

Guideline for Palliative Sedation

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Committee on National Guideline for Palliative Sedation

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For the online knowledge file on palliative sedation, see the website www.medischcontact.tv
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Summary

Palliative sedation is the deliberate lowering of a patient's level of consciousness in the last stages of life. It may be administered in two distinct ways:

1. continuous sedation until the moment of death;
2. temporary or intermittent sedation.

Palliative sedation may be superficial or deep. Continuous sedation is always administered in the final stages of life to patients who are dying and are experiencing unbearable suffering.

The object of palliative sedation is to relieve suffering; lowering the level of consciousness is the means to that end. The object is not to lengthen or cut short the patient's life. It is crucial that palliative sedation should be applied proportionately and adequately, in response to the appropriate medical indications. It is the degree of symptom control rather than the degree to which consciousness must be reduced that determines the dose, combinations, and duration of the drugs administered.

Medical indications for palliative sedation are present when one or more intractable or 'refractory' symptoms are causing the patient unbearable suffering. A symptom is considered to be refractory if none of the conventional modes of treatment is effective or fast-acting enough, and/or if these modes of treatment are accompanied by unacceptable side-effects.

The physician will have to decide whether a symptom is treatable or not on the basis of accepted good medical practice, bearing in mind the specific circumstances of a patient in the last stages of life. Determining whether there are indications for palliative sedation is a medical decision. The decision to administer palliative sedation is not based on a specific moment in time, but is a possible outcome within the context of a palliative care plan. Patient and physician have together arrived at a point where they find themselves, through a complex of problems, with their backs to the wall. The decision-making is influenced by factors such as the views of the patient and the physician concerning a 'good death', the quantity and severity of symptoms, the impact of the somatic complaints on feelings such as fear, the fear of death and of the actual process of dying, powerlessness, uncertainty, grief, anger, sadness, the duration of the illness, the burden on informal carers, and the strength and endurance of the patient and of his informal carers. Physical exhaustion (intense fatigue) may also play a role at this stage, and may exacerbate the degree of suffering. Physical exhaus-

tion is one of the factors contributing to a patient's endurance. This may lead to the conclusion that there is no more scope for any other reasonable interventions aside from palliative sedation.

Pain, dyspnoea and delirium are the most common refractory symptoms. In practice, it is frequently a non-linear combination of diverse dimensions of one or more symptoms that leads to a situation in which the patient experiences unbearable suffering. The context is a contributory factor in this respect. Diverse symptoms and diverse contextual aspects may occur in combination with one another. In such cases it may become clear that it is technically possible, from a medical perspective, to control a specific symptom, but that the presence of other symptoms makes it pointless to do so. The patient's setting (whether he or she is at home, with or without home care, or in a hospice, nursing home or hospital) is also part of that context. Institutions often have different scope for interventions than exist in the home. As a result, it must be recognised that in a home situation, patient and carer have often taken a different route to palliative care and may therefore be at a different stage of the decision-making process than would have applied in the case of clinical care.

In addition to pain, 'existential suffering' may be among the refractory symptoms that go to make up unbearable suffering. Such suffering cannot be alleviated, for instance by communication or spiritual support. These patients are often extremely ill and weak, close to death, and have a range of physical complaints, some of them often severe. Some do not want to experience their final days consciously and may request continuous sedation. The feeling that one's existence is empty or meaningless, which is what we mean by existential suffering, may cause unbearable suffering. This comes within the scope of the approach to palliative care and the guideline. Existential suffering also belongs to the domain of medicine, but it is not open to infinite interpretation. In assessing existential suffering, in addition to medical expertise, expertise in the areas of psycho-social and spiritual problems will also be required. The focus here is on the meaninglessness of existence when death is expected within one or two weeks. In other words, the issue here is never solely existential suffering.

Besides the presence of medical indications, a precondition for the use of continuous sedation is the expectation that death will ensue in the reasonably near future – that is, within one to two weeks. In these circumstances, a medical practitioner may decide to initiate sedation and in principle to continue it until the moment of death. In principle, there is no artificial administration of fluids in the case of continuous sedation.

It is not always easy to estimate how long a patient is likely to live. But once a number of characteristics of the phase of dying have been observed, it can be assumed that the patient is approaching the point at which death is inevitable. The most characteristic feature is that patients virtually cease to eat and drink. In addition, they are frequently cachectic, tired and debilitated, and bedridden. They may also be drowsy and disoriented. It is up to the physician to factor these matters into the decision-making, along with the worsening symptoms of disease, without the expectation that the moment of death can be predicted precisely.

The point is therefore not so much to estimate the time until death, but to observe the progress of the signs described above and to conclude that the patient is dying. It is this that the physician must focus on.

Palliative sedation is a medical procedure, and the responsibility for assessing medical indications, decision-making and implementation therefore lies with the attending physician. Just as in any other area of normal medical procedure, the physician must demonstrably possess the necessary expertise and experience. Given the nature and content of palliative sedation and the indications listed in this guideline, the committee sees no reason to impose the condition that a physician with specific expertise must always be consulted before making the decision to administer palliative sedation.

Where a physician has doubts regarding his own expertise or has difficulty balancing the different considerations involved in deciding whether to start continuous sedation (indications, life expectancy, and the importance of exercising due care), it is standard professional practice to consult the appropriate expert in good time.

This is a general principle of medical practice. One exception to this rule is the compulsory consultation in the case of termination of life on request, since this is an exceptional case and does not come under the heading of normal medical procedure. This in no way applies to continuous sedation until the moment of death or other forms of palliative sedation.

Nonetheless, every physician must be aware that continuous sedation is a radical medical procedure, since it lowers the patient's level of consciousness until the moment of death.

In 2005, continuous sedation was administered in about 12,000 cases. It may be inferred from this that individual physicians have limited experience with the decision-making process and actual practice of continuous sedation. Both decision-making and practical application will often require the support of, and consultation with, other carers.

Continuous sedation within the context of palliative care is highly complex and requires specialist knowledge. The impact of the problems involved here may be such that consultation and cooperation with other carers, not just organisationally but also in matters of substance, is essential. The committee advises physicians to consult the appropriate expert(s) with specialist knowledge of palliative care in good time.

Palliative care characteristically relies on a multidisciplinary approach. Nursing staff can play an important part in providing input for drawing up the indications, estimating whether the conditions have been met, and implementing palliative sedation. That does not absolve the physician of his own responsibility. This applies most particularly to the administration of continuous sedation, the start of which is an emotionally charged event. What is more, situations may occur in which the physician must be able to intervene.

The physician must himself be present at the beginning of continuous sedation.

The physician and the nursing staff would be well advised to discuss this, as well as the evaluation criteria, in advance. This can prevent nursing staff, to whom the subsequent administration of the drug will in many cases be largely entrusted, from finding themselves in an undesirable position and situation.

Introducing sedation in phases is highly to be recommended. If an adequate dose does not produce the desired effect, one may proceed to the next phase. According to current received opinion, midazolam is the drug of choice. In general, subcutaneous is preferable to intravenous administration.

	Drug	Bolus	Continuous administration
Phase 1	Midazolam	Start with 10 mg s.c. If necessary every 2 hrs 5 mg s.c.	Initial dose 1.5-2.5 mg/hr s.c./i.v. If the desired effect is not achieved, increase the dose by 50% after a minimum of 4 hrs, <i>always</i> in combination with a bolus of 5 mg s.c. If risk factors are present (age>60, weight<60 kg, severe kidney or liver function disorder, very low serum albumin and/or co-medication that could exacerbate the effect of sedation): - lower initial dose (0.5-1.5 mg/hr), and - longer interval (6-8 hrs) before increasing maintenance dose. In the case of doses higher than 20 mg/hr, see phase 2.
Phase 2	Levomepromazine	25 mg s.c./i.v., possibly 50 mg after 2 hrs	0.5-8 mg/hr s.c./i.v. in combination with midazolam. After 3 days, halve the dose to prevent drug accumulation. If the desired effect is not achieved, stop administering midazolam and levomepromazine; see phase 3.
Phase 3	Propofol	20-50 mg i.v.	20 mg/hr i.v., increase by 10 mg/hr every 15 minutes. Administration under the supervision of an anaesthesiologist is advisable. In hospital, this may be considered for phase 2

The initial doses are based on the average patient. The physician should base his decisions on the effect of the medication. In the presence of extreme risk factors, such as a patient with a high (e.g. 100 kg) or low (40 kg) body weight, the initial and subsequent doses may be adjusted upward or downward correspondingly. In case of doubt concerning the dose to be administered, the opinion of a palliative care consultant should be sought. If the patient fails to respond satisfactorily to the initial drug of choice (midazolam), it should be ascertained whether the method of administration and the medication are in order, or whether any disruptive and remediable factors (e.g. a full bladder, constipation) are playing a role.

If a very rapid decrease of consciousness is desirable in an **acute situation**, bolus injections may be administered more frequently.

For **intermittent sedation** (in practice, always nocturnal), midazolam is in principle the only appropriate drug. In this case, phase 1 is maintained, and the medication is started when the patient is falling asleep and stopped 30 min to 1 hr before the desired time of awakening.

The object of palliative sedation is to alleviate the patient's suffering. The evaluation must focus on the patient's comfort. There is no scale available for measuring and scoring a patient's comfort during continuous sedation. A sedation score can be used for the purpose of describing the depth of sedation. However, the point of this is not to score the effect of the drug, but to alert the physician if the sedation is too deep.

The problems and symptoms that prompted the decision to administer continuous sedation should serve as the basis for evaluation. Agreements must be made regarding the observation points and times (including who does what, and when), and these should be evaluated by the carers concerned at least once a day. New symptoms may arise in addition to the existing ones. These must be evaluated in the same way.

The attending physician should visit the patient at least once a day. Attention should focus in particular on any complications (decubitus, urine retention) if these require treatment. The physician will discuss the course of the treatment with the other carer or carers involved.

Meetings may be scheduled with the person's family to evaluate the situation. Nurses too have a definite role here in identifying, observing, measuring and reporting on developments. For the person's family, it may be very important to achieve clarity on the points that could prompt a review of the management of the case.

In situations where continuous, deep sedation until the moment of death is being considered, morphine is often already being given to treat pain or dyspnoea; in these circumstances, it may seem attractive to increase the dose of morphine substantially in the hope of expediting loss of consciousness and death. Closer consideration reveals that its use in this way often has two different aims: first, to render the patient unconscious and second, to hasten death. For neither of these aims, however, is morphine the drug of choice. High doses of morphine frequently produce drowsiness, but not always loss of consciousness. Therapeutic doses of

opioids (that is, doses tailored to the degree of pain or dyspnoea) are not at all likely to shorten life, even if they are high. Moreover, morphine has major side-effects. For instance, it can increase delirium or induce myoclonus.

The committee regards the use of morphine as a sedative as bad practice. Morphine should only be given or continued (alongside sedatives) to relieve pain and/or dyspnoea; the dose should be calculated to relieve the actual or assumed extent of the pain and/or dyspnoea.

Both at policy level and in practice, there is some confusion about the distinction between continuous, deep sedation until the time of death, and euthanasia. As described in this guideline, continuous, deep sedation is a way of ensuring that patients are unaware of their symptoms and hence of alleviating suffering in the period immediately prior to death.

Continuous, deep sedation differs from euthanasia in that its aim is not to shorten life. Indeed, there is no evidence that continuous deep sedation, if carried out in accordance with good medical practice, does shorten life. Consequently, a clear distinction should be drawn between the two.

In recent years it has been suggested that physicians might view continuous, deep sedation as a way of 'avoiding' euthanasia. This implies that continuous, deep sedation is an alternative to euthanasia that is being put forward as such by medical practitioners. The two procedures should be distinguished from one another as clearly as possible. The preconditions that must be fulfilled for continuous sedation and euthanasia do not necessarily coincide. Continuous sedation can only be administered in the terminal phase, which does not apply in the case of euthanasia. However, rare situations may arise in which the indications and necessary preconditions for continuous sedation and euthanasia both apply, such that the patient may be able to choose between these options. In these cases, it is important to ascertain carefully how the patient wishes to put an end to the unbearable suffering he or she is experiencing:

- by lowering the level of consciousness until the time of death, in which case the preferred option would be continuous sedation until the time of death;
- or by remaining conscious until a moment chosen by the patient for the end of life, in which case euthanasia would be the preferred option.

The patient's own wishes are decisive in this situation.

1 Introduction

Historical background

Palliative care has been the subject of considerable interest since the late 1990s, partly because the government has actively promoted it. The past few years have witnessed a proliferation of expertise and skill in this area, and one of the resulting debates has focused on terminal, or as it is now generally called, 'palliative' sedation (see refs. 1-5). The term 'palliative sedation' has thus been added to the existing spectrum of medical decisions at the end of life (MDELs). Figures on palliative sedation were first mentioned in the context of the third empirical MDEL study, published in 2003 (see ref. 6). In its response to this third study, the government urged the medical profession to draft national guideline on terminal sedation (see ref. 7), after which the Dutch Medical Association (KNMG) agreed to appoint a multidisciplinary committee to do so.

After the Guideline for Palliative Sedation were adopted by the KNMG's executive committee at the end of 2005, the state secretary for health, Clémence Ross-van Dorp, presented them to the House of Representatives of the States-General (see ref. 8). The guideline describes the conditions in which palliative sedation is good medical practice. Besides defining the professional standard, they also possess legal significance. In January 2006 the Public Prosecution Service stated that it saw no reason to prosecute physicians who keep to the guideline. Any physician who deviates from them, however, must bear in mind that his actions may be the object of a criminal investigation (see ref. 9).

The need for revised guideline

The debate on palliative sedation has continued since the publication of the guideline in 2005, most notably in relation to continuous, deep sedation.ⁱ When it issued the initial guideline, the KNMG stated that it would actively monitor their content. To this end, it convened the Committee on National Guideline for Palliative Sedation in 2007 (for the composition of which, see annexe I).ⁱⁱ

ⁱ Palliative sedation may take a variety of forms: deep or superficial, and temporary/intermittent or continuous.

ⁱⁱ Three meetings were held in 2007 and four more in 2008. In addition, several topics were discussed by email. After this, diverse parties and experts in the field were consulted and the text was revised in response to their comments (see annexe II).

