NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation document

The Danis stent for oesophageal variceal bleeding

The National Institute for Health and Care Excellence (NICE) is producing guidance on using the Danis stent in the NHS in England. The medical technologies advisory committee has considered the evidence submitted by the company and the views of expert advisers.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the public. This document should be read along with the evidence (see the committee papers).

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and resource savings reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?

Note that this document is not NICE's final guidance on the Danis stent. The recommendations in section 1 may change after consultation.

After consultation the committee will meet again to consider the evidence, this document and comments from the public consultation. After considering the comments, the committee will prepare its final recommendations which will be the basis for NICE's guidance on the use of the technology in the NHS in England. For further details, see the medical technologies evaluation programme process and methods guides.

The key dates for this guidance topic are:

Closing date for comments: 12 February 2021

Second committee meeting: 19 March 2021

Details of the advisory committee are given in section 5.

NICE medical technologies guidance addresses specific technologies notified to NICE by companies. The 'case for adoption' is based on the claimed advantages of introducing the specific technology compared with current management of the condition. This case is reviewed against the evidence submitted and expert advice.

If the case for adopting the technology is supported, the specific recommendations are not intended to limit use of other relevant technologies that may offer similar advantages. If the technology is recommended for use in research, the recommendations are not intended to preclude the use of the technology in the NHS but to identify further evidence which, after evaluation, could support a recommendation for wider adoption.

1 Recommendations

1.1 Evidence supports the case for adopting Danis stent for treating acute variceal oesophageal bleeding. Danis stent improves the short-term control of bleeding compared with a balloon tamponade and can be left in place for longer allowing time for stabilisation.

1.2 Danis stent should be considered for people aged 16 and over with acute oesophageal variceal bleeding that does not respond to endoluminal therapy and whose oesophageal varices are being considered fordefinitive treatment. Also, Danis stent should be considered for people when definitive treatment is not appropriate and who are likely to be offered palliative care.

1.3 Cost modelling shows that Danis stent is cost saving compared with balloon tamponade for acute oesophageal variceal bleeding being considered for definitive treatment. This is because having Danis stent results in a shorter stay in intensive care. To be cost saving, Danis stent needs to decrease intensive care stay by 0.6 days or more compared with balloon tamponade.

Why the committee made these recommendations

The Danis stent puts pressure on enlarged veins (varices) in a person's food pipe (oesophagus) when they are bleeding uncontrollably. Enlarged veins can develop when a person has longstanding scarring liver disease (cirrhosis) that affects blood flow through the liver. This causes pressure in the blood vessel that drains blood from the gut into the liver and enlargement of these veins in the oesophagus can predispose to bleeding. The Danis stent is designed to be used as a bridging treatment to control the bleeding until a decision on definitive treatment to manage the underlying pressure problem (such as a transjugular intrahepatic portosystemic shunt [TIPS] procedure, or band ligation) can be made.

Studies show that the Danis stent is better than the balloon tamponade device (a balloon inflation device that compresses the bleeding veins) in controlling bleeding in the short term. It can stay in place for up to 7 days. This is longer than the balloon tamponade, which needs to be removed after 24 hours. This allows more time to stabilise the person before their next treatment and also means that they do not usually need to stay in intensive care. Cost analysis concludes that Danis stent is cost saving compared with balloon tamponade because it reduces the number of days a person needs to stay in intensive care.

2 The technology

Technology

2.1 The Danis stent is a self-expanding and removable stent used to stop acute bleeding from oesophageal varices. The stent is a variable weave, made of nitinol with a silicone membrane. It is 135 mm long and 25 mm in diameter, inflating to 30 mm in diameter. During insertion, a balloon is inflated in the stomach to make sure the stent self-expands in an accurate position at the gastro-oesophageal junction, providing direct compression of oesophageal varices. The aim of the Danis stent is to stabilise the bleeding, until the person can have definitive treatment to manage the underlying problem. Features of the stent include radiopaque

markers for visibility, a security pressure valve and retrieval loops with gold markers. The company recommend that the Danis stent stays in place for no longer than 7 days. A specially designed removal device, the Ella extractor, is needed to remove the stent unless a definitive treatment has been done, in which case the risk of re-bleed may be considered low and the stent may be removed with grasping forceps.

