

Information for doctors of patients with a brain tumor in the end-of-life phase

Online: <https://hersentumorcentrum.nl/eol-artsen/>

Introduction

Your patient has a brain tumor for which anti-tumor therapy is no longer effective or available. The patient, family and friends are aware of the situation and are aware of the possibility of a rapid further deterioration. As a general practitioner, hospital doctor or nursing home doctor, we ask you to take over the guidance and care in this final phase of life. We realize that you may not come into contact with this specific problem and of course you can always contact us. Our contact details are at the bottom of this information letter.

This letter provides explanations and (treatment) advice for some common symptoms and other problems in the last phase of life. The symptoms listed have a link to the respective symptom in the appendix "[Dexamethasone, symptoms and symptom management](#)".

A life expectancy for a patient with a brain tumor cannot be reliably predicted. Sometimes a patient with a brain tumor recovers and turns out not to be in the last phase of life.

The symptoms listed below have a link to the respective symptom in the appendix "[Dexamethasone, symptoms and symptom management](#)".

Palliative care in the last phase of life

Efficient coordination and transfer between all care providers involved is essential for brain tumor patients in the last phase of life. With this letter, we hope to contribute to that. It is equally important that your colleagues and service observers are aware of the patient's situation and the agreements that have been reached.

In the last phase of life, brain tumor patients can often no longer be involved actively in end-of-life decisions due to [cognitive disorders](#), [aphasia](#) or [consciousness disorders](#). We cannot emphasize enough that starting counseling early (advance care planning) and providing information about the palliative process and the necessary decisions that are made around the end of life make the process more bearable. This can help maintain or improve quality of life.

The expected course

The symptoms listed below have a link to the respective symptom in the appendix "[Dexamethasone, symptoms and symptom management](#)".

Neurological failure

Progression of the brain tumor will eventually lead to (increase of existing) [neurological deficits](#). This mainly causes [\(hemi\) paresis, gait disturbances, aphasia, a hemianopsia](#) and problems with attention, memory or concentration. [Behavioral changes](#) may also occur. Many patients react less spontaneously and above all more slowly, show fewer emotions and become increasingly passive. Others are busy, uninhibited, easily irritated, chaotic and restless. Often the patient has little insight into his disease. Sometimes, but not always, [epileptic seizures](#) can occur or increase in severity and frequency.

Due to the increasing neurological deficit, behavioral changes and epilepsy, the patient will become more dependent. Many people with brain tumors eventually become bedridden.

Complications

Complications that can occur include infection (especially pneumonia), leg thrombosis, and pulmonary embolism. Make clear agreements about which complications should no longer be treated. Also discuss with the patient, family and loved ones that the patient will not be resuscitated. Respiratory or cardiac arrest is often caused by progression of the brain tumor. The chance that a resuscitation will succeed (without increased brain damage) is therefore very small.

The dying phase

Usually someone with a brain tumor dies from the effects of the brain tumor itself. The most common symptoms in brain tumor patients in the dying phase are a [decrease in consciousness](#), swallowing disorders, an increase in neurological deficits, communication problems, epilepsy, incontinence, [headache](#), progressive cognitive impairment and agitation or confusion. [Nausea and/or vomiting](#) is relatively uncommon. The decline in consciousness may initially manifest as lethargy, somnolence, or increased need for sleep, but eventually the patient often becomes comatose. It does happen that consciousness is variable. Decrease in consciousness and swallowing disorders often go hand in hand and mainly occur in the last week before death. If the patient is no longer responsive (comatose), we advise to discontinue the dexamethasone.

General common symptoms and complaints in the dying phase are discussed in the (Dutch) guideline "Care in the dying phase" on pallialine (Dutch): <https://www.pallialine.nl/stervensfase>

See also (Dutch): <https://www.knmg.nl/advies-richtlijnen/dossiers/levenseinde-2/levenseinde-zorg.htm>

Palliative sedation

Despite the generally progressive neurological deficit, patients with a brain tumor in the last phase of life often do not experience their situation as 'unbearable and hopeless suffering'. Possible complaints (for example headaches) can usually be effectively treated with medication. Palliative sedation for inadequate symptom control is sometimes necessary in difficult-to-treat epilepsy or severe restlessness.

