help guide you regarding the best treatment for you.

Words highlighted in **colour** are defined in the glossary at the end of the document.

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WHAT'S INSIDE

Cancer pain: A summary of key information

This summary is an overview of the key information provided within the Cancer Pain guide. The following information will be discussed in detail in the main pages of the guide.

Introduction to cancer pain

- Patients with cancer commonly experience pain due to the cancer itself, the cancer treatment, or a combination of both.
- How much pain a patient experiences is not necessarily related to the growth of the cancer. It is important that patients tell their doctor or nurse about their pain, including any new pain arising from new or unknown locations.
- Pain is routinely assessed as a part of cancer care. Different assessment scales are available, and numerical scales are widely used. Patients may be asked to grade their pain on a numerical scale (e.g. 0–10, with a score of 0 for no pain and 10 for the worst pain) and an appropriate pain relief strategy will be initiated. Patients should ask their doctor or nurse to explain the numerical rating scale and ask if they can report their worst pain as well as average pain.
- Cancer pain can arise from various sources and includes different types of pain. Therefore, if patients can accurately describe their pain, their doctor or nurse will be more able to prescribe adequate measures for pain relief.
- A number of effective treatments are available to provide pain relief at all stages and types of cancer. Patients should not have to tolerate pain.

Treatment for cancer pain

- There are many ways to manage different types of cancer-related pain. The pain relief offered depends upon the type and severity of the pain, as well as the patient's general health and level of fitness. Patients should be fully informed and involved in decisions about treatment options.
- Treatment options for cancer pain include non-opioid **analgesic** drugs, opioid **analgesic** drugs, **radiotherapy** and, in some cases, surgery. **Adjuvant** drugs are also an important part of pain control.
- Treatment for cancer pain varies between individual patients, but in general:
  - Mild cancer pain may be treated with non-opioid **analgesics** such as **paracetamol** or **non-steroidal anti-inflammatory drugs** (**NSAIDs**; e.g. **aspirin**, **ibuprofen**, **diclofenac**). These may be used alone or in combination with opioids.
  - Mild to moderate cancer pain may be treated with weak opioids such as **codeine**, **dihydrocodeine** or **tramadol**. These might be given alongside non-opioids.
  - Moderate to severe cancer pain is usually treated with strong opioids, including **morphine**, **oxycodone**, **fentanyl**, **hydromorphone** and **methadone**. **Morphine** is the most commonly used opioid for moderate to severe cancer pain.

- Episodes of breakthrough cancer pain are typically treated with fast-acting opioids, usually **morphine** or **fentanyl**.
- Cancer-related bone pain caused by bone **metastases** can be treated with **radiotherapy**, **bisphosphonates** and **denosumab** as well as **analgesic** drugs. **Bisphosphonates** and **denosumab** are not considered pain medications as such, but can delay the onset of bone pain and prevent bone complications such as fractures. **Percutaneous vertebroplasty** can also reduce spinal pain by stabilising the bones.
- Pain from **spinal cord compression** caused by **metastases** is typically treated with **radiotherapy** with or without **steroids**, and occasionally with surgery to remove the **tumour** or stabilise the **vertebrae**.
- **Neuropathic pain** can be caused by the cancer itself, cancer therapies or infections (such as **herpes zoster**). It causes unpleasant sensations and can be difficult to treat. **Neuropathic pain** in patients with cancer is treated with opioids as well as **adjuvant** drugs that can reduce nerve pain, including **anticonvulsants**, **antidepressants** and **lidocaine** patches.
- **Refractory pain** (persistent pain that is not relieved by standard drug treatments) may rarely require more invasive strategies, such as **intrathecal** opioid treatment, **peripheral nerve block**, **neurolytic blockade**, **spinal cord stimulation** or **cordotomy**.

Side effects of treatment for cancer pain

- The side effects from cancer pain treatments are usually mild and not serious.
- Common side effects of **NSAIDs** include effects on the **gastrointestinal system**, and **paracetamol** can be associated with a skin rash or itching.
- The common side effects of opioid **analgesics** include constipation, drowsiness, nausea and vomiting. Hydration may be necessary to ensure that the by-products of opioids pass through the kidneys without causing problems. Many of the side effects of opioids can be managed by reducing the dose of the opioid, switching to a different opioid or using specific additional drugs to treat the side effect.
- Possible side effects of **radiotherapy** include **fatigue** and skin irritation around the treatment area. Occasionally **radiotherapy** can cause a temporary flare up of pain.

Emotional support

- Specialist counsellors or psychologists can help patients to deal with the emotional challenges associated with cancer and cancer-related pain.
- Local, national and international patient support groups are available for specific types of cancer. These groups can provide help for patients to better understand their disease, allow them to share their experiences with other patients, and help them to learn how to cope with cancer.

What is cancer pain and how common is it?

Patients with cancer commonly experience pain. This can be due to the cancer itself, the cancer treatment, or a combination of both.

Pain is particularly common in the advanced stages of cancer, affecting more than 60% of patients with advanced, **metastatic** or terminal disease. However, cancer pain is also a frequent occurrence at the earlier stages of disease – around a third of patients who have undergone **curative** treatment experience pain. Some types of cancer are particularly associated with a high prevalence of pain at earlier disease stages, including pancreatic cancer and head and neck cancer *(Fallon et al., 2018)*. It is important to understand that how much pain you have is not necessarily related to the growth of your cancer – a very small **tumour** pressing on a nerve can be extremely painful, while a very large tumour somewhere else might not cause any pain at all.

The amount of pain you have is not necessarily related to the growth of your cancer

Cancer treatments, including surgery and **radiotherapy**, can cause pain. Pain can also be a long-term side effect of **chemotherapy**, and post-treatment pain can appear or worsen months or years after treatment. Cancer pain can be distressing for patients and their families, but a range of effective treatments are available to provide pain relief for all stages and types of cancer. It is important to understand that cancer pain can be effectively managed; multiple treatments are available and **patients should not have to tolerate pain**.

How is cancer pain assessed?

