HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

NATIONAL COMMITTEE FOR THE EVALUATION OF MEDICAL DEVICES AND HEALTH TECHNOLOGIES (CNEDiMTS)

OPINION

14 September 2010

CONCLUSIONS	
Name:	**RELAY**, thoracic aortic stent-graft
Models and references:	Those proposed by the applicant (see page 4)
Manufacturer:	**Bolton Medical Espana, SLU**
Applicant:	**ABS – Bolton Medical**
Available data:	• Data not specific to RELAY Two articles by national health assessment agencies assessing vascular stent-grafts in the treatment of disease of the thoracic aorta are available: - the report by the National Institute for Health and Clinical Excellence (NICE) - 2005 - the report by HAS (Haute Autorité de Santé) - 2006 • Data specific to RELAY Three studies that specifically involve the RELAY thoracic aortic stent-graft were submitted. These studies are ongoing. The study reports were provided. - 3-year results of the non-comparative multi-centre study. Thirty patients were enrolled. Number of patients being followed up (had neither died nor been lost to follow-up) at 6 months was 26; at 1 year, 24; at 2 years, 20; at 3 years, 13; and at 4 years, 5. The planned duration of this study was 5 years. The endpoints were major morbidity and mortality. The total number of deaths during the follow-up period was 8. There were six cases of device-related major morbidity. - preliminary results of the non-randomised, comparative, phase II multi-centre study (involving 30 centres in the United States). The objective of this study was to compare safety and performance of the RELAY thoracic aortic stent-graft in patients with thoracic aortic aneurysm with a control group of patients receiving surgical treatment. 120 patients were to be enrolled in the endovascular treatment arm, and 60 patients in the surgical arm. Currently, 93 patients are enrolled in the endovascular treatment arm (the RELAY arm), and 7 patients in the surgical arm. Number of patients being followed up (had neither died nor been lost to follow-up) at 6 months was 55; at 1 year, 40; at 2 years, 13. - Preliminary results of RESTORE (Relay Endovascular registry for thoracic diseases), a European prospective post-marketing multi-centre study (22 centres in 7 countries). The objective of this study was to assess safety and

	performance of the RELAY thoracic stent-graft in patients with thoracic aortic disease (e.g. thoracic aortic aneurysm, penetrating atherosclerotic ulcer, dissection). The planned duration of follow-up was 2 years. The primary endpoint was mortality (procedure or device related death) and morbidity (serious adverse events and events either device or procedure related) at 2 years. 304 consecutive patients were enrolled. 114 patients had a 1-year follow-up, and 50 a 2-year follow-up. Mean duration of follow-up was 334 days [CI not recorded]. Mean length of hospital stay was 18 days (21 - 370 days). Mean number of stents used per patient was 1.26 (237 patients each had 1 stent implanted, 56 patients had 2, and 11 had 3). The number of patients who had died at 30 days was 22/304 (7.2%), and 6 of these deaths were either device or procedure related. ***The Committee considers that the ratio of therapeutic effect to adverse effects of the RELAY thoracic aortic stent-graft is sufficient for it to be used in the treatment of diseases of the descending thoracic aortic: aneurysms of more than 6 cm in diameter, acute aortic dissection where surgery is indicated, penetrating ulcers if there are complications, traumatic rupture of the isthmus in the context of multiple trauma.*** ***The Committee does note, however, that there is a lack of long-term data, and that the interim analysis (which was not planned for in the protocol) of studies involving RELAY specifically is not easy to interpret.***
Actual Benefit (AB):	**Sufficient,** for the following reasons: **- the therapeutic usefulness** of the product, as seen in the data provided and existing guidelines (NICE, HAS and OHTAC); - **the expected public health benefit**, given the serious nature of the diseases involved and the existence of an unmet treatment need, in cases in which conventional surgery is contraindicated.
Indications:	The following diseases of the descending thoracic aorta: - Aneurysms greater than 6 cm in diameter; - Acute dissections if surgery is indicated; - Penetrating ulcers, if there are complications; - Traumatic rupture of the isthmus in the context of multiple trauma.
Factors determining the AB: - Technical specifications: - Conditions for prescription and use:	No requirements in addition to the technical specifications proposed by the manufacturer. Implantation of the RELAY thoracic aortic stent-graft must be done in compliance with the guidelines issued by the Haute Autorité de Santé (HAS), which include the following: - Implantation must be done in centres that have expertise in both types of treatment (endovascular and surgical), and that have suitable technical capability. - There must be a multidisciplinary discussion process, particularly concerning the risks of conversion to open repair and possible use of cardiovascular bypass. - There must be a proximal section of aorta of at least 2 cm in length, which will enable the stent-graft to be inserted. - Patients must be informed of the advantages and drawbacks of the available repair techniques, i.e. open surgery and endovascular aortic repair (EVAR). - There must be annual monitoring using CT scan, or MRI + X-ray. Implantation of RELAY must lead to the use of one or two devices. In