See (Dutch): <https://www.pallialine.nl/sedatie>

See (Dutch): <https://www.knmg.nl/advies-richtlijnen/dossiers/palliatieve-zorg-en-palliatieve-sedatie.htm>

Supportive guidance for patients, family and friends (most only in Dutch)

- The Voluntary Organization for Palliative and Terminal Care (VPTZ).
Website: www.vptz.nl
- Mezzo (National association that stands up for everyone who takes care of another)
Website: www.demantelzorger.nl
- The informal care center (Professional organization for all informal carers)
Website: <https://paletwelzijn.nl/mantelzorg/>
- Drop-in centers and Psycho-oncology centers of the IPSO network
Website: www.ipso.nl
 - The Vruchtenburg in Rotterdam
Website: www.defruitenburg.nl

- The Helen Dowling Institute in Utrecht
Website: www.hdi.nl
- Palliative care networks
Website: www.stichtingfibula.nl

More and more home care institutions employ a specialized oncology or palliative nurse who can provide support at home

If necessary, consult with (telephone number)

Further information

During office hours you can contact:
Telephone numbers and email addresses

Outside office hours you can contact:
Telephone numbers

Colophon

The two information letters for doctors and patients, family and friends** regarding the end of life in brain tumor patients were written by Dr. Walter Taal¹ under the auspices of LWNO. Translation by Eva van Diest and Walter Taal.

Helpful suggestions for improving these letters have been provided by (in alphabetical order): Prof. dr. dr. Martin J. van den Bent¹, dr. Jacqueline E.C. Bromberg¹, Mrs. Marit Eland¹, Dr. Johan A.F. Koekoek^{2,3}, Dr. Tjeerd J. Postma⁴, Prof. dr. Dr. Carin C.D. van der Rijt⁵, dr. Tom J. Snijders⁶, Prof. dr. Dr Martin J.B. Taphoorn^{2,3} and Mrs. Hanneke Zwinkels – van Vliet².

¹Department of Neuro-Oncology/Neurology, Erasmus MC Cancer Institute, Rotterdam. ²Department of Neurology, MCH, The Hague. ³Department of Neurology, LUMC, Leiden. ⁴Department of Neurology, VUMC, Amsterdam. ⁵Department of Internal Oncology, Erasmus MC Cancer Institute, Rotterdam. ⁶Department of Neurology, UMCU, Utrecht.

** In addition to this information letter for doctors, there is also a letter for patients, family and friends.
See <https://hersentumorcentrum.nl/eol-patienten/>

Appendix: Dexamethasone, Symptoms and Symptom Management

Below are some common symptoms that can be caused by a brain tumor. Possible other (treatable) causes are mentioned. The treatment of symptoms is briefly discussed, sometimes with references to existing guidelines (most only in Dutch). There are many more symptoms that can occur in the last phase of life. For this, see palliative (Dutch): <https://www.palliative.nl/index.php>

Dexamethasone

In patients with a brain tumor, dexamethasone is almost always prescribed. Dexamethasone reduces the edema caused by the brain tumor. Dexamethasone often helps (certainly in the beginning) against symptoms caused by the brain tumor.

Please note! Continuing or increasing dexamethasone in the last phase of life can also prolong the suffering of the brain tumor patient!

The dose of dexamethasone

The dose of dexamethasone is highly dependent on the individual situation. In general, about 4mg dexamethasone per day is a good starting dose and it is believed that a daily dose of more than 16mg dexamethasone is not useful. Dexamethasone has a long half-life and can be dosed once or twice daily. In the case of increased [neurological deficit](#) and/or [headaches](#), the dose of dexamethasone should be increased considerably (eg doubling), so that a rapid effect occurs. After that, it can be gradually reduced (e.g. every 3 days a reduction of the daily dose by 0.5 mg) to the minimum effective dose. If there is no positive effect after a few days, it is better to go back to the starting dose immediately, in order to prevent side effects. Sometimes a single high dose of dexamethasone can be given (e.g. 8 or 10mg once) in order to achieve a quick decrease of symptoms. In the last weeks before death, continuing or increasing dexamethasone can also prolong the patient's suffering! Consult with a neuro-oncologist about this if necessary.

In case of difficulties with swallowing, dexamethasone can be administered subcutaneously in equal doses. If the patient is no longer responsive, we advise to discontinue the dexamethasone.

Side Effects of Dexamethasone

Only the most important side effects for this situation are discussed here.

Increase in appetite, weight gain, altered fat distribution (face, trunk).

Advise patient not to give in to increased appetite. Try to encourage the patient to keep moving as much as possible (for example, walking), if the condition allow this.

Stomach issues

It is not necessary to give proton pump inhibitors preventively. Do give this in case of stomach problems. With a combination of dexamethasone, anticoagulation and opioids, it is advisable to prescribe proton pump inhibitors. (e.g., pantoprazole 20-40mg once or twice a day or esomeprazole 20-40mg once a day). NSAIDs are relatively contraindicated and also not rational with concomitant dexamethasone use; if deemed necessary, also combine NSAIDs with a proton pump inhibitor.

Hyperglycemia

Check the blood at least once every 1-2 weeks for the development of hyperglycemia.