Innovative aspects

2.2 The company states that the Danis stent can be used without direct endoscopic imaging, which may allow for more rapid control of variceal bleeds in emergency situations compared with balloon tamponade. The delivery system has a security pressure valve that prevents the gastric balloon from being inflated in the oesophagus, which may help minimise the risk of oesophageal perforation. The stent can stay in place for up to a week (compared with balloon tamponade, which should not be left in place for more than 24 to 36 hours). This may allow more time to plan definitive therapy (such as transjugular intrahepatic portosystemic shunt [TIPS] insertion, usually done more than 72 hours after Danis stent insertion) or secondary band ligation. It may also keep the bleeding stable for longer, allowing liver function to improve. The Danis stent keeps the oesophagus open, allowing oral nutrition to be maintained, which is an important element in recovery. Its variable weave stent body is designed to conform to oesophageal peristalsis, with the aim of preventing stent migration.

Intended use

2.3 The Danis stent is intended for use in acute refractory oesophageal variceal bleeding, after first-line therapy, such as variceal band ligation, has failed, to allow more time for a definitive procedure to be done. It is intended to be used as an

alternative to balloon tamponade or early TIPS insertion (that is, done within 72 hours), in people aged 16 and over.

2.4 The technology is intended to be used in secondary or tertiary care by gastroenterologists, hepatologists, emergency care practitioners, paramedics or nurse practitioners. Comprehensive training is needed and is delivered by the company.

Costs

2.5 The cost of the Danis stent is £1,495 (excluding VAT) per stent. The cost of the Ella extractor is £695 (excluding VAT).

For more details, see the website https://www.ukmedical.com/products/danis-stent/.

3 Evidence

Clinical evidence

The main clinical evidence comprises 9 studies

3.1 The evidence assessed by the external assessment centre (EAC) included 9 full text peer-reviewed studies including 247 people. Two of the studies were comparative, a randomised controlled trial (RCT) and a retrospective case-controlled study. The remaining 7 studies were non-comparative case series. For full details of the clinical evidence, see section 3 of the assessment report.

The comparative evidence is relevant to the decision problem but has limitations

3.2 Both comparative studies compare the use of the Danis stent with balloon tamponade. The studies report that using the Danis stent improves control of bleeding at 5 and 15 days. The RCT (Escrosell et al. 2016) is the strongest evidence for the Danis stent and reports a composite end point including control of bleeding and adverse events but it is underpowered for this result.

The retrospective case-controlled study only included patients with acute-on-chronic liver failure and there were significant differences between disease severity scores of the patients in the control group compared with the interventional group. The EAC reported that both studies have a moderate risk of bias.

The RCT (Escorsell et al. 2016) is not reflective of the UK care pathway

3.3 The RCT was done in Spain and differences in the care pathway limit the generalisability of the findings to the UK setting. Expert advisers stated that the definitive procedure, transjugular intrahepatic portosystemic shunt (TIPS), was delivered at an earlier stage after presentation in this trial than it would be in the UK.

The EAC did a meta-analysis on the 7 non-comparative studies

3.4 The 7 non-comparative studies are low in quality. The studies have broadly similar populations and outcomes. Outcomes with low heterogeneity were included in the analysis. Immediate bleeding control was found to have been achieved in 88% of cases (95% CI: 0.38 to 0.9) based on the 7 case series, one of which (Wright et al. 2010) was done in the UK. Survival rate at 30 days was 68% from 3 studies.