	exceptional cases, a maximum of 3 devices may be implanted. The various devices used are connected to the SAFEX end configuration, which enables the stent-graft to be extended. The committee requests that patients be included in a prospective registry of all implantations of thoracic aortic stent-grafts, and that patients be followed up.
Added clinical value (ACV):	RELAY provides no improvement in Added clinical value (level V) in comparison with other thoracic aortic stent-grafts.
Type of inclusion on reimbursement list:	**Brand name**
Duration of inclusion:	**3 years**
Renewal conditions:	Implantation and follow-up data in the registry will be requested when renewal of inclusion is applied for.
Target population:	Around 1600

Definitive opinion 2

EVIDENCE REVIEW

Nature of the application

Application for inclusion on the list of products and services qualifying for reimbursement (LPPR) mentioned under article L. 165-1 of the French Social Security Code.

- **Models and references**

RELAY stent-grafts are available in straight and tapered configurations.

Straight model

		Length (mm)			
		100	**150**	**200**	**250**
Diameter (mm)	**22**	28-M2 22 090 22 22 90S	28-M2 22 150 22 22 90S	28-M2 22 190 22 22 90S	-
	24	28-M2 24 090 24 22 90S	28-M2 24 150 24 22 90S	28-M2 24 190 24 22 90S	-
	26	28-M2 26 095 26 22 90S	28-M2 26 155 26 22 90S	28-M2 26 195 26 22 90S	-
	28	28-M2 28 095 28 22 90S	28-M2 28 155 28 22 90S	28-M2 28 195 28 22 90S	-
	30	28-M2 30 095 30 22 90S	28-M2 30 155 30 22 90S	28-M2 30 200 30 23 90S	-
	32	28-M2 32 095 32 22 90S	28-M2 32 155 32 22 90S	28-M2 32 200 32 23 90S	28-M2 32 250 32 24 90S
	34	28-M2 34 100 34 23 90S	28-M2 34 145 34 23 90S	28-M2 34 200 34 24 90S	28-M2 34 250 34 24 90S
	36	28-M2 36 100 36 23 90S	28-M2 36 145 36 24 90S	28-M2 36 190 36 24 90S	28-M2 36 250 36 24 90S
	38	28-M2 38 100 36 23 90S	28-M2 38 145 38 24 90S	28-M2 38 190 38 25 90S	28-M2 38 250 38 24 90S
	40	28-M2 40 105 40 24 90S	28-M2 40 145 40 24 90S	28-M2 40 195 40 25 90S	28-M2 40 250 40 25 90S
	42	28-M2 42 105 42 25 90S	28-M2 42 150 42 25 90S	28-M2 42 195 42 25 90S	28-M2 42 250 42 25 90S
	44	28-M2 44 105 44 25 90S	28-M2 44 155 44 25 90S	28-M2 44 200 44 25 90S	28-M2 44 250 44 25 90S
	46	28-M2 46 105 46 25 90S	28-M2 46 155 46 26 90S	28-M2 46 200 46 26 90S	28-M2 46 250 46 26 90S