There are three areas of debate. First, research has shown that in the past, physicians did not always act in accordance with earlier regional guidelines, which served in part as the basis for the KNMG Guideline (see ref. 10). Several questions therefore arise. Are physicians sufficiently familiar with the KNMG Guideline? Are they applied adequately in practice?^{III} The second area of debate relates to specific elements of the Guideline. When can a symptom be classified as 'refractory'? And do all physicians have the necessary skill to make that judgement? Should it not be compulsory to consult an expert opinion? To what extent is existential suffering an indication for palliative sedation? And as regards the requirement that continuous sedation can only be initiated if death is expected within one to two weeks, is it possible to estimate time of death in this way? (see refs. 11-20). The third area of debate concerns the relationship between continuous, deep sedation and euthanasia (see refs. 21-27).

The committee has taken due note of these discussions, and has concluded that there is now a clearer picture of the practice of palliative sedation, including its relationship to euthanasia. Nonetheless, a number of problems remain that require further attention:

1. The physician and the patient determine together whether or not a specific symptom is 'refractory'. But what exactly makes a symptom 'refractory'? And what happens if an unacceptable situation arises as a result of a combination of symptoms that are not defined individually as refractory? And how much weight is accorded to existential suffering as an indication for palliative sedation?
2. the pre-requisite that death must be expected to follow within one or two weeks poses difficulties in practice, since it is not always possible to predict that death will probably ensue within this time-frame.
3. There is some debate as to whether physicians can be assumed to possess sufficient expertise to decide that continuous sedation is indicated and to carry it out without consultation. Would it not be better to make it compulsory to consult an expert?
4. Stopping – or not starting – the administration of fluids if the patient himself has ceased to take fluids is sometimes seen as problematic in combination with continuous sedation, especially if it is believed that the patient is likely to die sooner as a result of dehydration.
5. The guideline do not provide enough information regarding acute sedation.
6. It has become clear that in practice, physicians are not always present at the beginning of palliative sedation.

^{III} The VU Medical Centre in Amsterdam and Erasmus Medical Centre in Rotterdam are researching this subject.

7. The impression exists, on the basis of a pharmaco-kinetic study (to be submitted for publication in the near future) and a number of observations in practice that the maintenance dose of midazolam given in the medication table is often increased too rapidly.
8. The fact that intermittent sedation is rarely recommended is generally felt to be a failing.
9. The practice of palliative sedation is primarily geared towards decision-making and its initiation. Another question that arises is the way in which the patient's comfort should be assessed.

The KNMG's 2009 Guideline for Palliative Sedation reflect the recent developments in science and medical practice, and clarify the matters listed above in comparison to the 2005 guideline.

Palliative sedation in perspective

The committee wishes to emphasise the following point. A decision to administer palliative sedation is not a one-off decision, but part of a process and course of palliative care. Palliative sedation is one option for alleviating suffering if the customary methods of controlling symptoms are not sufficiently effective and the symptoms are causing unbearable suffering. The patient (if able to make his wishes known) and the physician may reach the conclusion that continuous sedation is the only way of alleviating suffering, if life expectancy is less than one to two weeks. Continuous sedation is always administered in the final stages of life. The patients concerned are dying and experiencing unbearable suffering.

The physician's responsibility and the task of nursing staff

A multidisciplinary approach is a characteristic feature of palliative care. Nursing staff may contribute important input in helping to decide what procedure is indicated, in assessing whether the prerequisites are present, and in carrying out palliative sedation. That does not absolve the physician of his responsibility. This is particularly true in the case of continuous sedation, the initiation of which is an emotionally charged event. The physician must always be aware that continuous sedation is a radical medical procedure, since it lowers the patient's level of consciousness. Furthermore, situations may arise in which the physician must be able to intervene. The physician must therefore be present when continuous sedation is initiated. It is recommended that the physician and the nursing staff discuss this possibility, and the evaluation criteria, in advance. This can prevent nursing staff, to whom the subsequent administration of the drug will in many cases be largely entrusted, from finding themselves in an undesirable position.

Target group

The guideline are intended primarily for medical practitioners.

Basis

This new version of the KNMG Guideline was drafted using the 2005 version, regional guidelines previously drafted in the Netherlands and a number of international models (see refs. 8 and 28-37). In addition, the relevant national and international literature was consulted. Finally, the comments of individuals and organisations consulted by the committee were incorporated (see annexe II). The guideline has been approved by the KNMG's executive committee.

Significance of the guideline

This guideline was intended for use by the various medical specialists who may have to administer palliative sedation. They should be seen as an explicit formulation of the professional standard to be followed by medical practitioners when it comes to palliative sedation. Guidelines are not statutory regulations, but views and recommendations that are based as much as possible on evidence, which can help carers to provide qualitatively good care. Only a limited amount of systematic research has been conducted in the field of palliative sedation (see ref. 38). From the vantage point of medical ethics, it is scarcely possible to conduct randomised comparative clinical research in this area. This guideline is based on the findings in the national and international literature and expert opinion.

The guideline is intended for use in the case of seriously ill adult patients in a wide range of circumstances. Not only may a wide range of symptoms be involved, but the patients' backgrounds and circumstances, such as place of residence (home, hospice, hospital, nursing home) will also be very diverse. Every decision relating to palliative sedation takes full account of the context of the individual patient, who is dying. This will inevitably produce differences of interpretation. The guideline does not describe all the specific situations that may arise, but can be a useful aid in dealing with these intractable conditions. In some situations, circumstances may make it desirable or necessary to depart from this guideline; as is customary, any such departure must be properly argued and furnished with documentation.

The guideline will also need to be regularly updated to incorporate new knowledge. The KNMG will decide when the moment is ripe for an update in consultation with the other parties involved, and take the initiative to arrange it.

Contents

Chapters 2 to 7 discuss matters primarily relating to continuous sedation until the moment of death. These also apply where appropriate to brief, intermittent sedation, but with a few reservations, which the committee lists in chapter 8. In addition, there are subjects that matter in all cases of palliative sedation, but which do not apply primarily to the action taken by medical practitioners. These include dealing with the patient's family and care for carers. The committee deals with these matters in chapters 9 and 10. In chapter 11 the main conclusions on which this guideline are based are enumerated, together with the underlying scientific evidence.

2 What is palliative sedation?

A certain confusion surrounds the definition and usage of the terms palliative sedation, end-of-life sedation, palliative sedation in the final phase, terminal sedation and deep sedation (see refs. 33 and 39-49). In this guideline the committee has decided to use the term 'palliative sedation'. A full definition of the term is provided later in this chapter. The use of the adjective 'palliative' makes it clear that sedation is administered as part of an overall plan or process of palliative care. In addition, 'palliative sedation' refers not only to continuous, deep sedation, but also to temporary, intermittent and/or superficial forms of sedation.

This chapter sets out the relationship between palliative care and palliative sedation, the definition of palliative sedation, the structure of the guideline and the extent to which palliative sedation is practised in the Netherlands.

2.1 Relationship between palliative care and palliative sedation

Regarding palliative sedation as part of an overall plan or process of palliative care means that decisions about whether or not to initiate it are taken within the context of a palliative care plan. Palliative care is the care of patients with life-threatening conditions, who have no prospect of recovery and who will eventually die as a result of their illnesses.

It is defined in greater detail by the World Health Organisation (WHO 2002) as follows (see ref. 50):

'Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.'

Expanding on the definition, the WHO says that the palliative care approach:

- affirms life and regards dying as a normal process;
- intends neither to hasten nor to postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patient's illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if required;

- will enhance the quality of life, and may also positively influence the course of illness;
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage clinical complications (see ref. 51).

The needs of the patient and his/her family are paramount in palliative care. It is therefore not confined to purely medical care and can in principle be provided by anyone, including general practitioners, medical specialists, nursing home physicians, nurses, social workers, psychologists, spiritual counsellors, volunteers and family.

Palliative sedation may be considered where the relief provided by conventional modes of treatment is insufficient and symptoms prove to be refractory (see refs. 33 and 52-53).

2.2 Definition of palliative sedation

Palliative sedation is defined by the committee as:

The deliberate lowering of a patient's level of consciousness in the last stages of life.

The committee has deliberately opted for a definition that is as factual as possible. It does not think that the definition should include normative elements or descriptions that can be regarded as preconditions for good medical practice. These are discussed in subsequent chapters.

The definition has three elements, in that it refers to action that:

1. lowers the level of consciousness;
2. is deliberately taken;
3. relates to a patient in the last stages of life.

These three aspects are discussed below.

1. Action that lowers the level of consciousness

The aim of palliative sedation is to alleviate the patient's suffering. Lowering the level of consciousness is a means to that end. The aim of palliative sedation is not to shorten life (see annexe III) or indeed to prolong it. It is crucial that it should be applied proportionately and adequately, in response to the appropriate medical indications (see refs. 32, 43, 45 and 54-59). It is the degree of symptom control rather than the degree to which consciousness must

be reduced that determines the dose, combinations, and duration of the drugs administered (see ref. 60). Interim evaluations and other decision-making processes must be geared towards alleviating the patient's suffering in order to create a tranquil and tolerable situation.

The debate on the relationship between palliative sedation (in particular continuous, deep sedation) and action intended to terminate life (in particular euthanasia) has continued since the publication of the 2005 guideline. The committee continues to take the view that palliative sedation is a normal medical procedure and must be clearly distinguished from termination of life. For a further discussion of this point, see annexe III.

2. Action that is deliberately taken

The word 'deliberate' is included in the definition in order to exclude situations in which the lowering of the patient's consciousness is a (possibly unintended) side-effect of treatment. The definition of palliative sedation does not include situations where:

1. benzodiazepines are administered in normal doses to relieve insomnia and/or dyspnoea;
2. sedation is an unintended side-effect of medication (for example, as a result of the administration of morphine to relieve pain).

Opioids or other forms of medication not normally used primarily as sedatives are sometimes used, or are administered in raised doses, with the implicit or explicit aim of sedation. The committee regards this as an improper use of these substances and would not include this practice in its definition of palliative sedation (see refs. 4, 40, 41, 47, 52-54 and 61).

The committee would likewise exclude from its definition of palliative sedation any situation where sedation is merely employed during a painful or unpleasant medical procedure such as endoscopy.

3. Action that relates to a patient in the last stages of life

Lowering the patient's consciousness to relieve suffering is appropriate in the last stages of life, in which death is expected to ensue in the near future.

2.2.1 Brief, intermittent and continuous sedation

The term 'palliative sedation' refers to two different situations:

1. continuous sedation until the moment of death;^{IV}
2. brief or intermittent sedation.

In the view of the committee, these situations must both be seen against the wider background of the case and the overall process of palliative care. On the other hand, they differ as regards the substance and wording of the preconditions for good medical practice. It is the first of these situations that has been the main focus of the medical-ethical, legal, social and political debate that has taken place in the Netherlands on the subject of 'terminal sedation' over the past few years. For these reasons, the development of this guideline is important.

This distinction between the two forms of palliative sedation has dictated the structure of this guideline. Chapters 3 to 7 deal with various aspects of continuous, deep sedation until the moment of death, while chapter 8 discusses brief or intermittent sedation.

2.3 Structure of the guideline

The remainder of this guideline focuses first on the medical indications and preconditions for good medical practice in cases of continuous sedation until the moment of death. Key topics in this respect are:

1. The indications and preconditions for palliative sedation (chapter 3);
2. The decision-making process (including the issue of consultation) (chapter 4);
3. Administration of fluids (chapter 5);
4. Good medical practice in the administration of palliative sedation (chapter 6);
5. Record-keeping and evaluation (chapter 7).

2.4 Empirical data on the extent of the practice of palliative sedation

The symptoms most commonly experienced by patients in the last stages or final week of life are fatigue (83%), dyspnoea (50%), pain (48%), confusion (36%), anxiety (31%), depression (28%) and nausea and vomiting (25%). Fatigue is perceived as the greatest burden, followed by pain, anxiety, dyspnoea, depression, nausea/vomiting and confusion, in that order (see ref. 62).

^{IV} This situation (continuous sedation until the moment of death) is sometimes called 'terminal sedation'. Terminal sedation is then a species of the genus palliative sedation. The Committee prefers to use a single term (within which different situations can be distinguished).

Palliative sedation may be considered wherever the relief provided by the conventional mode of treatment is insufficient and symptoms prove refractory (see ref. 53).

The percentage of the total number of deaths in 2005 in which deep sedation was administered prior to death was 8.2%.^v Continuous, deep sedation was administered together with the non-administration of food or fluids in 5.4% of all deaths. Continuous, deep sedation until death is practised most often by medical specialists (45% of cases), followed by general practitioners (34%) and nursing-home physicians (19%). Of the cases in which continuous, deep sedation was administered until the time of death, 47% involved patients with cancer, 17% patients with cardiovascular disorders, 6% pulmonary diseases, 4% diseases of the nervous system and 26% 'other' disorders. In about three-quarters of all cases, the patients were aged 65 or over. The most common symptoms in 2005 in the last 24 hours preceding death were fatigue (55%), dyspnoea (48%), reduced level of consciousness (47%) and pain (42%) (see refs. 22, 25). The most commonly stated reasons for continuous, deep sedation in the Netherlands in 2001 were to relieve pain (51%), agitation (38%), dyspnoea (38%), anxiety (11%) and 'other' symptoms (29%) (see ref. 63).

In the international literature, the reported incidence of palliative sedation of patients receiving clinical care (generally in hospices) ranges from 15% to 52%. The commonest indications for palliative sedation are delirium or agitation in the last stages of life (57%), followed by dyspnoea (23%), pain (17%) and vomiting (4%) (see refs. 31, 32, 34, 36, 41, 59 and 64-66).

The vast majority of patients have virtually ceased eating and drinking by the time that palliative sedation needs to be initiated and most of them die within a few days of its initiation (see refs. 36, 60). Research shows that 47% of patients put into a state of continuous, deep sedation die within 24 hours, 47% within one to seven days, and 4% within one to two weeks (see refs. 22, 67).

The committee found that, for a variety of reasons (such as differing definitions and limited availability of research data from different parts of the world), it is difficult to compare the Dutch figures with findings elsewhere and hence to chart the extent to which palliative sedation is used around the world in any clear and reliable way.

^v In this study, palliative sedation is defined as 'keeping a patient continuously under deep sedation or in a coma until death'.

3 Indications and preconditions for palliative sedation

This chapter discusses the indications for palliative sedation, and clarifies the definition of a 'refractory' symptom. It also discusses the development of unacceptable situations as a result of a combination of symptoms that are not in themselves refractory. The discussion then moves to the consideration of existential suffering as a factor in deciding on the indications, and describes one exceptional situation.