Cost evidence

The company used a cost-calculator model to compare the cost of using the Danis stent with balloon tamponade

3.5 The cost comparison has a 6-week time horizon and is from an NHS and personal and social services perspective. The model estimates the cost associated with the use of the Danis stent compared with balloon tamponade as bridging treatment for patients aged 16 or over with acute refractory oesophageal variceal bleeding in whom first-line therapy is unsuitable or has failed. The model captures the cost of the initial procedures, the

likelihood of adverse events for both technologies and the cost and use of resources to remove the devices. The key model parameters are:

- The proportion of patients that have either balloon tamponade or the Danis stent as a bridging treatment and the proportion of patients that have either TIPS or band ligation as a definitive treatment.
- Survival 6 weeks after treatment and relative risk of dying at 6 weeks with balloon tamponade compared with the Danis stent.
- Proportion of patients that have adverse events after treatment.

For full details of the cost evidence, see section 4 of the assessment report.

The EAC updated 5 cost parameters

3.6 Updated cost parameters include:

- the cost of removing the Danis stent(company, £1,257; EAC, £1,452.00)
- the cost of re-bleed (company, £3,287.00; EAC, £4,978.75)
- the cost of definitive TIPS treatment (company, £3,928.00; EAC, £4,965.56)
- the cost of definitive band ligation (company, £1,114.00; EAC, £4,983.67)
- the cost of severe hepatic encephalopathy (company, £400.52; EAC £400.56)

The EAC's updates to the cost model change the direction of the cost case

3.7 With the updated cost parameters, the EAC's base case shows that the Danis stent is cost incurring by £923 per person. The

company also presented 3 scenario analyses, all of which the EAC considered relevant. Scenario 1 modelled the cost of using each technology by cumulating the costs of the resources needed. Scenarios 2 and 3 explored uncertainty in the assumed impact of the bridge treatment on the choice of definitive treatment including (scenario 3) and excluding (scenario 2) hepatic encephalopathy costs.

Two additional scenario analyses were done to include a second endoscopy for patients that have a balloon tamponade

3.8 Clinical experts highlighted that a second endoscopy at the time of balloon removal is needed for people that have balloon tamponade and that the choice of definitive treatment is done on a case by case basis regardless of the bridging treatment used. Therefore scenarios 4 and 5 were done to include the cost of a second endoscopy:

- Scenario 4 – An extension of scenario 2 but with the addition of a second endoscopy for people treated with balloon tamponade based on expert comments.
- Scenario 5 – An extension of scenario 1 to explore the impact of reduced intensive care unit bed days in the Danis stent group and a second endoscopy for people treated with balloon tamponade.

Resource parameters in the micro costed model were updated based on expert advice and data about hospital admissions

3.9 Estimates about resource use in the care pathway were updated based on expert advice and were reported as scenarios 5A and 5B. The key parameters that were changed are:

- The proportion of patients that had Danis stent inserted within a theatre setting was increased

- The intensive care unit (ICU) length of stay was reduced in the Danis stent group and increased in the balloon tamponade group
- The cost of the balloon tamponade procedure was increased
- Costs were modelled for the proportion of patients that needed transferring from a secondary care setting to a tertiary care setting (scenario 5B only).

4 Committee discussion

Clinical-effectiveness overview

The clinical care pathway is complex

4.1 The clinical experts explained that oesophageal variceal bleeding is an acute clinical emergency and clinical care is managed on a case by case basis. First-line treatment is an endoscopy followed by band ligation. However, in rare cases, balloon tamponade may be done to control the bleeding before an endoscopy. If first-line therapy fails, balloon tamponade or the Danis stent is used as a bridging therapy to stabilise the patient before a definitive treatment, such as transjugular intrahepatic portosystemic shunt (TIPS) insertion, can be done.

4.2 People who cannot have definitive treatment are given palliative care. The committee heard from experts that the Danis stent can be used to control bleeding as a component of palliative care after all other lines of treatment have failed or if the patient cannot have definitive treatment with TIPS or transplant surgery. The committee concluded that the care pathway is complex, and that practice varies depending on the individual circumstances of each patient.