Tapered model

		Length (mm)				
		150	**200**	**250**		
Proximal diameter (mm)	**28**	28-M2 24 155 28 22 90S	28-M2 28 155 28 24 90S	-	**24**	**Distal diameter (mm)**
	30	28-M2 26 155 30 22 90S	28-M2 30 155 30 26 90S	-	**26**	
	32	28-M2 28 155 32 22 90S	28-M2 32 155 32 28 90S	-	**28**	
	34	28-M2 30 145 34 23 90S	28-M2 34 145 34 30 90S	-	**30**	
	36	28-M2 32 145 36 24 90S	28-M2 36 145 36 32 90S	-	**32**	
	38	28-M2 34 145 38 24 90S	28-M2 38 145 38 34 90S	-	**34**	
	40	28-M2 36 145 40 24 90S	28-M2 40 145 40 36 90S	28-M2 36 195 40 25 90S	**36**	
	42	28-M2 38 150 42 25 90S	28-M2 42 150 42 38 90S	28-M2 38 195 42 25 90S	**38**	
	44	28-M2 40 155 44 25 90S	28-M2 44 155 44 40 90S	28-M2 40 200 44 25 90S	**40**	
	46	28-M2 42 155 46 26 90S	28-M2 46 155 46 42 90S	28-M2 42 200 46 26 90S	**42**	

- **Packaging**: single-unit, sterile

- **Applications**

The application for inclusion on the reimbursement list concerns the following diseases of the descending thoracic aorta:

- Atheromatous aneurysms
- Chronic type-B dissections
- Acute and post-traumatic dissections
- Pseudoaneurysms

Reimbursement history

Second request for inclusion of the RELAY thoracic aortic stent-graft on the LPPR.
The first request for inclusion of the RELAY thoracic aortic stent-graft on the LPPR was submitted in 2007. The Actual Benefit was insufficient (opinion dated 3 October 2007), in particular given the small number of subjects for which analysis was provided.

One thoracic aortic stent-graft is included in the LPPR for the indications accepted by the CNEDiMTS Committee (the ZENITH stent-graft - decree dated 6 July 2007).

Characteristics of the product and the associated service

- **CE marking**

Class III, declaration by SGS United Kingdom Ltd Systems & Services Certification (no. 0120), United Kingdom

- **Description**

The RELAY thoracic aortic stent graft is composed of self-expanding nitinol stents sutured to polyester fabric graft. The skeleton of the device is made up of a series of sinusoidal stents placed along the length of the graft fabric. A curved nitinol wire sutured along the length of the graft fabric provides longitudinal support.
Two configurations are available:

- SAFEX: proximal end configuration consists of uncovered, sinusoidal nitinol wires of varying heights, circumferentially projecting above the fabric end of the stent-graft.
- STRAIGHT: the circumference of the terminating nitinol stent on the distal end of the graft is covered with fabric.

The device is loaded into a delivery system (TRANSPORT).
Extended proximal and distal aortic grafts are available, to treat endoleaks or to increase the area of coverage.
The RELAY stent-graft is also available custom made.

- **Intended purpose**

Thoracic aortic stent-grafts are designed to provide endovascular repair of the descending thoracic aorta.
Implantation of a thoracic aortic stent-graft enables:

- isolation of aneurysms, false lumens and rupture sites
- re-establishment of blood circulation through the lumen of the stent-graft.