3.1 Indications for palliative sedation

Indications for palliative sedation are present when one or more intractable or 'refractory' symptoms are causing the patient unbearable suffering (see refs. 29, 31, 32, 34, 36, 37, 53, 64 and 68-70). A symptom is, or becomes, 'refractory' (see refs. 34, 35, 42 and 69) if the following applies:

None of the conventional modes of treatment is effective or fast-acting enough, and/or if these modes of treatment are accompanied by unacceptable side-effects.

The physician will have to decide whether a symptom is treatable or not on the basis of accepted good medical practice, bearing in mind the specific circumstances of a patient in the last stages of life. The indications for palliative sedation are therefore medical in nature. In addition, however, the feelings of the patient are extremely important, especially as regards the discomfort and side-effects of any possible mode of treatment. It will often be appropriate for the physician and patient to decide together whether or not, on balance, a symptom is refractory. A possible mode of treatment may be unacceptable to the patient if it involves too much discomfort and/or will have too little effect within a reasonably short time. Clearly, this factor may play a role in the physician's decision-making process. In short, therefore, the decision that a symptom is untreatable will be based on consideration of the following two factors in conjunction with each other:

- the expected effectiveness of the possible treatment;
- the discomfort or other side-effects associated with the possible treatment.

Pain, dyspnoea and delirium are the refractory symptoms that lead most frequently to the use of palliative sedation (see refs. 31, 32, 34, 36, 41, 59 and 64-67). Severe forms of nausea and vomiting also motivate its use, but do so less frequently. In practice, it will often be a

nonlinear combination of different dimensions of a symptom (e.g. extreme dyspnoea producing severe anxiety) and/or of differing symptoms that produces suffering that the patient finds unbearable and/or a situation that he finds unacceptable (see refs. 32 and 71).

The untreatable nature of the symptoms must be demonstrated beyond reasonable doubt. This means that reversible causes of suffering must be meticulously excluded before a decision is taken to administer palliative sedation. In the case of agitation, for example, there may be underlying causes which are treatable, such as pain, constipation or urine retention, side-effects of medication, withdrawal symptoms (from stopping medication like benzodiazepines or opioids, or from the cessation of nicotine or alcohol intake), electrolyte disorders (hyponatremia, hypercalcemia) or hypoglycaemia (see ref. 72). Consideration should also be given to psychological causes of agitation such as problems with coming to terms with and accepting the situation, anxiety and suchlike. Here too, the patient's feelings regarding issues such as the discomfort of further diagnostic tests will be important.

Definition of a refractory symptom

Physician and patient together decide whether or not to classify a particular symptom as refractory. The decision to administer palliative sedation is not taken in response to the circumstances at a specific moment in time, but is a possible outcome within the context of a palliative care plan. Patient and physician have together arrived at a point where they find themselves, through a complex of problems, with their backs to the wall. The decision-making is influenced by many factors, such as the views of the patient and the physician concerning a good 'death', the quantity and severity of symptoms, the impact of the somatic complaints on feelings such as anxiety, the fear of death and of the actual process of dying, powerlessness, uncertainty, grief, anger, sadness, the duration of the illness, the burden on informal carers, the strength and endurance of the patient and of his informal carers, and so on. Physical exhaustion (intense fatigue) may also play a role at this stage and may exacerbate suffering. It is one of the factors that help to determine the patient's endurance. All these factors may lead to a situation that a patient, his family and/or carers experience as 'overwhelming'. This may lead to the conclusion that there is no more scope for deploying any other reasonable interventions aside from palliative sedation.^{VI}

Nonlinear combination of symptoms in the context of approaches to palliative care

The judgement of whether one or more symptoms should be considered 'refractory' must be made within the context of the overall approach to palliative care (see the remarks on pallia-

^{VI} The term 'undeferrable' action has recently been introduced in this connection (see ref. 20).

tive care in perspective in the introduction). That is to say that a variety of problems and characteristics of the patient are taken into account.

In practice, it is frequently a nonlinear combination of diverse dimensions of one or more symptoms that leads to a situation that constitutes unbearable suffering for the patient. The context is a contributory factor. Diverse symptoms and diverse contextual aspects may occur in combination with one another. In such cases it may become clear that it is technically and medically possible to control a particular symptom, but that the presence of other symptoms makes it pointless to do so.

The patient's setting (whether he or she is at home, with or without home care, or in a hospice, nursing home or hospital) is also part of that context. Institutions often have different scope for interventions than exist in the home. As a result, it must be acknowledged that in a home situation, patient and carer have often taken a different route to palliative care and may therefore be at a different stage of the decision-making process than would have applied in the case of clinical care.

Existential suffering as a factor in the decision-making process

Like pain, existential suffering may be among the refractory symptoms that go to make up unbearable suffering.^{vii} In such cases, this existential suffering cannot be alleviated, for instance by communication or spiritual support. These patients have often been through a great deal of distress, and have gradually come to embrace the notion of continuous sedation. They are often extremely ill and weak, close to death, and have a range of physical complaints, some of them often severe. The patient's body has reached its end, literally and figuratively, and everything that needed saying has been said. Some of these patients do not want to experience their final days consciously and may request continuous sedation. The feeling that one's existence is empty or meaningless (existential suffering) may in itself cause unbearable suffering.

This comes within the domain of medicine, but it is not open to infinite interpretation. In assessing existential suffering, medical expertise cannot suffice; expertise in the areas of psycho-social and spiritual problems is also required.^{viii} For more observations on consultation, see also section 4.3.

^{vii} Existential suffering may be expressed as feelings of pointlessness, emptiness, existential distress, a desire not to experience death or the dying process consciously, psychosocial problems, spiritual problems, or for instance the desire to preserve one's dignity.

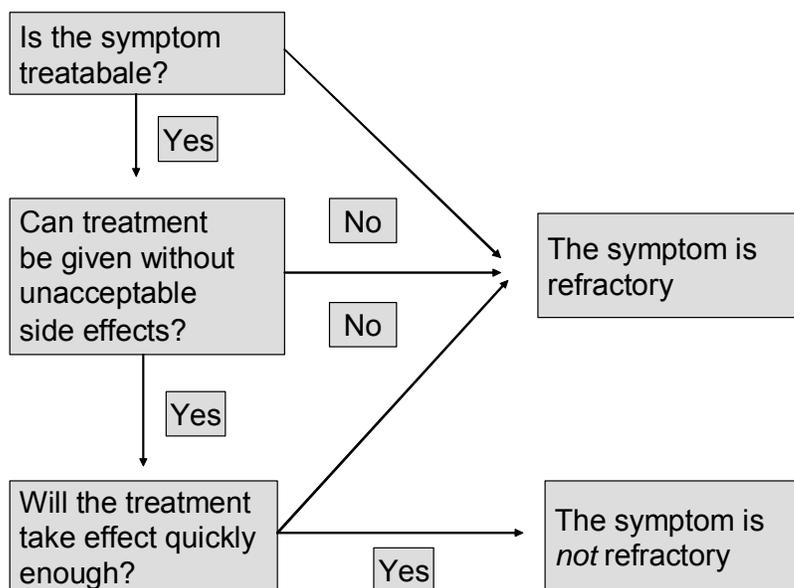
^{viii} Psychologists or spiritual counsellors might be consulted, for instance.

The focus here is on the meaninglessness of existence when death is expected within one or two weeks. The committee believes that this certainly falls within the scope of palliative care and the guideline for the following reasons. The patients to whom this applies are in practice very seriously ill, have a combination of symptoms, are in many cases no longer accepting food or drink, and their bodily functions are breaking down. In other words, the issue here is never solely existential suffering.

However, there are patients who have no refractory symptoms but simply want palliative sedation as a way of avoiding consciously experiencing the end of life. The committee does not regard this as an acceptable indication.

3.1.1 Refractory symptoms: flow diagram

The following flow diagram can be used to decide whether or not a symptom is refractory:



3.2 Preconditions for continuous sedation

Besides the presence of medical indications in the form of one or more refractory symptoms, a precondition for the use of continuous sedation is the expectation that death will ensue in the reasonably near future – that is, within one to two weeks (see refs. 31, 32, 36, 53 and 73). In these circumstances, a medical practitioner may decide to initiate sedation and in principle to continue it until the moment of death. In this situation, the committee assumes

that continuous sedation will not include the artificial administration of fluids (see also chapter 5). If the patient's life expectancy exceeded one to two weeks, the non-administration of fluids would cause dehydration and hasten the time of death.

The pre-requisite that death must be expected to follow within one or two weeks poses difficulties in practice, since it is not always possible to predict that death will probably ensue within this time-frame.

In practice it is not always easy to estimate how long a patient is likely to live.^{ix} But once a number of characteristics of the phase of dying have been observed, it can be assumed that the patient is approaching the point at which death is inevitable. The most characteristic feature is that patients virtually cease to eat and drink. In addition, they are frequently cachectic, tired and debilitated and bedridden. They may also be drowsy and disoriented. Such signs that a patient is dying, combined with the worsening symptoms of disease, guide the decision-making process. It is up to the physician to factor these matters into the decision-making, along with the worsening symptoms of disease, without the expectation that the moment of death can be predicted precisely. The point is therefore not so much to estimate the time until death, but to observe the progress of the signs described above and to conclude that the patient is dying. It is this that the physician must focus on.

Research shows that 47% of patients put into a state of continuous, deep sedation die within 24 hours, 47% within one to seven days, and 4% within one to two weeks. In 2% of patients, it proved necessary to administer continuous deep sedation for over two weeks (see refs. 22 and 67). It may be inferred from this that survival after the start of continuous, deep sedation is more than two weeks (the upper limit for the advance estimate of the time until death) in only 2% of patients. For 94% of patients, actual life expectancy after the start of continuous, deep sedation is less than one week. Furthermore, a meta-analysis reveals that patients actually live for a period that is 30% shorter, on average, than the life expectancy estimated by the physicians. Another important finding is that the poorer the patient's physical condition, the more accurate is the patient's life expectancy as estimated or predicted by physicians (see ref. 74).

3.3 An exceptional situation

A specific and highly exceptional situation arises when a patient exhibits refractory symptoms, but death is not expected to ensue in the near future (within one to two weeks). The

^{ix} With the exception of acute situations; see section 4.5.

committee is not thinking here of cancer patients, but of conditions such as muscular dystrophy, amyotrophic lateral sclerosis (ALS), or cardiac or respiratory insufficiency. In some cases of this kind, it is hard to be certain whether the patient is actually in the final stages of life. It is important to avoid the premature initiation of continuous sedation until the time of death.

In situations like this, brief or intermittent sedation may be initiated as a first step (see refs. 29, 31, 32 and 36). This provides the opportunity to establish whether a symptom is permanently refractory. Temporary or intermittent sedation gives the physician a chance to evaluate the situation with the patient and/or family and if necessary to review the management of the case. See chapter 8 for a further discussion of this point. On the issue of artificial hydration, see chapter 5, point 3.

The committee feels that, in situations where it is hard to judge whether the patient actually is in the final stages of life, particular care needs to be taken in establishing whether a particular symptom is permanently refractory and deciding on that basis to initiate continuous sedation. In such cases, the committee considers the advice of a consultant, preferably a palliative specialist, to be mandatory (see refs. 5 and 53).^x

^x The committee's view in this instance is based on the general rule that physicians should consult wherever insufficient expertise is available or wherever there is any doubt on the key issues. For the general views of the committee regarding consultation, see section 4.3.

4 The decision-making process

This chapter discusses the procedure for decision-making in relation to palliative sedation. But this is preceded by a different, extremely important, stage, namely that in which the patient is informed that there are no further curative treatment options. After briefly considering this stage, the discussion will move to the different phases and key aspects of the process culminating in the decision to administer palliative sedation. This decision-making process can be divided into three stages:

1. the initial proposal;
2. determining whether indications for palliative sedation are present;
3. consultation with the patient and/or his representative(s).

Although these three stages are interconnected, it is important to distinguish between them. The committee wishes to make the general observation that these stages are not one-off activities or decisions. Far more frequently, they are steps in a longer journey of palliative and other care. Some of the steps in that journey will have to be repeated. Acute situations may arise in which it is impossible to go through the stages listed above before deciding to administer palliative sedation. In such cases, the attending physician has the scope to opt for palliative sedation on the basis of the patient's condition. This point is elaborated in section 4.3.4.

4.1 Timely and open communication

When a patient hears that no curative treatment options remain, and that subsequent treatment will be merely palliative, the physician and patient must speak to one another openly and in good time about what is possible and what is not possible in decisions concerning the end of life.^{XI} The anxiety and fear regarding death may assume such dramatic forms for the patient and his family that the physician must attach considerable weight to them. The physician can be expected to adopt an open attitude and to raise any differences of opinion with the patient in good time.

^{XI} See the Dutch website www.alsjenietmeerbeterwordt.nl. In brief films, eight people describe their reactions when they were told that their illness was incurable. The films show the dilemmas that may arise, and help to open them up for discussion. The underlying premise is that such openness can help in making one's own choices, as well as diminishing the sense of isolation and helping to define a kind of meaningfulness that will enable a person who is dying to face the final stages of life as well as possible.

4.2 Reasons for considering palliative sedation

The issue of palliative sedation may be raised in various ways. The patient and/or his family may request it, either explicitly or indirectly in the form of a request to relieve suffering. Equally, staff caring for the patient may raise the possibility, if they believe that the patient's situation is developing such as to require it, now or in the near future (see refs. 32, 35, 36 and 53).

The committee views palliative sedation as a medical response to a serious medical problem. A patient cannot opt for continuous sedation unless the indications and preconditions for this option are fulfilled.^{xii} Only if the indications are present, in the physician's opinion, and the preconditions have been met does continuous sedation become a right that the patient may choose to exercise. Some patients, of course, may decide against starting continuous sedation at this stage.

4.3 Determining whether indications for palliative sedation are present

Once the question of initiating palliative sedation has been raised, the patient's situation must be assessed thoroughly in the light of the indications for palliative sedation set out in chapter 3. The decision to administer palliative sedation is not based on a specific moment in time, but is a possible outcome within the context of a palliative care plan and process. Nursing staff have a definite role to play here in drawing attention to important points; through their regular close contact with the patient, they are often in a good position to assess the patient's overall situation. All this information contributes to the decision to initiate palliative sedation. The information provided by the patient himself and by other professionals caring for him as well as by the patient's family may also be important.