Cancer pain is routinely assessed as an integral part of cancer care. Your doctor or nurse may ask you a question such as:

'What has been your worst pain in the last 24 hours on a scale of 0–10, where 0 is no pain at all and 10 is the worst pain imaginable?'

It is very important that you give your doctor or nurse an accurate answer so they can ensure you receive the appropriate pain relief. If you find it difficult to give your pain a number, you can try to express it in words; for example, "my pain is mild" (corresponding to 1–3 on the number scale), "my pain is moderate" (numbers 4–6), or "my pain is severe" (numbers 7–10).

Using the question above, if your worst pain level is less than 3, you will typically be monitored, re-assessed regularly and pain relief medication may be prescribed. If your worst pain level is 3 or more, or if your pain is causing you distress, then a more detailed assessment will be carried out (including details on the type, location and timing of the pain) and appropriate pain relief will be arranged. Once your **analgesic** treatment has started, your doctor or nurse will reassess your pain level and ask you about any side effects that you are experiencing from the pain relief medication. They will then adjust your treatment if necessary *(Fallon et al., 2018)*.

It is very important that you tell your doctor or nurse about all of the pain that you are experiencing, including any new pain arising from new or unknown locations. Your doctor or nurse may ask you for a detailed description about the sensations you are experiencing, for example "stabbing", "burning", "shooting" or "shock-like" pain. This can be difficult to describe but it is important that you provide as much information as you can.

Cancer pain is regularly assessed to ensure it is managed effectively

How is treatment for cancer pain determined?

At all stages of cancer, your medical team will support you and help to manage your pain. There are many ways to manage different types of cancer-related pain. The pain relief offered will depend upon the type and severity of your pain, as well as your general health and level of fitness. The choice of treatments will be discussed with you and your preferences will be taken into account.

A range of pain management options is available at every stage of disease

It is important that patients are fully involved in the treatment decision-making – when there are several options available, doctors should involve patients in making decisions about their pain relief so that the patients can choose the care that meets their needs and reflects what is important to them. This is called 'shared decision-making'.

It is important that patients are fully involved in discussions and decisions about their treatment

Your doctor will be happy to answer any questions you have about your pain relief treatment. Four simple questions that may be helpful when talking with your doctor or any healthcare professional involved in your care are:

- What is the cause of my pain?
- What pain relief options do I have?
- What are the possible advantages and disadvantages of these options?
- How likely am I to experience these advantages and disadvantages?

Your doctor may recommend one or more of the following approaches to pain management:

Analgesic drugs

Analgesic drugs reduce pain. They are used widely in the treatment of cancer pain and are broadly divided into two categories: non-opioids and opioids.

- Non-opioid **analgesics** include **paracetamol** and **non-steroidal anti-inflammatory drugs** (**NSAIDs**) such as such as **aspirin**, **ibuprofen** and **diclofenac**. These drugs can be taken as tablets, liquid, injection or as **suppositories**, and are usually used for the management of mild pain *(Fallon et al., 2018)*.
- Opioid **analgesics** are stronger painkillers and are commonly used in the treatment of cancer pain, particularly moderate or severe pain. There are several types of opioids (*Fallon et al., 2018)*:
  - Weak opioids, including **codeine**, **dihydrocodeine** and **tramadol**.
  - Strong opioids, including **morphine**, **methadone**, **oxycodone**, **hydromorphone**, **fentanyl**, **alfentanil**, **buprenorphine** and **diamorphine**. Legislation in different countries means that not all strong opioids are available in all countries.

Opioids are usually taken by mouth (e.g. tablets, capsules, **suspensions**), but other types of administration, including **transdermal**, **intravenous**, **subcutaneous** or **suppositories** are available if required.

The most common treatment for cancer pain involves the use of non-opioid and opioid analgesic drugs taken by mouth

It is important to take your **analgesic** medications regularly and at the correct time, according to the advice of your doctor or nurse. Sometimes patients delay taking their **analgesic** medication until the pain affects their normal daily activities, however this can lead to an inconsistent level of pain relief, therefore it's very important to take the next dose as instructed rather than waiting until the pain returns. It is a common mistake for patients to get into the habit of taking pain medication at mealtimes, but this can result in long periods between doses of medication, leading to incomplete pain relief.

Radiotherapy

Radiotherapy can reduce cancer pain in some cases by shrinking the **tumour** and relieving the pain caused by the **tumour** pressing against bone tissue or the spinal cord. **Radiotherapy** is therefore often used to reduce pain caused by bone **metastases** and **spinal cord compression** due to **metastases** *(Fallon et al., 2018)*.

Surgery

In a small number of patients, surgery to remove **metastases** may be used to relieve pain from **spinal cord compression** caused by **metastases** *(Fallon et al., 2018)*. Surgical removal of **metastases** reduces pain by relieving the pressure that the **tumour** exerts on the spinal cord. Stabilisation of the **vertebrae** may also be considered.

What are the treatment options for different types of cancer pain?

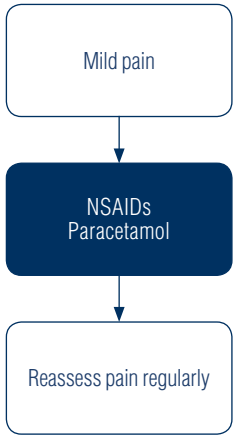
Whichever type of pain you experience, your doctor or nurse will begin treatment with the most suitable pain relief medication for the specific intensity of your pain.

What are the treatment options for mild cancer pain?

Mild cancer pain may be treated with non-opioid **analgesics** such as **paracetamol** or **NSAIDs**. These may be used alone or in combination with opioids when required *(Fallon et al., 2018)*.

Mild cancer pain is often managed with non-opioid analgesic drugs

Although effective for mild pain, increasing long-term doses of non-opioid analgesics can lead to serious side effects on the kidneys or liver. Therefore, these medications have maximum recommended daily doses, after which stronger **analgesics** such as opioids may be added.

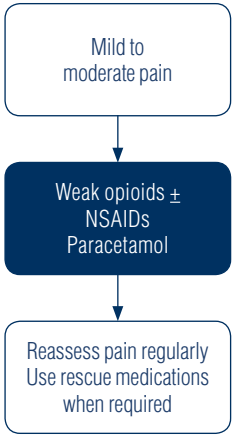


Flowchart showing treatment approaches for mild cancer pain.