- **Associated intervention or service**

Procedure listed in the Common Classification of Medical Procedures (CCAM): Chapter 4.3 Therapeutic procedures involving arteries; 4.3.1: Thoracic aorta; 4.3.1.2: intraluminal dilatation and insertion of thoracic aorta graft. Code DGLF003: insertion of covered stent-graft into thoracic aorta

Actual Benefit

1. Benefit of the product or service

1.1 Data analysis: assessment of the therapeutic effect/adverse effects, risks linked to use

Studies that do not specifically involve the RELAY thoracic stent-graft

There have been three studies by national assessment agencies assessing thoracic aortic stent-grafts in the treatment of diseases of the thoracic aorta: the reports by NICE (National Institute for Health and Clinical Excellence), HAS (Haute Autorité de Santé), and the technological assessment report by OHTAC (Ontario Health Technology Assessment Committee).

Report by NICE[1] - 2005

Objective: To assess the evidence for the efficacy and safety of the use of endovascular stent-graft in the treatment of thoracic aortic disease.

The review focused mainly on thoracic aortic aneurysms and dissections.

Methodology:

29 studies, published between 2000 and 2003, were used in the analysis: 27 were case series and 2 were comparative observational studies (surgical treatment versus endovascular treatment). In these studies, patient demographic and clinical characteristics were not similar in the two treatment arms, and comparative results are not presented.

The results of the assessment are given in the appendix.

The NICE guidelines, which are based on a systematic evidence review[2], state that:

- Endovascular treatment of thoracic aneurysms and dissections is a suitable alternative to surgery in appropriately selected patients.
- Clinicians should enter all patients having endovascular stent-graft placement into a registry.
- The procedure should be performed by a multidisciplinary team with access to facilities for cardiothoracic surgery and cardiovascular bypass.

NICE noted that the studies were of poor methodological quality, and that there was a need for better-quality studies, long-term follow-up and comparisons with alternatives.

Report by HAS[3] - 2006

Objective: To assess the efficacy and safety of endovascular stent-grafts in the treatment of thoracic aorta aneurysms and dissections.

Methodology:

54 studies reporting experiences of and/or points of view about endovascular treatment for thoracic aortic diseases were selected:

- 31 involved the descending thoracic aorta
- 5 involved the aortic arch
- 12 involved emergency situations
- 6 were systematic reviews

Seven comparative studies were selected, none of which were randomised. Five of these studies compared endovascular treatment with surgical treatment.

Only two studies compared groups of patients that were statistically similar (Brandt et al 2004[4],

[1] National Institute for clinical Excellence. A systematic review of the recent evidence for the efficacy and safety relating to the use of endovascular stent-graft placement in the treatment of thoracic aortic disease. NICE; 2005

[2] National Institute for clinical Excellence. Endovascular stent-graft placement in thoracic aortic aneurysms and dissections. Guidance. NICE; 2005

[3] Haute Autorité de santé "Assessment des endoprothèses dans le traitement des anévrismes et des dissections de l'aorte thoracique" [Assessment of endovascular stent-grafts in the treatment of thoracic aorta aneurysms and dissections]. February 2006. www.has-sante.fr

[4] Brandt M et al. J Endovasc Ther 2004; 11(5): 535-8

Nienaber et al 1999[5]).
In this report, a comparison was made between emergency and elective treatment. Patients who undergo emergency stent-graft treatment do not have the same characteristics as those who receive elective treatment. Patients treated as emergencies have a very high risk of death during surgery, comparable to the risk involved in conventional surgery. Eleven studies report separate mortality figures for patients treated as elective cases and those who receive emergency treatment.

Early and late mortality are greater with emergency treatment:

	Elective treatment	Emergency treatment
30-day mortality rate	5.9% (0%-16%)	16% (2.5%-23%)
Overall mortality (20.5 months)	13.3% (4%-45%)	28.2% (5%-38.5%)

HAS recommendations and conclusions:

Endovascular repair (EVAR) for thoracic aortic diseases, including aneurysms, dissections and ruptures of the isthmus, seems to provide a real benefit in terms of operative mortality and severe morbidity, though a rigorous medium-term assessment is needed (mean rates of paraplegia are 2.1% (range: 0-7%) for EVAR versus 5% (range: 3-15%) for surgery).