On the basis of their observations, monitoring and recording of symptoms, nursing staff and other carers can frequently provide background information in support of the expressed desire or need for sedation. From this information a picture can be built up of the patient's overall situation, in terms of case history, diagnosis and prognosis. The committee would emphasise that the continuity of cooperation, coordination, exchange of information and communication among the various carers is crucial. Poor cooperation and coordination can produce discrepancies in the information received by the various parties involved and these can cause anxiety for the patient, family and indeed staff. To avoid this, clear agreements are needed between all concerned, especially when the patient is being nursed at home, where contact between the parties will generally be less regular. The attending physician

^{xii} Palliative sedation may be administered to a patient who is incapable of making an informed decision. See section 4.4 of the guidelines.

must ensure that those taking over in the evenings, nights and weekends (for instance the doctor on duty at the local after-hours GP clinic) are given all the relevant information. If a substitute physician decides to administer palliative sedation, he must likewise ensure that the attending physician is apprised of all the facts.

The assessment must culminate in a decision on palliative sedation by the attending physician (see ref. 52). This decision should specify the aim of sedation (relieving suffering by treating a particular refractory symptom), its nature (temporary/intermittent or continuous), the choice of drugs, and the dose to be administered. The decision itself and the considerations on which it is based must be recorded in the patient's file. The file should also contain a record of consultations with the patient and/or with his family, within the team of professional carers, and with any outside specialists. See also the section on record-keeping in chapter 7.

Since palliative sedation is a medical procedure, the attending physician bears responsibility for determining whether the medical indications are present, for decision-making and for the practicalities of administration. As in any other normal medical procedure, every physician must be able to demonstrate, where necessary, that he possesses the expertise and experience relevant to the case. Given the nature and content of palliative sedation and the medical indications set forth in this guideline, the committee sees no need to insist that an expert physician be consulted at all times before deciding to administer palliative sedation.

Where a physician has doubts regarding his own expertise or has difficulty balancing the different considerations involved in deciding whether to initiate palliative sedation (indications, life expectancy, and the importance of exercising due care), it is standard professional practice to consult the appropriate expert in good time.^{xiii} This is a general principle of medical practice. One exception to this rule is the compulsory consultation in the case of termination of life on request, since this is an exceptional case and does not come under the heading of normal medical procedure. This in no way applies to continuous sedation until the moment of death or other forms of palliative sedation. Nonetheless, every physician must be aware that continuous sedation is a radical medical procedure, since it lowers the patient's level of consciousness until the moment of death.

Research has shown that continuous sedation is administered each year in 8.2% of all deaths. In 2005 it was administered in 12,000 cases (see ref. 22). It may be inferred from

^{xiii} It should be added that just as in other kinds of medical procedure, the physician is free to disregard the advice. He or she must be able to explain, if the need arises, on the basis of professional expertise and arguments, why the advice was not followed.

this that individual physicians have limited experience with the decision-making process and actual practice of continuous sedation.

Both decision-making and administration will often require the support of, and consultation with, other carers. Continuous sedation within the context of palliative care is highly complex and requires specialist knowledge. The impact of the problems involved here may be such that consultation and cooperation with other carers, not just organisationally but also in matters of substance, may be essential (see refs. 5, 29, 32, 41). The committee advises physicians to consult the appropriate expert(s) with specialist knowledge of palliative care in good time (see refs. 32, 34, 53, 75 and 76).^{XIV XV}

4.4 Discussion with the patient and/or his representative

The general rules set out in the Medical Treatment Contracts Act (WGBO) also apply to palliative sedation. The main principle is that of the informed consent of the patient. If the patient is no longer competent to take an informed decision, the physician must consult his representative. In both cases, it is crucial that the information on which consent is to be based should be provided in a comprehensible form. There are three possible situations: 1) discussion with the patient, 2) discussion with the representative of the decisionally incompetent patient, and 3) acute situations in which neither the patient nor his representative can be consulted. These three situations are discussed below.

4.4.1 Discussion with the patient

Wherever possible, palliative sedation should only be initiated with the consent of the patient. Staff should be proactive in ensuring that consent is sought while the patient is still lucid (see refs. 32 and 35). This means that the possibility should be discussed with the patient, if at all possible, well before the stage when palliative sedation is the only remaining option. Staff caring for the patient will therefore have to take the initiative and explain to him why it is important to discuss the possibility of palliative sedation at that relatively early stage.

The discussion with the patient can be based on the following list of issues. They need not all be addressed on the same occasion and, indeed, may not all be relevant in the particular case. As noted earlier, the process of exchanging information and discussion may well be

^{XIV} For exceptional circumstances in which consulting an expert is a prerequisite, see section 3.3.

^{XV} In the Netherlands, every physician can enlist the assistance of a regional palliative consultation team. See www.ikcnet.nl. In principle, these teams are readily available and easy to reach, even outside office hours.

spread over a number of different conversations. The issues to be addressed can be divided into the following three categories:

Palliative sedation as such

1. The patient's condition, life expectancy and prospects.
2. The indications for and purpose of palliative sedation.
3. The options in the case of unbearable and untreatable suffering (continuous sedation and euthanasia).
4. The fact that, properly practised, continuous sedation does not shorten life.
5. The procedure in unforeseen (acute) situations.
6. The potential and limitations of palliative sedation, including the depth of sedation, the possibility of a (perhaps unintended) return to consciousness and the difference between temporary and continuous sedation.
7. The consequences of palliative sedation (including the partial or complete loss of powers of communication).
8. The medical procedure itself (including information on the drugs to be administered).

Specific wishes and views of the patient

9. The wishes and views (including fears or anxieties) of the patient with regard to the process of dying. It is important that these should be discussed as explicitly as possible.
10. Wishes of the patient concerning matters such as:
 - organ donation;
 - timing of farewells to family;
 - physical care during palliative sedation;
 - where he wants to die;
 - any medical procedures during palliative sedation:
 - non-administration of artificial nutrition/hydration (and the consequences of this);
 - continuing or withholding other kinds of treatment prolonging life (such as resuscitation, artificial respiration or kidney dialysis).
11. The desire of the patient to receive the support of a spiritual advisor or other individual in relation to religious or ethical matters.

Other aspects

12. Providing information and support for the patient's family, to help them understand the situation and the procedure to be adopted, and to help them cope with the experience.
13. Informing family about the point or otherwise of keeping vigil over the patient.
14. Properly informing the patient's designated representative during palliative sedation.

15. Providing information about consultations with additional experts (if applicable).

4.4.2 Discussion with the representative of a decisionally incompetent patient

If the patient himself is no longer competent to give consent, the decision must be discussed with his representative. The Medical Treatment Contracts Act lists the people eligible to take on this role.^{XVI} The patient's right of informed consent is then transferred to his representative. However, decisional competence is not a black-and-white matter. Patients may be only partially incompetent and even if they are completely so, they may still have relevant feelings on the matter and ways of making them clear. In such cases, the patient should be involved in the decision-making process as far as possible.

The discussion with the patient's representative can be based on the list of issues given above. The Act states that the patient's representative should take the decision on his behalf. However, this does not preclude the possibility that the representative (usually a relative) may elect to leave the decision to the physician(s) involved in the case, either because he feels they have greater expertise or because he is unwilling to assume the responsibility of taking such a momentous decision. Another possibility – at least in theory – is that the representative may refuse to give consent for palliative sedation. In that case, however, the physician has discretion – in the interests of the patient – to ignore the feelings of the representative and decide to initiate palliative sedation without consent. In such a situation, the physician can always consult a specialist if he wishes. As a rule, however, it is extremely important that a consensus should be reached between medical staff and the patient's family about the aim of the treatment (to relieve suffering and not to shorten life), the procedure that is appropriate to achieve this, and the consequences that it is likely to have. Such agreement is in the interests both of the patient and his family. The latter aspect is discussed in more detail in chapter 9.

4.4.3 An exceptional situation: acute sedation or the absence of a representative

The general rule is that palliative sedation should not be initiated without the consent either of the patient himself or, if he is decisionally incompetent, his representative. The patient's condition may make it necessary to administer acute sedation. This means sedating a patient in a situation in which a complication (frequently one that is life-threatening) suddenly

^{XVI} In order of eligibility: the patient's legal representative (a guardian or mentor appointed by the Court), if he has one; whom failing a personal representative; whom failing his spouse, partner or companion; whom failing a parent, child, brother or sister (art. 7:465 of the Dutch Civil Code).

occurs that causes unbearable suffering. In that case, the physician may decide that acute sedation is the only sound option for alleviating the patient's suffering at the point in time.

Generally speaking, the patient himself will be beyond giving properly informed consent at such a moment and action will have to be taken too quickly for it to be possible to consult the representative. In these circumstances, responsibility for the decision lies with the attending physician(s). The patient's representative must, however, be informed as quickly as possible of the decision and its consequences.

Acute sedation may be called for in the event of suffocation, massive blood loss or cerebral vasoconstriction. Until the point at which the complication arose, the patient was not yet dying. Symptoms of this kind are always refractory. The possibility that such a complication may arise can sometimes be predicted, in which case it should be discussed with the patient, his family and nursing staff. Clear information regarding the risk that a situation of this kind may occur and the measures to be taken in this eventuality may have a calming effect. The patient can give prior consent and designate a representative. Those concerned must be given adequate instructions so that they know what to do if the physician is not present when the acute situation arises. If there is a realistic risk of such a situation developing, the drugs to be administered in this clearly-defined situation should be laid out ready for use. It is self-evident that as soon as possible the actions must be supported and examined by the physician, and all the relevant information entered in the case file.

In most cases, the person's family will be shocked by the circumstances at the initiation of acute sedation. It is important to explain clearly what has happened and to offer adequate support. If the patient survives the incident, it must be decided whether the indications for acute sedation are still present. There is generally a reluctance to allow the patient to awaken, out of fear that he or she may experience the same thing again. Switching from acute sedation to continuous sedation can only be regarded as good medical practice on the basis of the appropriate indications and preconditions. In the case of reversible problems, or if the complaints can be alleviated in some other way, the physician should cease the sedation.

In cases where the patient is decisionally incompetent but has no representative, the attending physician likewise has discretion to decide to initiate palliative sedation on the basis of the indications listed in this guideline and any other relevant information (views expressed by the patient in the past, signs of suffering, etc.).

5 Administration of fluids

This chapter discusses the relationship between palliative sedation and the issue of hydration.

In most cases, continuous sedation until the moment of death is administered in cases in which the patient is no longer able or willing to take any fluids, because he or she is dying as a consequence of the underlying disease (see ref. 77).

The often gradual cessation of voluntary absorption of fluids is an indication of approaching death. The vast majority of patients have virtually ceased eating and drinking by the time palliative sedation is initiated and die within a few days afterwards (see ref. 31). Research shows that 47% of patients put into a state of continuous, deep sedation die within 24 hours, 47% within one to seven days, and 4% within one to two weeks. In 2% of patients, it proved necessary to administer continuous deep sedation for over two weeks (see refs. 22 and 67). The committee feels that, provided that the patient has only a reasonably brief life expectancy (one to two weeks), hydration is not a relevant factor in decisions about continuous sedation (see refs. 3, 5, 32, 59 and 61).

If the patient has almost or completely ceased to take food, but continues to take fluids, death may not occur for many weeks and sometimes even longer, whereas if he has ceased to take sufficient fluids dehydration will hasten his death. In this respect, enteral nutrition must be regarded as a combination of nutrition and hydration. Stopping it is therefore equivalent to non-administration of fluids. The same is true of parenteral nutrition, but in practice this is extremely unlikely to be an issue in cases where palliative sedation is under consideration. The fact that, once sedated, the patient will receive no nutrition is seldom if ever raised as an issue and is not considered further in this guideline.

The situation at the point when palliative sedation is initiated can vary and may be a relevant factor in decision-making:

1. the patient is able to take fluids;
2. the patient is unable to take fluids;
3. the patient is able to take fluids or is having fluids artificially administered, but indicates that he wishes this to cease;
4. the patient is having fluids artificially administered.

The decision to stop the administration of fluids, or not initiate it if the patient himself has ceased to take fluids, is sometimes seen as problematic in combination with continuous sedation, especially if it is believed that the patient is likely to die sooner as a result of dehydration. The decision-making regarding fluids is in all cases a separate decision, which precedes the decision to initiate continuous sedation. If possible, the physician must discuss this with the patient. The committee wishes to emphasise that it is improbable that the patient will die sooner if there is not artificial administration of fluids, since the patient is already dying. Thus, in virtually all cases, the patient dies from the consequences of the underlying disease.

1. Able to take fluids

If the patient is decisionally competent and able to drink, the physician must discuss with the patient and his family the fact that the consequence of initiating continuous sedation will be that no more fluids can be taken (see chapter 4, 'The decision-making process'). If the patient then expresses the wish to continue taking fluids, superficial, brief or intermittent palliative sedation is a possible alternative. This will allow the patient to continue taking fluids. This course of action may also be chosen in cases in which the patient is not expected to die within one or two weeks.

2. Unable to take fluids

If the patient is no longer able to drink, the possibility of initiating artificial hydration may be an issue (see refs. 32, 45 and 53). The committee feels that artificially administering fluids to patients under continuous sedation is medically futile. Treatment may be regarded as medically futile if the resources involved unreasonably outweigh the potential benefits of the treatment (the principle of proportionality). In the circumstances discussed here, initiating artificial hydration may even prolong suffering or exacerbate it by increasing oedema, ascites, bronchial secretions, urine production and incontinence (see refs. 33, 53 and 78).

3. Does not wish to take fluids or have them administered

The patient can always decide for himself to stop taking fluids or having them administered. The patient's decision to stop taking fluids must be accepted and respected. In this situation, therefore, there will be no question of artificial hydration. If the patient is, or has become, decisionally incompetent, his or her representative must be consulted (see chapter 4, 'The decision-making process').

The patient's refusal to take fluids may play a crucial role in the exceptional circumstances described in section 3.3. In that case, it may be decided at a later stage to initiate continu-

ous, deep sedation. This decision (to initiate continuous sedation) can be taken by the physician only after the patient has decided to cease taking fluids. The actual initiation of continuous sedation will therefore only take place once the patient has decided to refuse fluids, has shown consistency in this respect, *and* exhibits a refractory symptom. During the decision-making process, it is extremely important that the physician should take – in consultation with the patient – a clear view of the point at which the symptoms are untreatable and cause unacceptable suffering. The committee would emphasise that two distinct decisions are involved here, which are taken together, but where the key lies in the initial decision by the patient himself. The order in which the decisions are taken and the existence of an interval between the two separate decisions are crucial.