Insomnia

Dexamethasone can cause [insomnia](#). Sometimes it helps to prescribe the daily dose in one go in the morning. If necessary, a benzodiazepine can be prescribed for the night.

Osteoporosis prevention

Osteoporosis prophylaxis with dexamethasone use is no longer recommended at this stage, due to an expected lifespan of less than 3 months. Incidentally, advice with regard to mobility, and in particular undertaking weight-bearing activities, such as walking, can be important.

Psychiatric disturbances

Dexamethasone can cause [psychiatric complications](#), including [delirium](#). This usually occurs at a high dose and usually starts within the first few weeks of starting or increasing dexamethasone. However, delirium can occur at any dose, at any time, and also during dexamethasone withdrawal. However, it is not always easy to distinguish with behavioral disorders caused by the brain tumor itself. Psychiatric disturbances due to dexamethasone, however, more often show similarities with a manic episode or manic psychosis. Patients are often cheerful, restless and uninhibited. But also easily irritated, chaotic and restless. Sometimes aggression occurs. If psychiatric side effects are suspected, the dexamethasone dose can be reduced as a first step. Sometimes antipsychotics are indicated, such as haloperidol (starting dose 1-2 mg twice daily or 0.5-1 mg s.c. twice daily) or olanzapine. Consult with a psychiatrist if necessary.

Progressive focal neurological deficit

Progressive focal neurological deficits, such as hemiparesis, aphasia and/or hemianopsia, is usually caused by the brain tumor. Consider (increasing the dose of) dexamethasone in case of progressive neurological deficit. Aids such as a cane, walker or wheelchair can be supportive. Sometimes (increased) focal failure has a metabolic cause. This can be seen especially in hypoglycemia and in hyponatremia. Depending on the situation, a routine laboratory examination can therefore sometimes be useful.

Behavioral changes

Behavioral changes are common. Disease insight is often reduced. Patients with a brain tumor may be bradyphrenic and usually respond less spontaneously. They sometimes show less emotions or are more easily irritated and become increasingly passive. Sometimes an increase in the dexamethasone can be useful, but often medication is not effective. Also consider other causes, such as silent delirium or side effects of medication, such as anticonvulsants.

Sometimes brain tumor patients, on the other hand, become busy and uninhibited. They are easily irritated, chaotic and restless. Very occasionally people are very confused and aggressive. In such situations antipsychotics can be indicated, such as haloperidol (starting dose 1-2 mg p.o. or 0.5-1 mg s.c. twice daily) or olanzapine. Consult with a psychiatrist if necessary. Also consider dexamethasone as a cause of this behaviour, especially if the dexamethasone has been started or increased in the last few weeks. Also consider other causes for delirium. See also the guideline delirium on palliative (Dutch): <https://www.palliative.nl/delirium>
See also (Dutch): <https://richtlijnen.nhg.org/standaarden/delirium>

Delirium

See behavioral changes and decreased consciousness.

Epilepsy

Always consult a neurologist in the event of a (partial) status epilepticus, severe and/or new epileptic seizures. However, not everyone with a brain tumor will get seizures.

Sometimes the epileptic seizure itself is not seen (for example, during sleep or a non-convulsive seizure) and only the (passing) postictal phase or decreased consciousness is observed. Typically, this postictal phase gradually recovers, but this can sometimes take days. In general, epilepsy in a brain tumor patient can be treated effectively with medication.

Anti-epileptics

The most commonly used anticonvulsants are: levetiracetam, sodium valproate, lacosamide, clobazam, carbamazepine, phenytoin, oxcarbazepine, topiramate, gabapentin and lamotrigine. Always consult a neurologist about this type of medication.

Medication to cut an attack

If the convulsions last longer than 5 minutes, it is advised to intervene with medication. Examples of drugs to stop an attack are midazolam (nasal spray), diazepam (rectal application) and clonazepam (oral drops). Midazolam nasal spray (27.8mg/ml; 2.5mg per spray) in a dose of 1 puff of 2.5mg in each nostril is the easiest to use and therefore the most prescribed. Opened packages of the midazolam nasal spray have a shelf life of 3 months.

Anti-epileptics in case of inability to swallow

More than a third of brain tumor patients experience seizures in the last week of life. It is therefore essential to continue the treatment with anti-epileptic drugs, even in case of swallowing difficulties and/or loss of consciousness. Rectal administration of carbamazepine, levetiracetam and sodium valproate is possible, but preparations have to be specially prepared by the pharmacist. A good alternative is an adequate dose of benzodiazepines, such as liquid clonazepam 2.5 mg/ml buccal or sublingual; with an initial dose of 1-2 mg and afterwards as a maintenance dose of 2-4 mg per day. It is also possible to opt for rectal diazepam starting with 10 mg 3 times a day. For patients with refractory epilepsy and insufficient effect of the above treatment, starting palliative sedation may be useful if the life expectancy is shorter than 1-2 weeks.