- This treatment may only be done in centres that have expertise in both types of treatment (endovascular and surgical), and that have suitable technical capability.
- In particular, there must be a proximal section of aorta of at least 2 cm in length, which will enable the stent-graft to be inserted. There must be a multidisciplinary discussion process in advance of EVAR, particularly concerning the risks of conversion to surgery and possible use of cardiovascular bypass.
- Patients must be informed of the advantages and drawbacks of the available repair techniques, i.e. open surgery and EVAR.
- Annual monitoring, with CT scan or MRI+X-ray, must be carried out.
- Patient follow-up procedures, in the form of a prospective registry of all procedures carried out that involve the thoracic aorta, must be put in place.

OHTAC health technology assessment report (2005) concerning descending thoracic aortic aneurysms

The assessment method used by OHTAC was based on systematic review of the literature, existing health technology assessment reports and medical device vigilance data.

A search of the literature databases was done for the date range 01/01/2000 to 11/07/2005: Of the identified references, 9 studies comparing endovascular treatment with surgery were used: 1 comparative retrospective study, 7 case series and one small comparative cohort study.
Thirty-day mortality rate observed in the observational studies ranged from 1 to 6% for patients receiving endovascular treatment. Late mortality rate was between 0 and 7%. The main cause of death at 30 days was rupture. The main causes of late death were cardiac events and aorto-bronchial and aorto-oesophageal fistula.

The multi-centre comparative study by Glade et al reported a 30-day mortality rate of 2/42 in the endovascular arm and 6/53 in the open surgery arm. Thirteen patients required repeat procedure in the surgical arm (post-operative haemorrhage (n=11), duodenal perforation (n=1)); this figure was 2 patients in the endovascular arm (1 access site haemorrhage and 1 paraplegia).

[5] Nienaber CA et al. N Engl J Med 1999; 340(20): 1539-45

The main complications are shown in the table below:

	Paraplegia	MI*	Stroke	Pneumonia	Renal failure	Intestinal ischaemia
Endovascular treatment (%)	2	2	0	9	2	5
Surgery (%)	8	4	4	28	11	0

* MI = myocardial infarction

The recommendations resulting from this assessment were as follows:

- There is no randomized controlled trial with long-term follow-up to support the treatment for repair of descending TAA as first choice treatment.
- Short-term and medium-term outcomes of endovascular grafting in the studies that are currently available are comparable to those of surgical intervention. OHTAC recommends endovascular treatment particularly in patients at high surgical risk and after a benefit/risk assessment of the two methods.
- The use of this technology should be restricted to certain centres with experience and expertise in the field of endovascular grafting.
- Informed consent by patients should include an understanding that the medium to long-term contraindications are unknown.

Studies that specifically involve the RELAY thoracic stent-graft

Three studies that specifically involve the RELAY thoracic stent-graft were submitted. These studies are ongoing. Only the study reports were provided.

- The 3-year results of the non-comparative, multi-centre study were provided at the time of the first application for inclusion. Thirty patients were enrolled: 26 had an aneurysm of the descending thoracic aorta, 4 patients had a penetrating ulcer. Number of patients being followed up (had neither died nor been lost to follow-up) at 6 months was 26; at 1 year, 24; at 2 years, 20; at 3 years, 13; and at 4 years, 5. The planned duration of this study was 5 years. The endpoints were severe morbidity and mortality. The results are reported in table 1.

Table 1: Major morbidity and mortality

	≤ D 30 n = 30	**> 30 days n = 28**	**Total n = 30**
Mortality	**2**	**6**	**8**
Severe device-linked morbidity	**5**	**1**	**6**
Cardiac complications	2	0	2
Pulmonary complications	2	0	2
Renal impairment	1	0	1
Neurological complications	1	0	1
Haemorrhage after the procedure	2	0	2
Other	2	0	2
Conversion to open surgery	0	1	1

10 cases of endoleak were reported: 4 type I endoleaks (1 at 1 month, 2 at 6 months and 1 at 2 years), 4 type II endoleaks (1 at 1 month, 2 at 6 months and 1 at 2 years), 1 preoperative type III endoleak and 1 endoleak of unknown origin.
1 migration was reported at 2 years.