What are the treatment options for mild to moderate cancer pain?

Patients with mild to moderate cancer pain may be offered weak opioids such as **codeine**, **dihydrocodeine** or **tramadol** *(Fallon et al., 2018)*. These might be given in combination with non-opioids.

Mild to moderate cancer pain may be treated with weak opioids



Flowchart showing treatment approaches for mild to moderate cancer pain.

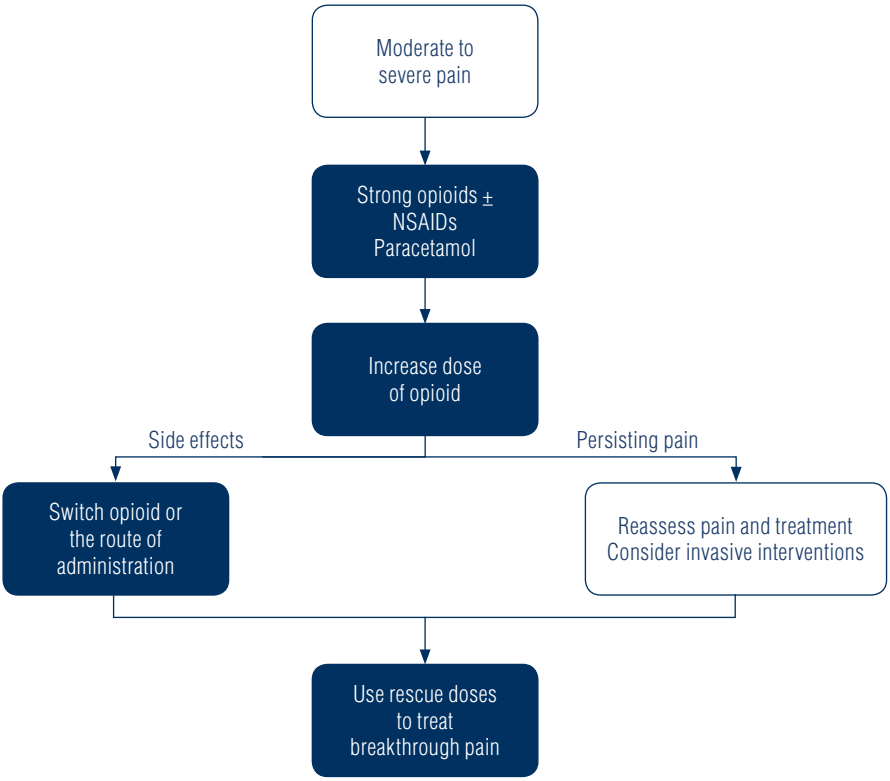
What are the treatment options for moderate to severe cancer pain?

Strong opioids are the standard treatment for moderate to severe cancer pain *(Fallon et al., 2018)*. **Morphine** is the most commonly used opioid in this setting. **Morphine** is usually given orally but can be given **intravenously** or **subcutaneously** if urgent pain relief is required. **Oxycodone**, **hydromorphone** and **methadone** are common alternatives to oral **morphine**. Once their pain has stabilised, some patients may be offered **transdermal fentanyl** or **buprenorphine** patches – these ensure a consistent dose of **analgesic** without having to remember to take medication.

Strong opioids are commonly used in the management of moderate to severe cancer pain

After a while, the effectiveness of an opioid might decrease (this is called opioid **tolerance**), or unpleasant side effects might occur. If this happens, your doctor may suggest switching to a different opioid. Opioid switching (also known as opioid rotation) can improve the opioid response by improving pain relief or by reducing the intensity of side effects. It is also possible to re-introduce a previously used opioid (after rotation) in some patients to prolong its use. Your doctor will carefully calculate the correct dose of the new opioid to avoid any increases in pain or side effects.

Patients who are unable to receive opioids orally or **transdermally** can receive them **subcutaneously**. If **subcutaneous** administration is not possible, or immediate pain relief is needed for severe pain, then **intravenous** administration can be used.



Flowchart showing treatment approaches for moderate to severe cancer pain.

What are the treatment options for breakthrough cancer pain?

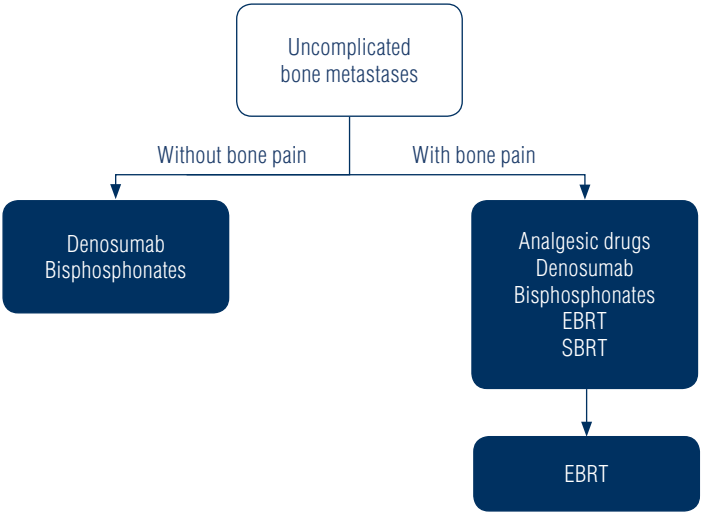
Breakthrough cancer pain is an episode of severe pain that occurs in patients who are already receiving treatment with opioids for persistent pain. Treatment for breakthrough cancer pain is usually managed using fast-acting opioids, particularly **morphine**. Various formulations of **fentanyl** can also provide rapid relief from unpredictable breakthrough cancer pain, including oral, **buccal** (between the gum and cheek), **sublingual** (under the tongue) and **intranasal** (through the nose) administration *(Fallon et al., 2018)*.

Morphine and fentanyl are common treatments for episodes of severe breakthrough cancer pain

What are the treatment options for cancer-related bone pain?