4. Having fluids artificially administered

Artificial hydration is a medical procedure. The initiation or continuation of a medical procedure cannot under all circumstances be regarded as beneficial. In line with the reports by the Health Council of the Netherlands and the KNMG's own Commission for the Acceptability of Life Terminating Action, the committee concludes that the artificial hydration of patients under continuous sedation can be regarded as medically futile (see refs. 47, 52, 79 and 80). Like the authors of these reports, the committee feels that this is justified because the patients have untreatable symptoms causing unbearable suffering and death as a consequence of the underlying disease is unavoidable. In the view of the committee, the decisive factor in such situations is that initiating or continuing artificial hydration may prolong suffering or even exacerbate it (see also point 2 above). Stopping artificial hydration is a medical decision for which the physician must be able to produce good reasons. The committee also endorses the view expressed in the reports that there can be no question of 'extra' suffering as a result of the cessation of artificial hydration. The patient's suffering is eliminated by the sedation. Here too, artificial hydration can prolong suffering or exacerbate it by increasing oedema, ascites, bronchial secretions, urine production and incontinence. In situations where the patient can no longer indicate his consent to the non-administration of artificial hydration, it is important to give his family or representative a clear explanation of the reasons for deciding to stop administering fluids, the consequences of doing so and the prognosis for the patient (see also chapter 4, 'The decision-making process').

6 Good medical practice

This chapter discusses good medical practice in the administration of palliative sedation. It focuses on: the preparations to be made, the initiation of sedation, proportionality, the drugs to be used and the method of administration, morphine and sedation, and – finally – accompanying measures. It is important that the choice of medication should be tailored as closely as possible to the circumstances of the individual case. This chapter discusses the main considerations regarding the choice of medication. More detailed information about drugs and dosages can be found in annexe IV.

6.1 Preparations

The following preparations should be made:

- ensure that the necessary medication is available;
- ensure that the equipment necessary to administer it is available;
- exchange information with the patient (if possible) about the arrangements;
- exchange information with family about the arrangements;
- exchange information with all the professionals involved in the case (and, where necessary, ensure their presence);
- establish the criteria for initiating palliative sedation together with the associated points to keep under observation and the record-keeping procedure;
- establish plans for the initiation procedure and later stages of the treatment (including details of how, when and by whom sedation may be initiated or the dose increased).

6.2 The initiation of sedation

Palliative care characteristically relies on a multidisciplinary approach. Nursing staff can contribute important input for drawing up the indications, estimating whether the conditions have been met, and implementing palliative sedation. That does not absolve the physician of his own responsibility. This applies most particularly to the administration of continuous sedation, the start of which is an emotionally charged event for the patient and his family, as well as for the person's carers, especially in situations leading to a rapid diminishing of consciousness so that the possibility for communication is lost.

It has become clear that in practice, physicians are not always present at the beginning of continuous sedation (see ref. 19). Every physician must be aware that continuous sedation is a radical medical procedure, since it lowers the patient's level of consciousness.

The physician must therefore himself be present at the beginning of continuous sedation. It is recommended that the physician and the nursing staff discuss this possibility, as well as the evaluation criteria, in advance. This can prevent nursing staff, to whom the subsequent administration of the drug will in many cases be largely entrusted, from finding themselves in an undesirable position (see refs. 19 and 47). Situations may arise in the initial stage in which the physician must be able to intervene (for example, the patient may become delirious or sedation may be too superficial, or indeed too deep). After this, the administration of sedation can be left in large measure to nurses and other carers. They should then be properly informed and instructed, in particular about when to consult the physician.

Due to unforeseen circumstances, the attending physician may be unable to be present at the initiation of palliative sedation. In acute situations, experienced nursing staff may initiate palliative sedation. However, this is only permissible in cases where the physician has already discussed the possibility of acute sedation with the patient, his family and nursing staff. The physician must give nursing staff a clear advance explanation of the indications for initiating sedation and good instructions on the procedure for doing so. The necessary drugs should be ready for use in this clearly defined situation. Needless to say, the actions performed by the nursing staff should be checked by the physician as soon as possible after the event.

6.3 Proportionality

It is extremely important for palliative sedation to be applied proportionately; that is, for consciousness to be lowered to the extent that is necessary and sufficient to relieve symptoms in the degree desired (see refs. 32, 45, 54, 59 and 95). It is the degree of symptom control rather than the degree to which consciousness must be reduced that determines the dose, combinations, and duration of the drugs administered. Interim evaluations and other decision-making processes must be geared towards relieving the patient's suffering by maintaining or adjusting the doses and/or type of medication in order to create a tranquil and tolerable situation.

6.4 Drugs and method of administration

It is strongly advisable to employ a step-by-step approach. If an adequate dose fails to achieve the desired effect, it is time to proceed to the next stage. Midazolam is currently regarded as the preferred drug. Arguments in its favour are its short half-life, which means that treatment can be rapidly adjusted, and the considerable experience already gained with it in cases of palliative sedation. In general, it is preferable to opt for subcutaneous rather than

intravenous administration. If the patient fails to respond adequately to midazolam, checks should be performed to see whether the mode of administration and the medication are in order, and whether any disruptive and remediable factors (e.g. a full bladder or constipation) are playing a role. Only then can consideration be given to the use of a different sedative, such as levomepromazine or propofol (see refs. 31, 33, 36, 41, 53, 54, 59 and 81-95). For further details, see annexe IV.

6.5 Morphine and continuous sedation until the moment of death

In situations where continuous, deep sedation until the moment of death is being considered, morphine is often already being given to treat pain or dyspnoea. In these circumstances, it may seem attractive to increase the dose of morphine substantially in the hope that the patient will lose consciousness and quickly expire. The study of medical decisions at the end of life conducted in 2005 found that 19% of specialists, 13% of general practitioners and 10% of nursing home physicians in the Netherlands use morphine in this way (see ref. 22). Closer consideration reveals that its use in this way often has two aims: firstly, to render the patient unconscious and secondly to hasten death. For neither of these aims, however, is morphine the drug of choice (see refs. 47, 52 and 54). High doses of morphine frequently produce drowsiness, but not always loss of consciousness. Therapeutic doses of opioids (that is, doses tailored to the degree of pain or dyspnoea) are not at all likely to shorten life, even if they are high. Moreover, morphine has major side-effects. For instance, it can increase delirium or induce myoclonus. The committee regards the use of morphine to achieve these aims as bad practice. Morphine should only be given or continued (alongside sedatives) to relieve pain and/or dyspnoea; the dose should be calculated to relieve the actual or assumed extent of the pain and/or dyspnoea (see ref. 54).

Midazolam and morphine can be combined in a single cassette; however, the disadvantage of this is that the dose of each cannot then be separately adjusted and that when a bolus injection of one drug is given, the other will also be administered.

6.6 Supplementary measures

In addition to tending to the patient, special attention should also be paid to:

- reviewing existing medication and ensuring an alternative (rectal or parenteral) method of administration of whatever medication needs to be maintained;
- stopping all medical and nursing procedures that are not strictly necessary;
- preventing withdrawal symptoms (e.g. nicotine plaster);
- installing a high-low bed in order to facilitate the care of the patient;

- catheterising the patient's bladder (in the case of deep sedation or urine retention) shortly after he has been effectively sedated;
- treating constipation;
- treating wounds;
- attending to stoma;
- oral hygiene;
- in the case of a death rattle: turning the patient onto his side or if necessary administering butylscopolamine 20 mg s.c. or i.v.

7 Record-keeping and evaluation

This chapter discusses record-keeping and the evaluation of the effects of continuous sedation.

7.1 Record-keeping

When palliative sedation is being administered, it is essential to keep accurate records. This helps to ensure the quality and continuity of care (including the proper exchange of information between staff). The relevant information about the patient and his situation must be recorded in his file.^{xvii} First and foremost, the file should contain the reasons why it was decided to administer palliative sedation and how sedation was administered (see ref. 47). This includes information about:

- the life expectancy and condition of the patient;
- the indications for palliative sedation;
- the views of the patient, his representative and/or other family;
- the outcome of consultation with specialists (if applicable);
- the drugs used to achieve sedation;
- any other medical interventions (accompanying measures) and drugs administered.

Other aspects of patient care that should obviously be recorded include:

- who bears ultimate medical responsibility;
- when and with whom the situation is to be evaluated each day;
- a clear definition of the factors that may lead to a review of the management of the case;
- if home care technology is to be used, what is to be used and who is to provide it;
- what additional medical procedures and forms of nursing care are or will remain necessary and who is to be responsible for them;
- who is to act as the contact person within the family and/or, in the case of decisional incompetence, the patient's representative;
- which of the professionals involved is to be responsible for liaison with the patient's family or representative.

The case records should include clear information on how the effect of the sedatives is to be evaluated and the criteria to be used to adjust the dose (see refs. 35, 60, 64 and 96). The

^{xvii} The Committee uses the general term 'file' without distinguishing between the medical file and the nursing file. However, the key information (medical indications for sedation and the means used to achieve it) will always have to be recorded in the patient's medical file.

degree of symptom control is the decisive factor in this respect. A sedation scoring system *may* be used to describe and record the condition of the patient:

- Level 1: a) awake and oriented;
 b) drowsy;
 c) eyes closed, responds promptly to verbal commands;
 d) eyes closed, arousable only by physical stimuli.
- Level 2: eyes closed, not arousable by physical stimuli.
- Level 3: basic brain functions affected (respiration depressed).

(Level 3 is undesirable and the dose of the sedatives should be reduced if it occurs).

7.2 Supervision and evaluation of the effects of palliative sedation

The object of palliative sedation is to alleviate the patient's suffering. The evaluation must therefore focus on the patient's comfort. There is no scale available for measuring and scoring a patient's comfort during continuous sedation. A sedation score can be used for the purpose of describing the depth of sedation. However, the point of this is not to score the effect of the drug, but to alert the physician if the sedation is too deep (see also section 7.1).

The problems and symptoms that prompted the decision to administer continuous sedation should serve as the basis for evaluation. Agreements must be made regarding the observation points and times (including who does what, and when), and these should be evaluated by the carers concerned at least once a day. New symptoms may arise in addition to the existing ones. This must be evaluated in the same way.

The attending physician should visit the patient at least once a day. He should check particularly for any possible complications (such as decubitus or urine retention) that may need treating. He will discuss the course of the case both with other professionals involved and with the patient's family, looking in particular for any signs of burn-out in the latter. Family can be an important source of information about the welfare of the patient. Set times can be agreed with them for periodic consultation and evaluation concerning issues such as whether the patient is still comfortable, whether new circumstances have arisen or the patient has expressed new wishes, etc. Nursing staff also have an important role to play in identifying changes, observing the patient, monitoring his condition and reporting developments. It can be extremely important to the patient's family to be clear about the factors that may lead to a review of the management of the case (see also chapter 9).

8 Brief or intermittent sedation

Chapters 3 to 7 discuss good medical practice with regard to continuous sedation until the moment of death. This chapter does the same for brief and temporary (intermittent) sedation. More detailed information about drugs and dosages can be found in annexe IV.

The difference between brief or intermittent sedation and continuous sedation is that the latter is administered until the moment of death, whereas in the case of brief or intermittent sedation the patient is only temporarily sedated and then wakes up again (see ref. 33).

The primary aim of brief or intermittent palliative sedation is to restore tranquillity to the situation and then allow the patient to return to consciousness. It can be used to give patients time out from breathing difficulties and/or anxiety or, for example, to administer deep sedation at night while allowing the patient to be alert during the day (see ref. 97).

In some situations, brief or intermittent sedation offers an opportunity to see whether a symptom is permanently refractory. It can be used to bridge the period between the administration of medication to relieve the symptom and its taking effect (for example, when administering haloperidol to treat delirium). Temporary or intermittent sedation provides the opportunity to assess the situation with the patient and/or his family and if necessary to modify the management of the case.

As in the case of continuous sedation, it is extremely important that brief or intermittent sedation should be applied proportionately; that is, for consciousness to be lowered only to the extent that is necessary and sufficient to relieve symptoms in the degree desired. It is the degree of symptom control rather than the degree to which consciousness must be reduced that determines the dose, combinations, and duration of the drugs administered to achieve these forms of palliative sedation. Interim evaluations and other decision-making processes must be geared towards relieving the patient's suffering by maintaining or adjusting the doses and/or type of medication in order to create a tranquil and tolerable situation. It is on this basis that the aim (and therefore the intention) of the treatment will be evaluated and assessed.

In the view of the committee, the principle is that the recommendations made in chapters 3 to 7 (on indications, decision-making, fluids, method of administration and record-keeping)

also apply and should be followed in relation to brief or intermittent sedation, albeit with the following reservations and modifications:

- the indications are the same (a refractory symptom), but brief or intermittent sedation can also be applied where a symptom is only temporarily untreatable (and therefore only temporarily refractory);
- in the case of brief or intermittent sedation, it is not a precondition that life expectancy should be less than two weeks;
- the general rules regarding informed consent by the patient or his representative still apply, but it will not be necessary to discuss all the issues listed in chapter 5;
- in the case of brief or intermittent sedation, it will not usually be necessary to discuss the cessation of taking or administering fluids. In principle, the taking or administration of fluids can continue.

The committee wishes to emphasise that dealing with the patient's family (chapter 9) and caring for the carers (chapter 10) are extremely important aspects of good practice regarding palliative sedation, even where such sedation is brief or intermittent.

9 Dealing with the patient's family

Earlier in this guideline, palliative sedation has been defined as part of a longer overall process of palliative and other care. This chapter discusses the issue of dealing with the patient's family.

Palliative care includes comforting, supporting and lending a sympathetic ear to the patient's family, who play an important role both when palliative sedation is being considered and while it is being carried out (see refs. 32, 53, and 97-99). They often serve as carers, observers, informants and the patient's representatives in addition to their role as partner, relative or friend. They each pass through their own emotional journey of doubt, guilt, fear, sorrow and mourning. Informing them and explaining things to them, as well as cooperating and evaluating the situation with them, are essential if the palliative sedation is to work to good advantage and those involved can bid a meaningful farewell. Carers should communicate to the patient's family in a language they can understand.