- The preliminary results of a non-randomised, comparative, phase II multi-centre study (involving 30 centres in the United States). The objective of this study was to compare safety and performance of the RELAY thoracic stent-graft in patients with thoracic aortic aneurysm with a group of patients receiving surgical treatment. 120 patients were to be included in the endovascular treatment arm, and 60 patients in the surgical arm. Currently, 93 patients are included in the endovascular treatment arm (the RELAY arm), and 7 patients in the surgical arm. Number of patients being followed up (had neither died nor been lost to follow-up) at 6 months was 55; at 1 year, 40; at 2 years, 13. The primary endpoint was the rate of device-linked adverse

events at 1 year. At 30 days the mortality rate was 7/93, and this was 10/60 later than 30 days. The preliminary results of this study are given in the appendix.

- Preliminary results of a European observational multi-centre study (22 centres in 7 countries), which was a prospective post-marketing study named RESTORE (Relay Endovascular registry for thoracic diseases). The objective of this study was to assess safety and performance of the RELAY thoracic stent-graft in patients with thoracic aortic disease (e.g. thoracic aortic aneurysm, penetrating ulcer, dissection). The planned duration of follow-up was 2 years. The primary endpoint was mortality (death linked to the procedure or to the device) and morbidity (serious adverse events and events linked to the device or procedure) at 2 years. 304 consecutive patients were enrolled. 114 patients were followed up at 1 year, and 50 at 2 years. Mean duration of follow-up was 334 days [CI not recorded]. Mean length of hospital stay was 18 days (21 - 370 days).
  Mean number of stents used per patient was 1.26 (237 patients each had 1 stent implanted, 56 patients had 2, and 11 had 3).
  The number of patients who had died at 30 days was 22/304 (7.2%), and 6 of these deaths were linked to the device or procedure. Patient demographic characteristics are summarised in table 2.

Table 2: Characteristics of patients included in the RESTORE observational study

	RELAY (n = 304)
Mean age (SD)	64.3 (18 - 88)
Sex (%)	
Male	245 (80.6)
Female	59 (19.4)
Type of thoracic aorta pathologies treated with RELAY	
Atherosclerotic aneurysm	161 (53.9)
Aortic dissection	91 (29.9)
Intramural haematoma	9 (3.0)
Penetrating ulcer	27 (8.9)
Degenerative	44 (14.4)
Marfan syndrome	1 (0.3)
Other	10 (3.2)
Traumatic lesion	40 (13.2)
Pseudoaneurysm	8 (2.6)
Infection complications	4 (1.3)
ASA score[6] (%) (n = 301)	
ASA 1	24 (8.0)
ASA 2	67 (22.2)
ASA 3	151 (50.2)
ASA 4	51 (16.9)
ASA 5	8 (2.7)
Mean diameter of aneurysm	57.3 mm (7-100 mm)
Mean length of aneurysm	86.4 mm (5-400 mm)
Mean diameter	57.3 mm (7-100 mm)
Mean length of dissection	55.8 mm (1-250 mm)

Mean length of hospital stay was 18 days (21 - 370 days).
Mean number of stents used per patient was 1.26 (237 patients each had 1 stent implanted, 56 patients had 2, and 11 had 3).
The number of patients who had died at 30 days was 22/304 (7.2%), and 6 of these deaths were linked to the device or procedure.
The perioperative complications reported during follow-up are given in table 3.