Bone pain in patients with cancer is commonly caused by bone **metastases**. **Radiotherapy**, **targeted therapy** and **analgesic** drugs are all used in the management of bone pain *(Fallon et al., 2018)*.

- **Bisphosphonates** are drugs than can prevent or slow down a reduction in bone density known as **osteoporosis**. They are also used to prevent bone complications such as bone fractures caused by cancer, with or without **radiotherapy** (if available).
- **Denosumab** is an injected **targeted therapy** that helps to prevent bone complications in patients with solid cancers that have spread to the bones. **Denosumab** is also used to prevent or slow down **osteoporosis** in patients who are receiving hormonal therapy for breast or prostate cancer.
- **External radiotherapy** directs **photon beams** to the **metastases** from a machine outside the body and is very effective for cancer-related bone pain. **Stereotactic body radiotherapy** may be offered to some patients who have only one or two **metastases**.
- **Radioisotope therapy** with **radium-223** is another form of **radiotherapy** which is used to reduce bone pain in some patients with prostate cancer. **Radium-223** is mildly radioactive and is readily absorbed by active bone cells, making it a good way of specifically targeting bone cancer cells. Once the **radium-223** is absorbed, it releases the radiation, providing internal **radiotherapy** directly in the bone. Other types of **radioisotope therapy** may also be considered in selected patients (e.g. strontium, samarium or rhenium).



Flowchart showing treatment approaches for cancer-related bone pain.
*EBRT, **external beam radiotherapy**; SBRT, **stereotactic body radiotherapy**.*

A procedure called **percutaneous vertebroplasty** may also be used to reduce cancer-related spinal pain. This involves injecting a type of cement into one or more **vertebrae**, which relieves pain from **compression fractures** by stabilising the bone *(Filippiadis et al., 2017)*.

What are the treatment options for cancer-related spinal cord compression?

Almost all patients with **spinal cord compression** caused by **metastases** experience pain in their back or neck that doesn't go away. **Radiotherapy** is the **first-line** treatment for most patients with **spinal cord compression**, although a minority of patients undergo surgery to remove the **tumour**, followed by **radiotherapy**. A **steroid** (usually **dexamethasone**) is also given as soon as **spinal cord compression** is diagnosed, in order to reduce swelling and inflammation *(Fallon et al., 2018)*.

What are the treatment options for cancer-related neuropathic pain?

Neuropathic cancer pain is caused by damage to nerves and is often experienced as abnormal sensations such as burning, shooting or tingling, which can be continuous or intermittent (often resembling electric shocks). Treatments include opioid combinations and, if needed, additional drugs that have been shown to reduce nerve pain, such as **anticonvulsant** agents (**gabapentin** and **pregabalin**) and **antidepressants** (agents used to treat anxiety and depression, including **duloxetine** and **tricyclic antidepressants**) *(Fallon et al., 2018)*. **It is important to remember that if your doctor recommends anticonvulsant or antidepressant agents for cancer pain, it is not because they think that you have epilepsy or depression.** Research has shown that these medicines are effective for nerve pain in patients who do not have epilepsy or depression *(Fallon et al., 2018; Smith et al., 2013; Jiang et al., 2019)*. The dose of **anticonvulsants** and **antidepressants** may need to be gradually increased over days or weeks to control the pain, so it's very important to keep taking them even if they don't work immediately.

Transdermal patches containing **lidocaine** (a type of **local anaesthetic**) are also an option in patients with **neuropathic pain**, providing non-invasive, effective pain relief in up to 80% of patients *(López Ramírez, 2013)*.

In addition to opioids, anticonvulsants and antidepressants can help to manage neuropathic cancer pain

What are the treatment options for refractory cancer pain?

Refractory pain describes pain that is not relieved by standard management strategies. The following methods are not commonly used, and can only be carried out by specialists, but may be considered for patients who are still experiencing significant pain when all other methods have been tried *(Fallon et al., 2018)*:

- **Intrathecal** drug delivery usually involves infusion of an opioid directly into the space around the spinal cord.
- **Peripheral nerve block** is the injection of **local anaesthetic** around a nerve to block the pain signals travelling to the brain.
- **Neurolytic blockade** involves injection of a chemical around a nerve to damage it, blocking pain signals to the brain for 3–6 months.
- **Spinal cord stimulation** uses a small implant that delivers mild electrical impulses to the spinal cord to modify and mask the pain signals travelling to the brain.
- **Cordotomy** is surgery to disable selected pain-conducting pathways in the spinal cord.

What is a clinical trial and should I participate?

Your doctor may ask you whether you would like to take part in a **clinical trial**. This is a research study conducted with patients in order to *(ClinicalTrials.gov, 2017)*:

- Test new treatments.
- Look at new combinations of existing treatments or change the way they are given to make them more effective or reduce side effects.
- Compare the effectiveness of drugs.
- Find out how treatments work.

Clinical trials can help to improve knowledge about cancer pain and develop new treatments, and there can be many benefits to taking part. You would be carefully monitored during and after the study and the new treatment may offer benefits over existing therapies. It's important to bear in mind, however, that some new treatments are found not to be as good as existing treatments or to have side effects that outweigh the benefits *(ClinicalTrials.gov, 2017)*.

Clinical trials help to improve knowledge about diseases and develop new treatments – there can be many benefits to taking part

For example, therapeutic **cannabinoids** are a new type of drug undergoing **clinical trials** for the treatment of cancer pain. In patients with advanced cancer, some studies have shown that **cannabinoids** can provide greater pain relief than **placebo** when given in combination with opioids *(Johnson et al., 2010; Portenoy et al., 2012)*. However, other studies have reported that **cannabinoids** were no more effective than **placebo** *(Fallon et al., 2017; Lichtman et al., 2018)*. Large **clinical trials** are needed to evaluate the effectiveness of cannabis-based therapies for pain relief. As such, they are not currently recommended as a treatment for cancer pain *(Fallon et al., 2018)*.

You have the right to accept or refuse participation in a **clinical trial** without any consequences for the quality of your treatment. If you want to find out more about this option, you can ask your doctor if there is a trial for cancer pain taking place nearby *(ClinicalTrials.gov, 2017)*.