Balloon tamponade is an appropriate comparator

4.3 The committee noted that TIPS was included as a comparator in the scope and that in the RCT, TIPS was done within 72 hours of presentation. The experts explained that when TIPS is done this early it could be considered as a comparator to the Danis stent. However, the experts explained that it usually takes between 5 and 7 days to deliver TIPS in the UK and that Danis stent would be used before this timepoint. The committee concluded, therefore, that in the UK NHS setting, balloon tamponade is the best comparator for the Danis stent.

The evidence shows that the Danis stent improves short-term clinical outcomes

4.4 The comparative evidence reported that the Danis stent improves control of bleeding for patients in the short term (15 days). The committee recognised there were some key limitations in the evidence. For example, the population included in the retrospective case-controlled comparator study (Maiwall et al. 2018) was limited to patients with acute-on-chronic liver failure and the RCT study (Escorsell et al.,2016) was underpowered and was done in a non-UK setting. The committee considered the RCT to be the most robust evidence for the Danis stent and recognised the difficulties in doing controlled studies and generating evidence in this patient population. While the committee acknowledged the limitations in the studies it concluded that on balance the evidence shows that the Danis stent improves short-term clinical outcomes.

The evidence does not reflect potential use of the Danis stent in the UK care pathway

4.5 The RCT (Escrosell et al. 2016) was done in Spain and the clinical experts advised that TIPS was more accessible in this trial than it would be in the UK. They explained that TIPS procedures

are arranged and done in regional tertiary centres in the UK and that this procedure may only be suitable for people with less severe liver disease (Child-Pugh score A). In contrast, the experts explained that in the RCT, patients with more severe liver disease were given a TIPS procedure (Child-Pugh score B or C) and at an earlier timepoint than in the UK. The committee concluded that the protocol used in the RCT does not accurately reflect UK practice.

Side effects and adverse events

Adverse events are unlikely if users are well trained in using the Danis stent

4.6 Stent migration is reported to happen in 20% of cases. Clinical experts explained that in their experience, this figure is likely to be an overestimation and that stent migration happens rarely if operators are fully trained in using the device. Experts advised that there is a small risk of lung aspiration with the procedure and that patients should initially be managed in an intensive care setting after stent insertion. The risk of oesophageal perforation is higher in patients that have had balloon tamponade first. The committee concluded from the evidence and the expert advice received that using the Danis stent does not increase the risk of an adverse event.

Outcome measures

The evidence is limited to a 6-week follow-up time but this is acceptable

4.7 The evidence is limited to a follow-up time of 6 weeks or less. The committee recognised that some patients that have definitive treatment will live beyond 6 weeks, however it noted that the clinical evidence did not report a significant difference in mortality at 6 weeks between the Danis stent group and the balloon tamponade group. The committee also understood that people with oseophgeal variceal bleeding have other co-morbidities that

are likely to affect survival beyond 6 weeks and so it concluded that the time horizon to definitive treatment was appropriate for the cost modelling.

NHS considerations

The evidence does not capture all the system benefits of using the Danis stent

4.8 The Danis stent can be left in place for up to 7 days compared with a balloon tamponade which needs to be removed after 24 hours. Experts commented that in secondary or tertiary care settings, this additional time allows healthcare professionals the time to stabilise and monitor patients and arrive at a carefully considered clinical decision about the next stage of treatment. The experts highlighted that when patients need to be transferred to a tertiary care centre for definitive treatment, using the Danis stent can increase patient safety during the transfer. The committee recognised that there are limitations in the evidence and accepted expert advice about the additional patient and system benefits.

Training

The Danis stent users need training and regular reskilling

4.9 Healthcare professionals are trained to use the Danis stent. The committee heard from experts that training is straightforward for healthcare professionals with experience of endoscopic procedure and it is also possible to acquire the necessary skills even without this experience. Experts described that maintaining clinical competence within a large team is challenging because of the limited number of patients needing this procedure per year which necessitates regular reskilling. The committee considered that a lack of clinical confidence in using the Danis stent during a medical emergency situation might serve as a barrier for adoption

and suggested that the company should make sure centres that use the device have access to training and reskilling support.