The role of family in relation to the indications for palliative sedation and the decision-making process has been discussed in chapters 3 and 4 respectively. In cases where acute sedation has had to take place for medical reasons, the indications, decision-making process and sedation procedure will all be discussed with the family in retrospect.

Since palliative sedation is a medical procedure, it is the physician who bears final responsibility for assessing the indications for it and deciding to carry it out. At this stage, the main role of the family is to provide information and non-medical care (especially if the patient is being nursed at home). It is only once the patient is decisionally incompetent that his representative plays any formal role in decision-making. Because the patient will be decisionally incompetent during continuous sedation, one of his family will generally take on the role of representative. The active involvement of this person in the initial decision-making process may help to ensure continuity later. The remainder of this chapter considers various aspects of the situation once the decision has been taken:

1. the sedation procedure;
2. the patient's approaching death;
3. aftercare;
4. problems experienced by family themselves.

1. The sedation procedure

Once the option of palliative sedation has been raised, it is important to provide the patient's family with clear information, to prepare them, to agree how things are to be done and to apportion roles.

In the first place, the aim is to prepare them by providing information about what they can expect to happen when the patient is sedated. They will tend to be a frequent presence at the patient's bedside and providing such information will prevent them being confronted with unexpected or confusing situations. In this context, it may be important to discuss the following issues.

- The decision to withhold fluids and the fact that this need not cause the patient any suffering.
- The extent to which it will be necessary to lower the patient's level of consciousness (to achieve adequate relief of symptoms).
- The uncertainty about the speed with which the necessary lowering of consciousness can be achieved and the possibility that the patient may recover consciousness after first losing it.
- The fact that involuntary movements or agitation need not mean that the patient is in pain or discomfort.
- The fact that some clinical symptoms, such as haemorrhages, vomiting or diarrhoea will not be prevented or relieved by palliative sedation alone. The sedated patient will no longer be aware of such symptoms, but they may come as a shock to family who are not prepared for them.
- The patient's life expectancy and the fact that palliative sedation will not influence it.
- The care that family can provide during sedation.
- The availability of emotional support for family (for example, in relation to the approaching death of the patient).
- The point of holding a vigil and the benefits of leave-taking rituals.

In addition, practical information should be given (preferably in writing) about the professional care of the patient, such as:

- who bears ultimate medical responsibility and how the attending physician can be reached;
- when, how, and with whom the situation is to be evaluated each day;
- a clear definition of the factors that may lead to a review of the management of the case;
- if home care technology is to be used, what is to be used and who is to provide it;

- what additional medical procedures and forms of nursing care are or will remain necessary and who is to be responsible for them;
- what to do about problems, who can be called in to help and how to contact them;
- who can provide help with any problems of their own that family may experience while caring for the patient.

The provision of information should not be a matter of one-way communication. It is equally important that the patient's family are encouraged to offer the staff involved in the case information they gain through spending time with the patient and observing him. It is important to make agreements and apportion roles. During sedation, staff will retain their professional responsibility for medical and nursing care. Agreements with family must at least address the issue of how the patient is to be represented in decision-making. The following issues can be raised with family.

- Who is to act as the patient's representative.
- How liaison between the family and medical staff is to be organised.
- How daily evaluations are to be conducted.
- How family observations are to be recorded/discussed and used in deciding on further medical or nursing procedures to ensure the patient's comfort. These may relate to new problems but also to adjusting existing medication if, for example, the patient shows signs of pain or agitation, or of an insufficient or excessive lowering of consciousness.
- What care is to be provided by the family themselves and where they would like help.
- Who must alert the physician and nurse in the case of acute problems and how this is to be done.
- If roles need to be changed or modified, how this is to be discussed and with whom.

Discussions of the roles of the family should include explicit consideration of the roles of the professional carers themselves and concrete agreements should be made in this respect (see above).

2. The patient's approaching death

The patient's family must also be offered support and a sympathetic ear as the patient approaches death. It will often be impossible to offer a precise prognosis; sometimes death may clearly be imminent, but sometimes it may take longer than expected or the patient may suddenly expire. It is better for leave-taking and associated rituals to take place before sedation is initiated. This is also the best time to make agreements about who is to be present when the patient dies and about the laying out of the body and any post-death rituals. In the lead-up to death, family members may be in great doubt about the suffering being experienced by the patient; they may once again fear complications or be unsure about their own

ability to cope. In some patients, the existing symptoms may become worse or new problems may emerge, such as Cheyne-Stokes respiration, death rattle, ischemia, cyanosis and decubitus. Family will need extra emotional support and information to cope with these. It is crucially important to their grieving process that symptoms continue to be effectively managed at this stage.

3. Aftercare

Aftercare includes the filling out of the death certificate (death by natural causes following correctly induced palliative sedation) and any arrangements for agreed organ donation. Family may need practical advice about burial, cremation, financial arrangements etc. This is certainly the time to give them a chance to express their feelings about the way the patient died, as a preparation for the grieving process. This will provide a release valve for their emotions and their feelings about the role they played and the support (or lack of it) they received from others and from the professionals involved in the case. After this, follow-up appointments will usually be made with their own general practitioners and/or the nurse. In addition to the usual bereavement counselling, time can be made on these later occasions to talk about the problems that led to the decision to administer sedation and about their memories of the course of the sedation process and the patient's death while under palliative sedation.

4. Problems experienced by family themselves

In the last stages of the patient's life, attention needs to be paid not only to the situation of the patient, but also to the feelings of family, the various roles they play, the burden placed upon them and the problems they may face. The initiation of sedation can lead to feelings of emotional and physical relief: the patient has been put out of his suffering, relative calm has been restored and there will often be good (more extensive) professional help if the patient is still being cared for at home. On the other hand, this may be the time at which it dawns on the family that the patient's death is relatively imminent. The intimacy of family care may be disrupted by the introduction of technology and extra professional staff. Continuous sedation can feel like a loss not only of intimacy, but also of contact with the patient and as the moment of leave-taking. Family may have doubts about their own role in the lead-up to the decision to initiate sedation. What is more, their role will be changed by the initiation of sedation and may well not be clear to the various parties. Feelings of loss and anticipatory grief must be suspended because the patient is still alive. The result may be feelings of uncertainty, helplessness and alienation and there is an increased risk of stress, exhaustion or burn-out among family. The burden will be especially hard to bear if the period of continuous sedation is longer than they had expected. Every new symptom and complication in the pa-

tient's condition and every problem with the technology, professional care or communication may then prove too much.

The professionals involved in the case need to respond adequately to this situation. By providing information and making it clear to the family what their role is, but that the professional responsibility for the case lies elsewhere, they can ensure that family remain involved in the whole process without experiencing stress, anxiety or doubts about the part they should be playing. Daily evaluation of the patient's comfort, the organisation of care, and the feelings and needs of family can reduce feelings of exhaustion and helplessness. If, despite all this, those around the patient start to put pressure on staff to step up sedation or even to resort to action that will shorten life, the first step should be to explore the feelings of family about the patient's suffering and their own ability to cope with the situation. Staff should proceed tactfully in this respect, by showing that they are sympathetic to family problems and prepared to talk about them. This in no way changes the fact that the management of the patient's condition is a medical matter and responsibility. There is no place in it for incorrect use, doses or combination of drugs. As discussed earlier in this chapter (see point 3), the care of the patient's family should continue in the period immediately following death.

10 Caring for the carers

As discussed in chapters 4 and 9, it is important not only to provide the best possible information and emotional support for the patient and his family, but also to care for the various professionals involved in the case. The emphasis in this guideline is on the tasks and responsibilities of the attending physician, but in practice other professionals – in particular nursing staff and other carers – will also have a role to play.

Palliative care includes caring for the carers. Only if carers show consideration for their own and each other's practical and emotional needs and if their organisations support them in this respect will they be capable of continuing to provide proper care for patients and their family. Since the process of dying takes longer than in the past and dying patients require the support of professional staff in addition to that of their family, professionals have to cope more frequently with the demands of the dying and their family (see refs. 98-101).

Providing palliative care for people in the last stages of life is inspiring, challenging, interesting and – in more than one way – worthwhile. At the same time, it has to be recognised that such work can be emotionally and physically demanding.

Like the patient and his family, all professional carers need support (see ref. 102). Four areas can be distinguished in this respect (see ref. 103):

1. information;
2. clinical and practical support;
3. emotional support;
4. reflection.

Support in these areas is, of course, necessary for physicians as well as other professionals caring for the patient.

1. Information

It is important that everybody in the care team should be informed without delay of the diagnosis, prognosis, plans with regard to palliative care, and the indications on which these are based. This is important both to promote good practice by the relevant professional carers and to avoid misunderstandings between them and the patient and/or his family as a result of disparities in information. The physician should be particularly alert to the fact that nursing staff and other carers and professionals may experience doubts, moments of difficulty or

even ethical dilemmas when caring for patients in the last stages of life. The organisation of the team must be clear to all its members.

2. Clinical and practical support

All patient care is based on good teamwork between the professionals involved in the case. There must be regular meetings between the physician and the person coordinating the care provided by other professionals to discuss the care plan. The care coordinator must be approachable and easy for staff to contact if questions or dilemmas arise. He or she must in turn be able to consult the physician about the management of the case and any questions raised by professional carers involved in it.

Where staff feel the need for a meeting to assess the case, time should be made for one. All of them should be sufficiently knowledgeable about and skilled in the various forms of palliative care. As well as knowing how to organise it and how to communicate effectively with all involved, they should have an adequate understanding of the somatic, psychological, social, spiritual and ethical aspects of palliative care. Proper training (both of the team and of the individuals within it) is essential in this respect.

The work must be well resourced; staff must have access to the equipment they need to facilitate it. In the case of palliative sedation, this means ready access to infusion pumps, intelligible files containing clear agreements about the management of the case, transparent protocols, and lists of telephone numbers to enable staff to contact each other easily if problems arise (see also chapter 7).

3. Emotional support

Their professional role of supporting patients and their family does not always leave staff with sufficient time and energy to deal promptly and adequately with their own emotions. Like family, the physician and other professionals may experience the moment at which the patient loses consciousness and can no longer communicate as a kind of bereavement. Staff should show consideration for each other's emotions as such times. Caring for the carers means, therefore, ensuring that staff feel safe to express their emotions to each other and that they receive sympathy and emotional support in return.

4. Need for reflection

The regular confrontation with suffering, the dying process and death brings staff face to face with their own mortality. This creates a need for personal and group reflection. Questions which may arise in this context are: What is a good death? When is a particular mode

of treatment still beneficial and how long should it be continued? What can be done to alleviate the suffering of the patient and his family? What are the patient's remaining wishes and options regarding any unfinished business in his life and how can the patient and his family take leave of each other? What sources of inspiration are available in this respect? What norms and values are driving the patient, his family and us as professionals? How can we explicitly and implicitly recognise the patient as a unique individual, so that he and his family will feel safe and supported?

Caring for carers means communicating well with them, guiding them, and offering them the opportunity to reflect on what is happening. Taking time to think back and reflect on the entire situation after the patient's death helps provide clarity and identify areas that could be improved, thus improving the overall quality of care.

11 Conclusions and quality of scientific evidence

This chapter summarises the main conclusions reached in this guideline. These conclusions are based on the findings reported in the national and international literature and on the opinions of respected authorities. Each conclusion is accompanied by bibliographical references.

Depending on the relative persuasiveness of the underlying scientific evidence, the literature is categorised as follows:

- A1 Systematic reviews of a fair number of level-A2 studies, where the results of the different studies are consistent;
- A2 Randomised comparative clinical studies of good quality and adequate size and consistency;
- B Randomised clinical trials of mediocre quality or inadequate size, or other comparative research (non-randomised, comparative cohort study, case-control study);
- C Non-comparative studies;
- D Opinion of respected authorities, e.g. members of the working group.

The persuasiveness of the evidence is categorised as follows:

- Level 1 Based on 1 systematic review (A1) or at least 2 level-A2 studies conducted independently of each other;
- Level 2 Based on at least 2 level B-studies conducted independently of each other;
- Level 3 Based on 1 level-A2 or level-B study, or on level-C research;
- Level 4 Opinion of respected authorities.

Little systematic research has yet been conducted in the field of palliative sedation. For ethical reasons, it is virtually impossible to conduct randomised comparative clinical research in this area (see ref. 38).

What is palliative sedation? For discussion, see p. 17

The basic term used by the committee in this guideline is 'palliative sedation'. This term has been chosen to make it clear that sedation is administered as part of an overall plan or process of palliative care. It refers not only to continuous, deep sedation, but also to superficial and temporary or intermittent sedation. Following a study of the literature and extensive discussion, the committee has opted for the following definition:

Conclusion 1 Palliative sedation is 'the deliberate lowering of a patient's level of consciousness in the last stages of life'.

Level 4 Beel (ref. 46), Chabot (ref. 48), Chater (ref. 59), Cowan (ref. 41), Morita (ref. 43), Ondersteuningspunt Nijmegen (ref. 29), and Verhagen (ref. 31).

The word 'deliberate' is included in the definition in order to exclude situations in which the lowering of the patient's level of consciousness is a (perhaps unintended) side-effect of treatment.

Conclusion 2 The use of drugs not normally used primarily as sedatives cannot be regarded as palliative sedation.

Level 4 Boorsma (ref. 47), Cowan (ref. 41), Deijck (ref. 52), Hallenbeck (ref. 61), Quill (ref. 53), Schuurmans (ref. 4), Sykes (ref. 54), Swart (ref. 40).

Relationship between palliative sedation and action intended to terminate life. For discussion, see pp. 19 and 66, 67

The aim of palliative sedation is to relieve suffering and not to shorten or prolong life. Palliative sedation is a normal medical procedure and must be clearly distinguished from euthanasia.

Conclusion 3 Palliative sedation is a normal medical procedure and is of a different order from euthanasia.

Level 4 Bood (ref. 3), Boorsma (ref. 47), Broeckaert (ref. 45), Gevers (ref. 5), Schuurmans (ref. 4), Verhagen (ref. 31)

Conclusion 4	Administered proportionately, palliative sedation does not hasten death.
Level 3	Broeckaert (ref. 45), Chiu (ref. 55), Kohara (ref. 58), Morita (ref. 43), Stone (ref. 56), Sykes (ref. 54), Ventafridda (ref. 57), Wein (ref. 32).