What are the possible side effects of treatment?

As with any medical treatment, you may experience side effects from your cancer pain treatment. However, serious side effects from pain medications are relatively uncommon and most side effects are mild or moderate.

The most common side effects for each type of treatment are highlighted below, along with some information on how they can be managed. You may experience side effects other than those discussed here. It is important to talk to your doctor about any potential side effects that are worrying you.

Doctors classify side effects by assigning each event a 'grade', on a scale of 1–4, by increasing severity. In general, grade 1 side effects are considered to be mild, grade 2 moderate, grade 3 severe and grade 4 very severe. However, the precise criteria used to assign a grade to a specific side effect varies depending on which side effect is being considered. The aim is always to identify and address any side effect before it becomes severe, so you should always report any worrying symptoms to your doctor as soon as possible.

It is important to talk to your doctor about any treatment-related side effects that are worrying you

Non-opioid analgesics

Serious side effects from non-opioid **analgesics** are rare. Common side effects of **NSAIDs** include effects on the **gastrointestinal system** such as heartburn, indigestion and stomach ulcers. Some patients who are treated with **paracetamol** might experience a skin rash or itching. The table below summarises the important side effects of non-opioids **analgesics** that you should be aware of. It is important to note that some of these side effects are rare.

Serious side effects from non-opioids are rare, but patients are monitored for kidney and liver effects

DRUG CLASS	IMPORTANT SIDE EFFECTS	HOW THE SIDE EFFECTS MAY BE MANAGED
NSAIDs	• Kidney failure • Reduction in **platelet aggregation** • Stomach ulcers and **gastrointestinal** bleeding	• Tell your doctor or nurse immediately if you experience swelling in your legs, ankles or feet. In the event of kidney damage, **NSAID** treatment will be stopped. The kidneys usually recover to pre-treatment function after **NSAID** treatment has been stopped. • If you have a blood clotting disorder or are taking medication to reduce blood clotting, you will typically not be treated with **NSAIDs**. • Let your doctor or nurse know if you begin to bruise more easily than usual or if you experience bleeding from the gums/nose, prolonged bleeding from cuts or unusually heavy periods – these can be signs of reduced **platelet aggregation**. • Tell your doctor or nurse immediately if you experience dark tar-like stools, blood in your vomit or sudden sharp pains in your stomach, as these can be symptoms of **gastrointestinal** bleeding. Some patients may be offered enteric-coated **NSAIDs**, which have a special coating to prevent irritation of the stomach lining, or additional drugs that can protect the lining of the stomach during treatment with **NSAIDs**.
Paracetamol	• Liver damage • Reduction in **platelet aggregation**	• Liver damage is a rare side effect that is usually associated with high daily doses and long-term use of **paracetamol**. Let your doctor or nurse know if you experience nausea, vomiting, abdominal pain or yellow skin/whites of the eyes. If liver damage is suspected, you may need to be treated in hospital. You will be closely monitored if you have existing liver disease. • Let your doctor or nurse know if you begin to bruise more easily than usual or if you experience bleeding from the gums/nose, prolonged bleeding from cuts or unusually heavy periods – these can be signs of reduced **platelet aggregation**. Blood disorders such as a reduction in **platelet aggregation** are rare side effects of **paracetamol** use. If you have a blood clotting disorder or are taking medication to reduce blood clotting, you will be carefully monitored for signs of a reduction in **platelet aggregation**.

Important side effects associated with non-opioid analgesics used in the treatment of cancer pain. *The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Opioid analgesics

Side effects from opioids vary depending upon the drugs and the doses used. The main areas of the body affected by opioids are the **gastrointestinal system** and the **central nervous system**. Transient sleepiness can occur when opioids are first started or when the dose is increased. Constipation, nausea and dizziness are very commonly experienced when patients first start taking opioids, but these are usually temporary. Hydration may be necessary to ensure that the by-products of opioids pass through the kidneys without causing problems. The table below summarises the important side effects of opioids that you should be aware of. It is important to note that some of these side effects are rare.

Tell your doctor about any side effects you experience with opioids – most can be effectively managed

DRUG CLASS	IMPORTANT SIDE EFFECTS	HOW THE SIDE EFFECTS MAY BE MANAGED
Opioids	• Nausea • Constipation • Dizziness • Drowsiness • **Fatigue** • Nightmares • Confusion/hallucinations	• Your doctor might recommend that you take a treatment (typically **metoclopramide** or an **antidopaminergic** drug) to reduce opioid-induced nausea and vomiting. • Constipation is a very common side effect of opioids. Constipation can be treated with **laxatives** (which can also be taken in advance to prevent constipation) and lifestyle changes such as increasing the amount of fibre and fluid in the diet (if you are able to drink enough) and exercising as much as possible. For persistent constipation, your doctor might recommend treatment with a class of drugs called **peripherally acting mu-opioid receptor antagonists** (**PAMORAs**), such as **naloxegol**. **Naloxone** is a **PAMORA** that is available in combination formulations with some opioids to reduce the risk of constipation. • Dizziness, drowsiness and **fatigue** usually wear off after a few days, but it is important not to drive or operate machinery when feeling drowsy. Persistent drowsiness can be treated with **psychostimulants** (e.g. **methylphenidate**). • Tell your doctor or nurse if you or the people around you notice that you are feeling confused, or if you are experiencing troublesome nightmares.

Important side effects associated with opioid analgesics used in the treatment of cancer pain. *The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Bisphosphonates and denosumab

Treatment with **bisphosphonates** can result in side effects including flu-like symptoms and low calcium levels. If you have existing kidney disease, your dose will be reduced, or you may be unable to take some types of **bisphosphonates**. A common side effect of **denosumab** therapy is low calcium levels. You should be examined by a dentist before starting treatment with **bisphosphonates** or **denosumab** as this significantly reduces the risk of damage to the jaw bone *(Ripamonti et al., 2009)*. The table below summarises the important side effects of **bisphosphonates** and **denosumab** that you should be aware of. It is important to note that some of these side effects are rare.