See also the epilepsy guideline of the Dutch Association for Neurology (Dutch): <https://epilepsy.neurologie.nl>

Headache

A brain tumor can cause a headache, but certainly not always. However, it is important to also consider other causes for headaches, such as constipation and side effects of medication.

Headaches caused by the brain tumor are best treated with (an increase in) dexamethasone. Prescribe analgesics if the headache is mild or (an increase in) dexamethasone does not help or does not help sufficiently.

Paracetamol and NSAIDs

It is recommended to start with paracetamol up to 1000mg 4 times a day. With concomitant use of dexamethasone, the use of NSAIDs is not rational and not recommended, due to the risk of gastric bleeding.

Opioids

Do not wait too long before giving opioids if paracetamol and dexamethasone have insufficient effect, especially with more severe headaches. Weak-acting opioids, such as tramadol or codeine, should be skipped in case of severe headaches. Depending on the severity of the headache one can start oral morphine 20-60mg/day or an equivalent. If the patient is unable to swallow properly, the fentanyl patch (starting dose 12 or 25 micrograms)

is a good option. In addition to a modified-release opioid, always prescribe “rescue” medication in the form of a fast-acting opioid, preferably of the same class. See also cancer pain on palliative (Dutch): <https://www.palliative.nl/pijn-bij-patienten-met-kanker>

Nausea and vomiting

Nausea and/or vomiting is relatively uncommon for brain tumor patients, unless the tumor is located in the posterior cranial fossa. Therefore, it is important to consider other causes, such as side effects of medication (opioids), terminal renal failure, vestibular causes (dizziness) or an ileus.

Nausea and vomiting caused by the brain tumor should be treated with (an increase in) dexamethasone. If the effect of the dexamethasone is insufficient, one can start with oral or rectal metoclopramide (3 dd 10-20 mg oral or rectal). In case of extrapyramidal side effects (rigidity/dystonia) of metoclopramide, a switch is made to domperidone (3-4 dd 10-20 mg oral or 3-4 dd 60-120 mg rectal). Especially in case of simultaneous hallucinations and/or delirium, haloperidol (2 dd 1-2 mg oral or 2 dd 0.5-1 mg subcutaneous.) can also be chosen. A scopolamine patch (1-2 patches of 1.5 mg every 3 days) may be considered for vestibular causes (dizziness). In our experience, aprepitant (1 dd 80 mg p.o.) can be effective for treating nausea and vomiting as a result of a brain tumor in the posterior cranial fossa (consult this with the neurologist if necessary).

See also (Dutch): <https://www.palliative.nl/misselijkheid-en-braken>

Decreased consciousness

An increased need for sleep, somnolence and/or coma is often caused by the progressive brain tumor. The decline in consciousness is progressive, but can (certainly in the beginning) still be somewhat variable. Consider (increasing) dexamethasone in case of decreased consciousness which seems to be caused by the brain tumor. However, there are also many other (sometimes treatable) causes for decreased consciousness in the last phase of life.

Metabolic Causes

Decreased consciousness can have a metabolic cause, such as fluid deficiency, liver and/or kidney function disorders with medication use or hyperglycemia with dexamethasone use. In case of a metabolic cause, negative myoclonias are regularly seen (flapping tremor or asterixis).

Drug Causes

Medications such as antipsychotics, benzodiazepines, opioids and anticonvulsants can also play a role. For example, valproic acid can cause isolated hyperammonemia. In this case negative myoclonias are seen (flapping tremor or asterixis).

Epilepsy

Epilepsy can also cause decreased consciousness and is not always accompanied by convulsions. Sometimes the convulsions are not seen, for example when occurring during sleep. It is also possible that non-convulsive epileptic seizures occur. Often, after an epileptic seizure, consciousness recovers in minutes to hours.

Sleeping disturbances

There are many causes for poor sleep in the last phase of life. It can be the first manifestation of delirium. In case of a bad night's sleep, it is good to keep someone awake as much as possible during the day.

Dexamethasone can also cause insomnia. Sometimes it makes sense to take dexamethasone only in the morning. Sometimes a short prescription of benzodiazepines is necessary.

See also (Dutch): <https://www.pallialine.nl/slaaproblemen>

Incontinence

Urinary incontinence is a common symptom in brain tumor patients. Fecal incontinence is less common. If possible, the underlying cause and/or the influencing factors are treated, such as a urinary tract infection or medication with an anticholinergic effect.

See also (Dutch): <https://www.pallialine.nl/urogenitale-problemen>

This guideline also provides clear advice regarding supportive measures, catheterization and any drug symptomatic treatment.