It is the form of palliative sedation involving continuous, deep sedation until the moment of death that has been the main focus of the medical-ethical, legal, social and political debate that has taken place in the Netherlands on the subject of palliative sedation over the past few years. For this reason, the main emphasis in this guideline is on this specific form of palliative sedation.

The indications and preconditions for palliative sedation. For discussion, see p. 22

Conclusion 5	Indications for palliative sedation are present if the patient is suffering unbearably as a result of one or more untreatable or 'refractory' symptoms.
Level 3	Cherny (refs. 34, 64), Cowan (ref. 36), Hawryluck (ref. 70), Morita (ref. 37), Ondersteuningspunt Nijmegen (ref. 29), Quill (ref. 53), Rousseau (refs. 68-69), Verhagen (ref. 31) and Wein (ref. 32).
Conclusion 6	A symptom is considered to be refractory if none of the conventional modes of treatment is effective or fast-acting enough, and/or if these modes of treatment are accompanied by unacceptable side-effects.
Level 4	Braun (ref. 35), Cherny (ref. 34), Morita (ref. 42) and Rousseau (ref. 68).

Conclusion 7	In practice, pain, dyspnoea and delirium are the refractory symptoms that lead most frequently to the use of continuous deep sedation.
Level 4	Cherny (ref. 34, 64), Cowan (refs. 41, 36), Chater (ref. 59), Fainsinger (ref. 84), Rietjens (ref. 63), Verhagen (ref. 31), Voltz (ref. 65), Wein (ref. 32).

Besides the presence of one or more refractory symptoms (indications), a second precondition is the expectation that death will ensue in the reasonably near future – that is, within one to two weeks. In these circumstances, a medical practitioner may decide to initiate palliative sedation and in principle to continue it until the moment of death. If the patient's life expectancy exceeds one to two weeks, the non-administration of fluids could affect the time of death, since it is not impossible for death to be hastened by dehydration.

Conclusion 8	A precondition of deep, continuous sedation until the moment of death is that the patient's life expectancy should not exceed one to two weeks.
Level 4	Cowan (ref. 36), Smith (ref. 73), Quill (ref. 53), Verhagen (ref. 31), Wein (ref. 32).

Conclusion 9	In cases where life expectancy is longer than one to two weeks, superficial, temporary or intermittent sedation may be considered.
Level 4	Cowan (ref. 36), Ondersteuningspunt Nijmegen (ref. 29), Verhagen (ref. 31), Wein (ref. 32).

The committee feels that particularly careful consideration is needed to establish whether a certain symptom is permanently refractory and to decide on that basis to initiate continuous sedation in any situation where it is difficult to judge whether the patient is in the last stages of life. After lengthy discussion, the committee arrived at the following conclusion:

Conclusion 10	The advice of a consultant, preferably a palliative specialist, is mandatory if the attending physician possesses insufficient expertise and/or is in doubt about key issues such as medical indications and life expectancy.
Level 4	Gevers (ref. 5), Quill (ref. 53).

The decision-making process. For discussion, see p. 28

The question of whether to initiate palliative sedation may be raised by the patient and/or his representative(s). Equally, staff caring for the patient may raise the possibility, if they believe that the patient's situation is developing in such a way that the indications for palliative sedation are present, or soon will be.

Once the question has been raised, the patient's situation must be assessed thoroughly in the light of the indications and preconditions for palliative sedation. This assessment should include information provided not only by the professionals involved in the case but also by the patient himself and his representative(s).

The assessment must culminate in a decision on palliative sedation by the physician responsible for the case. This decision should specify the objective (relieving suffering by treating a particular refractory symptom), the nature of the sedation (temporary, intermittent or continuous), the choice of drugs, and the dose to be administered.

Given the nature and content of palliative sedation and the indications set forth in this guideline, the committee sees no need to insist that an expert physician be consulted at all times before deciding to administer palliative sedation (for an exception to this, see conclusion 10).

Conclusion 11	As with other forms of medical intervention, it is unnecessary to consult an expert physician if the attending physician possesses sufficient expertise to take a sound decision on his own.
Level 4	Cherny (ref. 34), Keizer (ref. 76), Ponsioen (ref. 75), Quill (ref. 53), Wein (ref. 32).

In acute situations where it is impossible to consult with all concerned before deciding to administer palliative sedation, the attending physician has the discretionary power to make the decision on the basis of the patient's condition. In such cases, the steps normally taken before the decision should be taken as soon as possible after it: that is, all relevant information should be recorded in the patient's file, and consultations should be held with the other carers and/or a specialist consultant where applicable.

Conclusion 12	Palliative sedation should be administered only after a careful exploration of the patient's situation, in the light of the general indications and preconditions for the procedure. Information provided by the patient, his representative(s) and the professionals involved in the case will be an essential factor. Only in acute situations, where there is no time to consult with all concerned before taking the decision to administer sedation, does the attending physician have the discretionary power to decide on palliative sedation on the basis of the patient's condition alone.
Level 4	Braun (ref. 35), Quill (ref. 53), Wein (ref. 32).

Administration of fluids. For discussion, see p. 35

The vast majority of patients have virtually ceased eating and drinking by the time palliative sedation is initiated and die within a few days afterwards. In cases where the patient has a life expectancy of no more than one to two weeks, hydration is not a relevant factor in the decision on initiating continuous sedation. The committee feels that artificially administering fluids to patients under deep, continuous sedation is medically futile and may even exacerbate suffering.

Conclusion 13	In cases of continuous, deep sedation until the moment of death, there should be no artificial administration of fluids.
Level 4	CAL (ref. 80), Deijck (ref. 52), Fine (ref. 33), Gezondheidsraad (ref. 79), Hallenbeck (ref. 61), Janssens (ref. 78), Quill (ref. 53), Verhagen (ref. 67).

Good medical practice in the administration of palliative sedation. For discussion, see p. 38

It is crucial that palliative sedation should be administered proportionately. In other words, consciousness should be lowered only to the extent necessary and sufficient to relieve symptoms. It is not the degree to which consciousness is lowered, but the degree of symp-

tom control or the comfort of the patient that should determine the dose, combinations, and duration of the drugs administered to achieve palliative sedation.

Interim evaluations and decision-making processes must always be geared to relieving the patient's suffering by maintaining or adjusting doses and/or drugs in order to create a tranquil and tolerable situation.

Conclusion 14	Palliative sedation should be administered proportionately: it is not the degree to which consciousness is lowered, but the degree of symptom control that should determine the dose, combinations, and duration of the drugs administered to achieve palliative sedation.
Level 4	Broeckaert (ref. 45), Chater (ref. 59), Rousseau (ref. 60), Sykes (ref. 54), Wein (ref. 32).

Midazolam is the drug of choice. In general, it is preferable to opt for subcutaneous rather than intravenous administration. If life expectancy exceeds one to two days, it is best to administer midazolam by means of a continuous subcutaneous infusion pump. If the patient fails to respond adequately to midazolam, checks should be performed to see whether the mode of administration and the medication are in order, and/or whether any disruptive and remediable factors (e.g. a full bladder or constipation) are playing a role. Only then can consideration be given to the use of a different sedative, such as levomepromazine or propofol.

Conclusion 15	Continuous, subcutaneous administration of sedatives is the preferred method. This should be based on a step-by-step approach. If an adequate dose fails to achieve the desired effect, it is time to proceed to the next stage.
Level 4	Bottomley (ref. 92), Burke (ref. 95), Chater (ref. 59), Chiu (ref. 55), Fainsinger (refs. 66, 84-87), Greene (ref. 82), Mclver (ref. 81), McNamara (ref. 93), Morita (ref. 94), Moyle (ref. 88), Muller-Busch (ref. 91), Stiefel (ref. 89), Stone (ref. 56), Swart (ref. 40), Ventafridda (ref. 57), Verhagen (ref. 31).

Record-keeping and evaluation of palliative sedation. For discussion, see p. 42

It is essential to keep accurate records in cases of palliative sedation. This helps to ensure the quality and continuity of care. The relevant information about the patient and his situation should be recorded in his file: why it was decided to administer palliative sedation, how it has been administered, how the effect is being evaluated and what criteria are to be applied when adjusting the dose of sedatives.

The attending physician should visit the patient at least once a day. He should check particularly for any complications and should evaluate the situation with other professional carers, with the patient himself (if possible) and with the patient's family. The management of the case can then be reviewed and modified on the basis of this evaluation.

Conclusion 16	Accurate records must be kept of the decision-making process, the way palliative sedation is being administered and the effect of the intervention. The management of the case can be modified on the basis of daily evaluations.
Level 4	Braun (ref. 35), Cherny (ref. 64), Rosseau (ref. 60), Quill (ref. 96).

Brief or intermittent sedation. For discussion, see p. 44

The difference between brief or intermittent palliative sedation and continuous palliative sedation is that the latter is administered until the moment of death, whereas in the case of brief or intermittent sedation the patient is only temporarily sedated and then wakes up again. The primary aim of brief or intermittent palliative sedation is to restore tranquillity to the situation and then allow the patient to return to consciousness.

In some situations, brief or intermittent sedation offers an opportunity to see whether a symptom is permanently refractory. It also gives the attending physician the chance to assess the situation with the patient and/or his family and if necessary to modify the management of the case. As in the case of continuous sedation, it is extremely important that brief or intermittent sedation should be applied proportionately.

The recommendations for continuous sedation apply equally to brief or intermittent sedation, albeit with the following reservations and modifications:

- brief or intermittent sedation can also be applied where a symptom is only temporarily untreatable and it is not a precondition that life expectancy should be less than two weeks;
- in the case of brief or intermittent sedation, it will not usually be necessary to discuss the non-administration of fluids. In principle, the administration of fluids can continue.

Conclusion 17	Brief or intermittent palliative sedation can be used to create a period of tranquillity. It also provides the opportunity to see whether a symptom is permanently refractory and to evaluate the management of the case with the patient himself and if necessary modify it. The administration of fluids can continue (intermittently). Life expectancy is not a limiting factor.
Level 4	Fine (ref. 33), Morita (ref. 97).

Dealing with the patient's family. For discussion, see p. 46

Palliative care includes comforting, supporting and lending a sympathetic ear to the patient's family, who play an important role both when palliative sedation is being considered and while it is being carried out. They often serve as carers, observers, informants and the patient's representatives in addition to their role as partner, relative or friend. They each pass through their own emotional journey of doubt, guilt, fear, sorrow and mourning. Informing them and explaining things to them, as well as cooperating and evaluating the situation with them, are essential if the palliative sedation is to work to good advantage and those involved can bid a meaningful farewell. Carers should communicate to the patient's family in a language they can understand. The care of the patient's family should continue in the period immediately following his death.

Conclusion 18	Informing and supporting the patient's family is an essential part of caring for a patient receiving palliative sedation, not only up to the time of the patient's death, but also afterwards. The information that they give in return will be extremely valuable in the evaluation and modification of case management.
Level 4	Morita (refs. 97-99), Quill (ref. 53), Wein (ref. 32).

Caring for the carers. For discussion, see p. ...

Palliative care includes caring for the carers: throughout the entire process, attention should be paid to the team of professionals involved in the case. Like the patient and his family, professional carers need support. Caring for carers means communicating well with them, guiding them, and offering them the opportunity to reflect on what is happening. Taking time to think back and reflect on the entire situation after the patient's death helps provide clarity and identify areas that could be improved, thus improving the overall quality of care.

Conclusion 19 **The circumstances surrounding palliative sedation can make heavy demands on the professional carers involved. The provision of information and practical and emotional support for staff is extremely important.**

Level 4 Morita (ref. 98-100), Papadatou Danai (ref. 103), Unen (ref. 102).

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Annexe II Organisations and individuals consulted by the committee

- Public Prosecution Service, Board of Procurators General
- Health Care Inspectorate (IGZ)
- Netherlands Association of Nursing Home Physicians (NVVA)
- Dutch College of General Practitioners (NHG)
- Netherlands Association of Palliative Care Consultants (NAPC)
- Netherlands Society of Neurology (NVN)
- Netherlands Society of Anaesthesiologists (NVA)
- Netherlands Society for Medical Oncology (NVMO)
- Netherlands Association of Pulmonologists and Specialists in Tuberculosis (NVALT)
- Netherlands Association of Oncology Nurses (V&VN Oncology)
- Netherlands Association of Palliative Nurses (V&VN Palliative Nursing)
- Voluntary Euthanasia Society (NVVE)
- Association of Comprehensive Cancer Centres (VIKC)
- Regional Euthanasia Review Committees (RTC)
- Royal Netherlands Society for the Advancement of Pharmacy (KNMP)
- Professor B. Broeckaert (Catholic University of Leuven)
- Professor J.J.M. van Delden (Utrecht University)
- Professor J.K.M. Gevers (University of Amsterdam)
- Professor G.A. den Hartogh (University of Amsterdam)
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* Both also representing the Netherlands Society of Anaesthesiologists (NVA)

Annexe III Relationship between continuous, deep sedation and action intended to terminate life

The debate on continuous, deep sedation and its relationship to action intended to terminate life is a medically, socially and politically sensitive issue. The committee takes the view that palliative sedation is a normal medical procedure and must be clearly distinguished from termination of life. This annexe sets out its position in this regard.

Towards the end of the patient's life, a variety of medical and other procedures and decisions may become necessary. They may include decisions to withdraw particular kinds of treatment, to intensify symptom control measures, not to resuscitate, to abstain from artificially administering fluids, to provide continuous, deep sedation and even to terminate life (via euthanasia, assisted suicide or termination without request). It should be stressed that, although these procedures or decisions may be closely interconnected, they each have their own particular characteristics and specific medical indications. It is not uncommon for a number of different procedures to be employed or decisions taken, either simultaneously or sequentially, during the last stages of a patient's life.

Both at policy level and in practice, there is sometimes a lack of clarity about the distinction between continuous, deep sedation until the moment of death and euthanasia. Continuous, deep sedation as described in this guideline is a way of ensuring that patients are unaware of their symptoms and therefore relieved of suffering in the period immediately prior to death. Continuous, deep sedation differs from euthanasia in that its aim is not to shorten life. Indeed, there is no evidence that such sedation, if carried out in accordance with good medical practice, does shorten life. Consequently, a clear distinction should be drawn between the two.