DRUG CLASS	IMPORTANT SIDE EFFECTS	HOW THE SIDE EFFECTS MAY BE MANAGED
Bisphosphonates	• Damage to the jaw bone (**osteonecrosis** of the jaw) • Irritation of the **oesophagus** (with oral **bisphosphonates**)	• Teeth should be cleaned regularly and carefully, and any oral problems should be reported to your doctor and dentist. • If you are taking oral **bisphosphonates**, you should remain standing or sitting upright for an hour after taking the medication to avoid irritation of the **oesophagus**. Tell your doctor or nurse if you have heartburn or develop any symptoms in your **oesophagus** such as pain or difficulty swallowing.
Denosumab	• Damage to the jaw bone (**osteonecrosis** of the jaw)	• Teeth should be cleaned regularly and carefully, and any oral problems should be reported to your doctor and dentist.

Important side effects associated with bisphosphonates and denosumab used in the treatment of cancer pain. *The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Anticonvulsants

Common side effects associated with the **anticonvulsants** used to treat cancer-related pain include dizziness, **fatigue**, sleeping for unusually long periods (**somnolence**), swelling of the hands and feet, weight gain, weakness (**asthenia**) and dry mouth with **gabapentin**, and dizziness, **somnolence** and swelling with **pregabalin** *(Esin and Yalcin, 2014)*. The table below summarises the important side effects of **anticonvulsants** that you should be aware of. It is important to note that some of these side effects are rare.

DRUG CLASS	IMPORTANT SIDE EFFECTS	HOW THE SIDE EFFECTS MAY BE MANAGED
Anticonvulsants	• Dizziness • Hallucinations • Sleeping for unusually long periods (**somnolence**)	• Let your doctor or nurse know if you experience dizziness, hallucinations or long periods of sleep. Your doctor may decide to reduce the dose of **anticonvulsant** or opioid, or switch to a different **analgesic** medication.

Important side effects associated with anticonvulsants used in the treatment of cancer pain. *The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Antidepressants

Tricyclic antidepressants are commonly associated with dry mouth, sleeping problems, blurred vision and **urinary retention**. The most common side effect of **duloxetine** treatment is nausea, but this is markedly reduced if the drug is taken after meals. The table below summarises the important side effects of **antidepressants** that you should be aware of. It is important to note that some of these side effects are rare.

DRUG CLASS	IMPORTANT SIDE EFFECTS	HOW THE SIDE EFFECTS MAY BE MANAGED
Antidepressants	• Constipation • Dizziness • Agitation • Impairment in memory and thinking	• Constipation can be treated with **laxatives** and lifestyle changes such as increasing the amount of fibre and fluid in the diet and exercising as much as possible. • You might experience some dizziness and impairment in general attention and concentration – if this occurs you should not drive or operate machinery.

Important side effects associated with antidepressants used in the treatment of cancer pain. *The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Steroids

Serious side effects from **steroids** are rare. Common side effects of **steroids** may include changes in blood sugar levels, difficulty sleeping, indigestion and swelling in the face. The table below summarises the important side effects of **steroids** that you should be aware of. It is important to note that some of these side effects are rare.

DRUG CLASS	IMPORTANT SIDE EFFECTS	HOW THE SIDE EFFECTS MAY BE MANAGED
Steroids	• Increased risk of infection • Increased appetite and weight gain • Mood changes • **Osteoporosis** • Swelling of the hands and feet	• Tell your doctor or nurse immediately if you experience signs of infection, such as fever, headaches, aching muscles, cough, sore throat, pain passing urine or feeling cold and shivery. Infections are usually treated with antibiotics. It's important that any symptoms of infection are reported, as **steroids** reduce the activity of the immune system, resulting in an increased risk of infection. • **Steroids** frequently increase appetite which can make it difficult to control your weight. You can talk to a dietitian about how to safely control your weight while taking **steroids**. Your appetite will return to normal when you stop taking **steroids**. • Feeling anxious or emotional are common side effects of **steroids** – let your doctor or nurse know if you or anyone in your family has a history of depression or bipolar disorder so they can decide if **steroids** are the appropriate treatment for you. • Patients at risk of **osteoporosis** (e.g. post-menopausal females) will be monitored for any signs of bone weakening. You can reduce your risk of **osteoporosis** by stopping smoking, limiting your intake of alcohol, taking more exercise and taking supplements to ensure you are getting enough calcium and vitamin D. • Swelling in the feet may be reduced by avoiding standing for long periods of time, and by putting your feet up when you are sitting down.

Important side effects associated with steroids used in the treatment of cancer pain. *The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Lidocaine

Lidocaine patches are associated with few side effects; the most common are skin reactions such as **pruritus**, **erythema**, burning, rash, swelling and dermatitis at the patch application area. These are usually temporary and clear up soon after patch removal. The table below summarises the important side effects of **lidocaine** patches that you should be aware of. It is important to note that some of these side effects are rare.

DRUG CLASS	IMPORTANT SIDE EFFECTS	HOW THE SIDE EFFECTS MAY BE MANAGED
Lidocaine patches	• Skin irritation • **Hypersensitivity** reaction	• Irritation around the patch application area is a common side effect of **lidocaine** patches, but if this gets too painful you should remove the patch and tell your doctor or nurse so they can arrange alternative pain relief. • Tell your doctor or nurse immediately if you develop a rash or fever, as these can be signs of a **hypersensitivity** reaction and the **lidocaine** patch may need to be removed.

Important side effects associated with lidocaine used in the treatment of cancer pain. *The most recent Summary of Product Characteristics (SPC) for any individual drug can be located at: http://www.ema.europa.eu/ema/.*

Radiotherapy

The side effects of **radiotherapy** for pain relief are usually mild and will depend on which part of the body is treated. Possible side effects include **fatigue** and skin irritation in the treatment area. **Radiotherapy** to the ribs, stomach area, pelvic area or skull can cause nausea, but this can be reduced with anti-sickness drugs taken before the treatment. **Radiotherapy** to the pelvis or bowel area can result in diarrhoea, but again, medicines are available to counteract this side effect. Occasionally, **radiotherapy** can cause a flare up of pain for 1 or 2 days after the treatment, in which case additional painkillers may be temporarily needed. **Radiotherapy**-related **neuropathic pain** can occur as a late side effect of **radiotherapy** in cancer survivors.