Other patient benefits or issues

The Danis stent has benefits for people for whom further treatment may not be suitable

4.10 The clinical experts advised that for a small proportion of the patient cohort, estimated at between 5 and 6%, further definitive treatment may not be appropriate. Experts advised that the Danis stent can be used where all previous lines of therapy have failed, and in patients for whom either transplant surgery or a TIPS procedure is not suitable. After the stent is inserted, patients can be extubated, moved off a high dependency ward and managed in a more comfortable and less intensive environment where interaction with family and friends is more possible. The experts explained that when used in this way, the Danis stent can stay in place for at least 7 days and even longer. This scenario was not included in the cost modelling however the committee recgonised that data collection is unrealistic in this population. It concluded that, in the proportion of people for whom definitive therapy is not appropriate, the use of the Danis stent may offer substantial patient benefits in alleviating suffering and allowing compassionate care.

Cost-modelling overview

The base-case assumptions are not reflective of UK practice

4.11 The EAC base-case cost model used clinical parameters based on the RCT (Escorsell et al. 2016) and case series data. The committee received the following expert advice:

- definitive treatment is decided on a case by case basis in the NHS and is not impacted by the choice of bridging treatment.

- a second endoscopy is needed in the balloon tamponade group which was not included in the base case model.
- use of multiple healthcare resource group (HRG) costs could result in an overestimation of procedure costs.
- the incidence of hepatic encephalopathy should not differ between arms.

The committee concluded that the assumptions used in the base case did not accurately reflect the cost of using the Danis stent in the UK.

Scenarios based on expert advice to estimate resource use in the care pathway are acceptable

4.12 The EAC developed scenarios 5A and 5B based on clinical advice so that the cost model better reflected UK practice. Scenario 5A reported that using Danis stent was cost saving by £2,423. Scenario 5B included the cost of transferring a proportion of people from secondary to tertiary care, although this cost had little effect on the results. This scenario reported Danis stent to be cost saving by £2,426. The main cost drivers of these scenarios were the risk of rebleeding, the procedure costs and the estimated length of ICU stay. The committee recognised that there were uncertainties in the parameters because they were primarily based on expert advice but concluded that scenarios 5A and B were the most appropriate models for estimating the cost of Danis stent in the NHS.

Danis stent is cost saving and length of ICU stay is the main cost driver

4.13 The committee noted that the estimated difference in length of ICU stay had the greatest effect on the direction of the cost case results. Experts estimated that length of ICU stay for the Danis stent group is 3.6 days and 6 days for the balloon tamponade group. The EAC did threshold analysis for this parameter and reported that Danis stent would be cost neutral or cost saving

when the balloon tamponade group had an increased length of ICUstay of 0.6 days or more compared with the Danis stent group. The committee accepted the expert clinical advice that the clinical effectiveness of Danis stent is likely to impact the length of ICU stay and concluded that in all probability, Danis stent will reduce time in ICU by more than 0.6 days in UK clinical practice. The committee concluded that Danis stent is very likely to be cost saving compared with balloon tamponade in people being considered for definitive treatment for oesophageal varices.

Further data collection is welcome to address uncertainties in the cost case

4.14 The committee recongised that there are uncertainties in the cost case because of the limited information available about resource use. The committee noted that a planned multi-centre UK RCT was not completed because of difficulties with recruitment. It recognised that generating evidence is challenging in this small and heterogenous population and accepted that expert advice was an appropriate alternative to definitive UK evidence. Further data collection is welcomed by the committee in order to inform more accurate assessments of the cost savings associated with the use of Danis stent in the future.

5 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technology advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technology advisory committee, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more technical analysts (who act as technical leads for the topic), a technical adviser and a project manager.

Rebecca Owens
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