In recent years it has been suggested that physicians might view continuous, deep sedation as a way of 'avoiding' euthanasia. This implies that continuous deep sedation is an alternative to euthanasia that is being put forward as such by medical practitioners. The committee considers it of great importance that the two procedures should be distinguished from one another as clearly as possible. The preconditions that must be fulfilled for continuous sedation and euthanasia do not necessarily coincide. Continuous sedation can only be adminis-

tered in the terminal phase, which does not apply in the case of euthanasia. However, rare situations may arise in which the indications and necessary preconditions for continuous sedation and euthanasia both apply, and in which the circumstances are such that the patient may be able to choose between these options (refs. 24, 26 and 27). In these cases, it is important to ascertain carefully how the patient wishes to put an end to the unbearable suffering he or she is experiencing:

- by lowering the level of consciousness until the time of death, in which case the preferred option would be continuous sedation until the time of death; or
- by remaining conscious until a moment chosen by the patient for the end of life, in which case euthanasia would be the preferred option.^{xviii} The patient's own wishes are decisive in this situation.

Continuous sedation until the moment of death is the treatment of choice if the patient no longer wishes to suffer but does not wish to take the assisted suicide or euthanasia route. If the patient feels that his suffering is such that he no longer wishes to remain alive, euthanasia is the more obvious choice. The patient may have good reasons for preferring euthanasia to continuous sedation; for example, he may wish to remain lucid enough to continue communicating with his family in his final days or he may not wish to die under sedation.

Another important difference is that continuous, deep sedation is in principle reversible, while euthanasia is not.^{xix} Because continuous, deep sedation, if properly practised, is a normal medical procedure, the decision to initiate it can if necessary be taken at a time when the patient is (temporarily or otherwise) incapable of giving consent, if the physician feels that this is the best course.

It follows from chapters 3 (What is palliative sedation?) and 4 (Indications and preconditions for continuous sedation) of this guideline that a patient with a life-threatening condition but without refractory symptoms cannot 'opt' for palliative sedation. Continuous sedation is only an option in the presence of an indication of the kind described in chapter 3. This means that, properly practised, continuous, deep sedation cannot be used to 'get round' the requirements and procedures for euthanasia and achieve the same aim (i.e. of shortening life) in a more gradual and surreptitious way. Continuous, deep sedation is therefore not a form of 'slow euthanasia'.

^{xviii} The conscious experience of death may be part of a person's concept of a good death.

^{xix} The committee would point out, however, that in the case of continuous, deep sedation, it is not desirable to allow patients to recover consciousness, since their refractory symptoms will then return.

Broeckaert summed up the key difference between euthanasia and palliative sedation in his remark that in the case of palliative sedation 'patients die, they are not killed' (see ref. 45). The main differences between the two options can therefore be summed up as follows.

1. Palliative sedation relieves suffering by lowering consciousness; euthanasia does so by terminating life.
2. Continuous, deep sedation does not in itself shorten life,^{xx} euthanasia certainly does. Indeed, palliative sedation may even prolong life to some extent (because it prevents exhaustion as a result of suffering).
3. Continuous, deep sedation is in principle reversible; termination of life is not.

If practised properly, palliative sedation must be described as a normal medical procedure (see refs. 3-5, 31, 45 and 47). This means that the indications for it and its use in medical practice are determined by current standards within the medical profession, and that it is the right of patients to receive palliative sedation (like other normal medical procedures), provided the accepted indications and preconditions are present. Euthanasia, and termination of life generally, is not regarded as a normal medical procedure; there is therefore no such thing as a right to euthanasia. Provided that continuous, deep sedation is administered proportionately (that is, using drugs and dosages tailored to achieve the requisite degree of symptom control), it cannot be regarded as a form of termination of life.

^{xx} Although it may occasionally do so in combination with the withdrawal of artificial hydration. See chapter 5.

The following table compares and contrasts continuous, deep sedation and euthanasia in greater detail:

	Continuous, deep sedation until the moment of death	Euthanasia
Aim	To relieve suffering	To end suffering
Means	Lowering consciousness	Terminating life
Medical procedure	Normal procedure	Exceptional medical procedure
Indications	Intractable (largely somatic) symptoms causing unbearable suffering	Unbearable suffering with no prospect of improvement
Only in the final stage of life	Yes, applicable in the case of a patient who is dying and who is expected to die within 1 or 2 weeks (precondition)	No
Patient consent	If possible	Invariably (well-considered request)
Consultation with independent physician	Not unless expertise lacking	Mandatory
Decision-making	If possible, consensus between patient, family and professional carers	Primarily patient and physician
Medication	Sedatives (esp. benzodiazepines)	Barbiturates and muscle relaxants
Dosage	Titrated to relieve suffering	Rapid overdosing
Administration	Physician and nurses	Physician
In principle reversible	Yes	No
Shortens life	No	Yes
Death by natural causes	Yes	No
Statutory controls	As for any other medical procedure	Separate legislation
Notification and review procedure	No	Mandatory

Annexe IV Drugs and dosages

Chapter 6 outlined the main considerations with regard to the choice of medication. This annexe addresses these considerations in greater depth and includes more detailed and technical information. Its content reflects the current state of knowledge in late 2008 (see refs. 31, 33, 36, 41, 44, 53, 59, 81-95).

The following medication can be used to achieve sedation:

Sedative	Means of administration	Maximum effect after	Half-life
Midazolam	s.c./i.v.	i.v.: 2.5 mins s.c.: 20 mins	1.5-2.5 hrs
Levomepromazine	s.c./i.v.	0.5-1.5 hr	15-78 hrs
Propofol	i.v.	1.5-2 mins	4-7 hrs
Diazepam	rectal	0.5-1.5 hrs	20-48 hrs
Lorazepam	s.l. (tablets or injection fluid)	60-90 mins	12-16 hrs
Clonazepam	s.l. (drops)	1-4 hrs	20-60 hrs

Continuous sedation until the moment of death

Palliative sedation is generally introduced in phases. If the initial appropriate dose does not produce the desired effect, one may proceed to the next phase. In a palliative setting, subcutaneously administered midazolam does not depress respiration if the dose is titrated to achieve the requisite degree of symptom control.

Chapter 1 noted that the entire guideline will be updated from time to time to incorporate new developments or knowledge. The impression exists, on the basis of a pharmaco-kinetic study (to be submitted for publication in the near future) and a number of observations in practice that in the context of continuous, deep sedation, the maintenance dose of midazolam given in the medication table in the previous version of the KNMG guideline on palliative sedation is often increased too rapidly. The 2005 guideline advised doubling the maintenance dose of midazolam administered in the first phase after 1-2 hours if the effect achieved was insufficient. However, pharmaco-kinetic research has shown that there is no stable serum concentration at that time. This means that the serum concentration may con-

tinue to rise after an adequate clinical effect has been achieved, as a result of which a deep intoxication may arise 8 to 24 hours after the initiation of sedation. The risk of this occurring is greater still if there is a failure to administer a bolus consistently in combination with any increase in dose. Another point is that Phenobarbital (phase 3 in the previous medication table) has proven hard to obtain, beside which it is difficult to dissolve for parenteral administration. Phase 3 (Phenobarbital) has therefore been removed from the updated table. These considerations lead to the following revised medication table.^{xxi}

	Drug	Bolus	Continuous administration
Phase 1	Midazolam	10 mg s.c. at the initiation of sedation, 5 mg s.c. every 2 hrs if necessary	Initially 1.5-2.5 mg/hr s.c./i.v., increase dose by 50% after a minimum of 4 hrs if effect is insufficient, <i>always</i> combined with a bolus of 5 mg s.c. If risk factors are present (age>60, weight<60 kg, severe kidney or liver function disorder, very low serum albumin and/or co-medication that could exacerbate the effect of sedation): - lower initial dose (0.5-1.5 mg/hr), and - longer interval (6-8 hrs) before increasing maintenance dose. In the case of doses > 20 mg/hr, see phase 2.
Phase 2	Levomepromazine	25 mg s.c./i.v., followed by 50 mg 2 hours later if desired	0.5-8 mg/hr s.c./i.v. in combination with midazolam. After 3 days halve the dose to prevent accumulation. If the desired effect is not achieved, stop administering midazolam and levomepromazine; see phase 3.
Phase 3	Propofol	20-50 mg i.v.	20 mg/hr i.v., increased by 10 mg/hr every 15 minutes. Administration under supervision of an anaesthetist advisable. In hospital setting, may also be considered for phase 2.

* The initial doses are based on the average patient. The physician should base his decisions on the effect of the medication. In the presence of extreme risk factors, such as a patient with a high (e.g. 100 kg) or low (40 kg) weight, the initial and subsequent doses may be adjusted upward or downward correspondingly. In case of doubt concerning the dose to be administered, the opinion of a palliative care consultant should be sought.

Midazolam is the sedative most commonly used for palliative sedation. In general, and certainly in the case of bolus injections, subcutaneous is preferable to intravenous administration, because of the practical advantages of subcutaneous infusion and the greater risk of

^{xxi} If necessary, this annexe will be updated more frequently than the guidelines themselves. The update will be publicised on the KNMG website and in other ways.

apnoea when bolus injections are administered intravenously. If life expectancy exceeds one to two days, it is best to administer midazolam by means of a continuous subcutaneous infusion pump.

On the basis of the above considerations and the modified medication table, if the effect achieved is insufficient after two hours, those administering palliative sedation are advised to give only a bolus of 5 mg midazolam, and only if the effect is still insufficient after a minimum of 4 hours, to increase the maintenance dose by 50% (not by 100%) (in combination with another bolus of 5 mg). If risk factors are present which might lead to delayed elimination or increase the effect of midazolam (age > 60, weight < 60 kg, severe kidney or liver function disorder, very low serum albumin and/or co-medication that could exacerbate the effect of sedation), it is necessary to wait longer (6 to 8 hours) before increasing the dose. These recommendations apply to subcutaneous administration. The result may be that it will take longer before the desired level of comfort is achieved. Patients and their family must always be told that the duration of the initial phase of sedation may vary widely.

In some rare cases, midazolam may prove insufficiently effective and/or the patient may unexpectedly recover consciousness. This is probably connected with metabolic changes (especially in the P-450 enzyme system) or with changes relating to the GABA receptor, on which midazolam acts (see ref. 83). For these and other reasons, the dosage of midazolam may have to be increased over time (tolerance); this is seen mainly in younger patients and more prolonged administration.

Where patients respond to the initiation of sedation by becoming delirious (a rare but not unknown complication, especially in children and elderly patients), it is advisable to increase the dosage rapidly. Patients with a history of intensive treatment with sedatives, antidepressants, anti-epileptics or antipsychotics are more likely to exhibit tolerance to midazolam and may require higher dosages.

If a patient is already being treated with opioids and/or antipsychotics, this medication should be repeated prior to sedation and maintained during sedation in accordance with the patient's needs. If a patient is delirious, sedation combined with an antipsychotic is the appropriate treatment. If the existing medication is being administered continuously via the parenteral route, it is preferable to administer the sedative drugs via a separate pump in order to avoid an undesirable increase in the existing medication when the doses of sedatives are increased.

If the administration of several boluses fails to render the patient unconscious, checks should be performed to see whether the mode of administration and the medication are in order, and whether any disruptive and remediable factors (e.g. a full bladder or rectum, withdrawal of nicotine or of corticosteroids used to treat elevated intracranial pressure etc.) are playing a role.

Whenever a patient recovers consciousness after initially being adequately sedated, it is important to check whether the patient is comfortable and whether the indications for continuous sedation are still present. In addition, the medication and mode of administration should be checked, as should the possible presence of other factors which may be disrupting sedation (urine retention, faecal impaction or abdominal cramps, inadequate analgesia, withdrawal from nicotine or medication, or delirium).

Only then can consideration be given to proceeding to the later phases in the table above and to the use of levomepromazine or propofol. In practice, however, the use of propofol is only very rarely necessary in cases of inadequate primary or secondary response to midazolam and/or levomepromazine.

Because of its long half-life, levomepromazine tends to accumulate; after three days, consideration should be given to halving the dose. The use of levomepromazine is not reimbursable under the Dutch system, but it is cheap. Few dispensing chemists in the Netherlands carry stocks of levomepromazine.

In some cases, it may be preferable to miss out phase 2 and proceed immediately to phase 3. This may be the case, for example, if the patient is in hospital, with the means of intravenous administration readily available and with an anaesthetist already involved in his treatment.

Especially where a patient is being cared for in the home, the use of a pump for continuous subcutaneous administration may not be desirable or indeed feasible. This is particularly the case where life expectancy is extremely short (1-2 days) and it may take longer than that to obtain a pump. In such circumstances, intermittent administration of sedatives may be an acceptable alternative. Depending on the situation, any of the following drugs can be selected for this purpose:

- midazolam administered via intermittent subcutaneous injections: 5-10 mg 6 times a day, if necessary an additional bolus after 2 hours; if the effect is insufficient, the dose of the bolus, to be administered every 4 hours, may be increased by 50%;
- diazepam administered rectally: 10 mg an hour until adequate sedation is achieved; on average, 40-60 mg will be necessary every 24 hours; however, rectal administration of diazepam has major practical and pharmacological disadvantages and will therefore be used only in exceptional circumstances;
- lorazepam administered sublingually: 1-4 mg every 4 hours;
- clonazepam administered sublingually: 1-2.5 mg every 6 hours.

Lorazepam and clonazepam are not registered for sublingual administration but experience has shown that tablets (or the contents of an ampoule) in the case of lorazepam or drops in that of clonazepam can be administered by this route. If intermittent sedation is to be administered subcutaneously, an infusion needle or butterfly can be inserted under the skin and connected to a three-way tap.

Acute sedation

In emergencies, when a very rapid lowering of consciousness is required, bolus injections can be given more frequently. In other situations, a calm atmosphere and gradual changes in consciousness are more important than speed.

Intermittent sedation

For intermittent sedation (in practice, always nocturnal), midazolam is in principle the only appropriate drug. In this case, phase 1 is maintained, and the medication is started at the time of going to sleep and stopped 30 min to 1 hr before the desired time of awakening. The following night, sedation will commence with the dose that induced the desired lowering of the level of consciousness the night before. If this desired level was not attained the night before, the maintenance dose will be further increased until the level of consciousness has fallen to the desired level. If the above-mentioned risk factors are present, there is a possibility that the patient may awaken far later than is desirable the next day.

Annexe V Bibliographical references

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