What can I do to improve my well-being?

During and after you have had treatment for cancer, you may feel very tired and emotional. Give your body time to recover and make sure you get enough rest, but there is no reason to limit activities if you are feeling well. It is important to take good care of yourself and get the support that you need.

- **Eat well and keep active:** Eating a healthy diet and keeping active can help improve your well-being. It is important to start slowly and build up as you start to feel better. Aerobic activity such as walking has been shown to increase well-being. It is very important to take the pain relief you need in order to stay active.
- **Take plenty of rest when you need it:** Give your body time to recover and make sure you get enough sleep. Complementary therapies, such as hypnotherapy, massage and meditation, may help you relax and cope better with pain. Your hospital may offer complementary therapy; ask your doctor for details.

Complementary therapies may help to manage pain

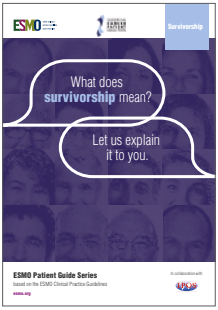
It is very important that you take the correct pain relief medications as instructed, to allow you to stay active and healthy. Additionally, the following eight recommendations form a good foundation for a healthy lifestyle during and after cancer *(Wolin et al., 2013)*:

- Don't smoke.
- Avoid second-hand smoke.
- Exercise regularly.
- Avoid weight gain.
- Eat a healthy diet.
- Drink alcohol in moderation (if at all).
- Stay connected with friends, family and other cancer survivors.
- Attend regular check-ups and screening tests.

A healthy lifestyle will help to improve your physical and mental well-being

Studies have shown that regular exercise is an important part of a healthy lifestyle, helping you to keep physically fit and avoid weight gain. It is very important that you listen carefully to the recommendations of your doctor or nurse, and talk to them about any difficulties you have with exercise.

Pain can be a long-term side effect of cancer treatment. It is important that you tell your doctor or nurse about any persistent or new pain so they can help you to manage it. Your doctor or nurse will also work with you to develop a personalised survivorship care plan.



For further information and advice regarding how to regain your life as far as possible during and after treatment for cancer, see ESMO's patient guide on survivorship (http://www.esmo.org/Patients/Patient-Guides/Patient-Guide-on-Survivorship).

For further information and advice about your specific type of cancer, see ESMO's cancer guides for patients (https://www.esmo.org/Patients/Patient-Guides).

Emotional support

It is common to be overwhelmed by your feelings when you are undergoing or have been through treatment for cancer. If you feel anxious or depressed, talk to your doctor or nurse – they can refer you to a specialist counsellor or psychologist who has experience of working with the emotional problems of people dealing with cancer and cancer-related pain. It may also help to join a support group so that you can talk to other people who understand exactly what you are going through.

Support groups

In Europe, there are patient advocacy groups which help patients and their families to navigate the cancer landscape.

Support groups are available for specific types of cancer. They can be local, national or international, and they work to ensure patients receive appropriate and timely care and education. These groups can provide you with the tools you may need to help you better understand your disease, and to learn how to cope with it, living the best quality of life that you can. Ask your doctor or nurse for information about support groups for patients with your type of cancer.

The European Cancer Patient Coalition is a large European cancer patients' association that supports and represents patients affected by all types of cancer in many European countries.

For further information about the European Cancer Patient Coalition visit: http://www.ecpc.org/

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GLOSSARY

ADJUVANT (TREATMENT)
Treatment given in addition to the primary treatment – for example **anticonvulsants** may be given as an **adjuvant** treatment alongside opioids

ALFENTANIL
A type of opioid **analgesic** drug

ANALGESIC
A drug that reduces pain

ANTICONVULSANT
A drug or other substance used to prevent or stop seizures or convulsions

ANTIDEPRESSANT
A drug used to treat depression

ANTIDOPAMINERGIC
A drug that prevents or counteracts the effects of dopamine

ASPIRIN
A type of non-opioid **analgesic** drug – **aspirin** is an **NSAID**

ASTHENIA
Abnormal feeling of weakness or lack of energy

BISPHOSPHONATES
Drugs that help prevent, or slow down, **osteoporosis**, and prevent broken bones and other bone problems caused by bone **metastases**

BUCCAL
Administered between the gum and cheek

BUPRENORPHINE
A type of opioid **analgesic** drug

CANNABINOID
A type of chemical in cannabis

CENTRAL NERVOUS SYSTEM
The brain and spinal cord

CHEMOTHERAPY
A type of cancer treatment using medicine that kills the cancer cells by damaging them, so that they cannot reproduce and spread

CLINICAL TRIAL
A study that compares the effects of one treatment with another

CODEINE
A type of opioid **analgesic** drug

COMPRESSION FRACTURE
A break in a bone caused by pressure, in which the bone collapses

CORDOTOMY
A surgical procedure to disable selected pain nerves in the spinal cord, without affecting other nerves in the body

CURATIVE
A treatment that is intended to cure the cancer

DENOSUMAB
A drug used to treat **osteoporosis** and prevent broken bones and other bone problems caused by bone **metastases**

DEXAMETHASONE
A type of **steroid**

DIAMORPHINE
A type of opioid **analgesic** drug

DICLOFENAC
A type of non-opioid **analgesic** drug – **diclofenac** is an **NSAID**

DIHYDROCODEINE
A type of opioid **analgesic** drug

DULOXETINE
A drug used to treat depression

ERYTHEMA
Redness of the skin

EXTERNAL BEAM RADIOTHERAPY
A type of **radiotherapy** that uses a machine to aim high energy rays at the cancer from outside of the body

FATIGUE
Overwhelming tiredness

FENTANYL
A type of opioid **analgesic** drug

FIRST-LINE
The initial treatment given to a patient

GABAPENTIN
A type of **anticonvulsant** drug

GASTROINTESTINAL SYSTEM
The system of organs responsible for getting food into and out of the body and for making use of food to keep the body healthy – includes the **oesophagus**, stomach and intestines

GLOSSARY

HERPES ZOSTER
A viral infection characterised by a painful rash with blisters – also known as shingles

HYDROMORPHONE
A type of opioid **analgesic** drug

HYPERSENSITIVITY
An exaggerated response by the immune system to a drug or other substance

IBUPROFEN
A type of non-opioid **analgesic** drug – **ibuprofen** is an **NSAID**

INTRANASAL
Administered through the nose

INTRATHECAL
Administered via injection into the fluid-filled space around the spinal cord

INTRAVENOUSLY
Administered into a vein

LAXATIVE
A substance that encourages bowel movements

LIDOCAINE
A type of **local anaesthetic**

LOCAL ANAESTHETIC
A medication that causes reversible absence of pain sensation around the site of administration

METASTASES
Cancerous **tumours** that have originated from a primary **tumour**/growth in another part of the body

METASTATIC (CANCER)
A cancer that has spread from its (primary) site of origin to different parts of the body

METHADONE
A type of opioid **analgesic** drug

METHYLPHENIDATE
A drug that is a **central nervous system** stimulant

METOCLOPRAMIDE
A drug that is used to treat nausea and vomiting

MORPHINE
A type of opioid **analgesic** drug

NALOXEGOL
A drug that is used to treat opioid-induced constipation – naloxegol is a **PAMORA**

NALOXONE
A drug that is used to treat opioid-induced constipation – naloxone is a **PAMORA**

NEUROLYTIC BLOCKADE
Injection of a chemical around a nerve to cause damage, blocking pain signals to the brain

NEUROPATHIC PAIN
Pain caused by damage or injury to the nerves that transfer information between the **central nervous system** and other parts of the body

NON-STEROIDAL ANTI-INFLAMMATORY DRUG (NSAID)
A type of non-opioid drug that decreases fever, swelling, pain and redness

OESOPHAGUS
The food pipe; the tube that connects your throat with your stomach

OSTEONECROSIS
Loss of blood flow to bone tissue, causing the bone to die

OSTEOPOROSIS
A decrease in the amount and thickness of bone tissue, which causes the bones to become weak and break more easily

OXYCODONE
A type of opioid **analgesic** drug

PARACETAMOL
A type of non-opioid **analgesic** drug

PERCUTANEOUS VERTEBROPLASTY
A procedure used to repair a bone in the spine that has a break. Bone cement is injected into the broken bone to make it stronger

PERIPHERAL NERVE BLOCK
Injection of **local anaesthetic** around a nerve to block the pain signals travelling to the brain

PERIPHERALLY ACTING MU-OPIOID RECEPTOR ANTAGONISTS (PAMORAS)
A class of drug that is used to treat opioid-induced constipation

PHOTON BEAMS
X-rays used to destroy cancer cells during **radiotherapy**

GLOSSARY

PLACEBO
An inactive substance that looks the same as, and is given the same way as, an active drug or treatment being tested

PLATELET
Tiny blood cell that helps your body form clots to stop bleeding

PLATELET AGGREGATION
The clumping together of **platelets** in the blood. **Platelet aggregation** is one of the events leading to the formation of a clot

PREGABALIN
A type of **anticonvulsant** drug

PRURITUS
Severe itching of the skin

PSYCHOSTIMULANT
A drug that is a **central nervous system** stimulant

RADIOISOTOPE THERAPY
A treatment that uses an unstable form of a chemical element that releases radiation as it breaks down and becomes more stable

RADIOTHERAPY
Treatment involving the use of high-energy radiation, which is commonly used to treat cancer

RADIUM-223
A radioactive liquid used to treat prostate cancer that has spread to the bone

REFRACTORY PAIN
Pain that does not respond to treatment

SOMNOLENCE
Sleeping for unusually long periods of time

SPINAL CORD COMPRESSION
Pressure on the spinal cord that may be caused by a **tumour**

SPINAL CORD STIMULATION
Application of mild electrical impulses to the spinal cord to modify and mask the pain signals travelling to the brain

STEREOTACTIC BODY RADIOTHERAPY
A type of external **radiotherapy** that uses special equipment to position the patient and precisely deliver radiation to a **tumour**

STEROID
A type of drug used to relieve swelling and inflammation. Some steroid drugs also have antitumour effects

SUBCUTANEOUSLY
Administered beneath the skin

SUBLINGUAL
Administered under the tongue

SUPPOSITORY
A solid drug formulation that melts at body temperature. For cancer pain relief, a **suppository** is inserted into the rectum

SUSPENSION
A liquid containing small pieces of drug. The drug is not complete dissolved in the solution

TARGETED THERAPY
A newer type of cancer treatment that uses drugs or other substances to precisely identify and attack cancer cells, usually while doing little damage to normal cells

TOLERANCE
When a patient no longer responds to a drug in the way they initially responded

TRAMADOL
A type of opioid **analgesic** drug

TRANSDERMAL
Absorption of a drug through unbroken skin

TRICYCLIC ANTIDEPRESSANTS
A type of drug used to treat depression

TUMOUR
A lump or growth of abnormal cells. **Tumours** may be benign (not cancerous) or malignant (cancerous). In this guide, the term '**tumour**' refers to a cancerous growth, unless otherwise stated

URINARY RETENTION
Inability to empty the bladder

VERTEBRAE
Small bones that form the spine

This guide has been prepared to help you, your friends and your family better understand the nature of cancer pain and the treatments that are available. The medical information described in this document is based on the clinical practice guidelines of the European Society for Medical Oncology (ESMO) for the management of cancer pain. We recommend that you ask your doctor about the types of treatments available in your country for cancer pain.

This guide has been written by Kstorfin Medical Communications Ltd on behalf of ESMO.

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GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

We can help you understand cancer pain and the available treatment options.

This guide has been prepared to help you, as well as your friends, family and caregivers, better understand cancer pain and its treatment. The medical information described in this document is based on the ESMO Clinical Practice Guidelines for the management of cancer pain.

For more information, please visit **www.esmo.org**