[6] ASA score
Score 1: A normal healthy patient
Score 2: A patient with mild systemic disease
Score 3: A patient with severe systemic disease that is not incapacitating
Score 4: A patient with severe systemic disease that is invalidating and a constant threat to life

Table 3: Perioperative complications (RESTORE observational study)

	Perioperative complications n = 304
complications linked to deployment of stent	
Deployment failure	4 (1.3)
Arterial thrombus or embolism	2 (0.7)
Occlusion of lateral branches	35 (11.5)
Rupture of thoracic aorta (not device-linked)	1 (0.3)
Bleeding or haematoma	51 (16.8)
Device-linked complications	
Unable to insert delivery system	2 (0.7)
Migration of stent-graft	8 (2.6)
Obstruction of stent-graft	2 (0.7)
Other	4 (1.3)
Systemic complications	
Pulmonary	40 (13.2)
Cardiac	14 (4.6)
Renal	15 (4.9)
Neurological complications	
Paraplegia	5 (1.6)
Paraparesis	7 (2.3)
Stroke	4 (1.3)
Stroke and paraplegia	1 (0.3)
Paraplegia and paraparesis	1 (0.3)
Endoleaks	**15 (4.9%)**
type 1	12
type 2	2
undetermined	1

During the follow-up period, 1 case of stent-graft migration and 40 endoleaks were reported.

The Committee considers that the ratio of therapeutic effect to adverse effects of the RELAY thoracic aortic stent-graft is sufficient for it to be used in the treatment of diseases of the descending thoracic aorta: aneurysms of more than 6 cm in diameter, acute dissection where surgery is indicated, penetrating ulcers if there are complications, traumatic rupture of the isthmus in the context of multiple trauma.
The Committee does note that there is a lack of long-term data, and that the interim analysis of studies involving RELAY specifically is not easy to interpret.

1.2 Therapeutic use

The conventional methods of treatment are medical and surgical. The former is primarily based on controlling arterial hypertension. Surgical treatment is taxing, and requires cardiovascular bypass. Only those patients for whom surgery carries an acceptable level of risk can undergo it.

Treatment strategy will vary depending on the disease.

Aneurysm of the thoracic aorta:
The conventional treatment is open surgery with excision of the lesion followed by implantation of a graft on cardiovascular bypass.

Reports of morbidity and mortality associated with surgery make the distinction between elective and emergency treatment, with particular attention paid to the risk of spinal cord ischaemia resulting in paraparesis or paraplegia. The mortality rate for elective surgery on descending aortic aneurysms varies between 6% and 15%, and is considerably higher for emergency surgery. The risk of paraparesis or paraplegia is estimated at between 3% and 15%.[3]

The main complications are as follows[3] (risk of each is around 5%):

- Haemorrhage with a requirement for repeat surgery;
- Respiratory failure with prolonged need for assisted ventilation;
- Acute renal failure;
- Infection;
- Central nervous system involvement (stroke, coma);
- Peripheral neurological involvement (sensory and motor deficit, paraparesis, paraplegia).

The contraindications for surgery are: patients aged over 80 years, chronic respiratory failure, renal failure, coronary artery disease and systemic disease (e.g. neoplastic disease).[3]

Thoracic aortic dissection:
The conventional treatment varies, depending on whether the dissection is type A (originating in the ascending aorta) or type B (originating in the descending aorta).
Type A dissections require emergency surgical treatment.
For uncomplicated type B dissections, medical treatment to reduce blood pressure is the gold – standard treatment. If there are complications, surgery is indicated.

The main contraindications to surgical treatment are advanced patient age and specific cardiac and respiratory conditions. Severe hemiplegia and intestinal ischaemia lasting over 6 hours are also contraindications to surgery.[3]
During the acute phase, mortality from surgery is between 20 and 35% and spinal cord complications occur in between 10 and 20% of cases.

In cases of ulcer and ruptures of the isthmus, surgery is also the gold-standard treatment.

Potential indications for thoracic aortic stent-grafts for thoracic aortic aneurysms and dissections are in all cases also indications for surgical treatment.
In thoracic aortic trauma, the use of thoracic aortic stent-grafts can be considered in particular in multiple trauma, in which associated injuries can constitute a contraindication to definitive surgical repair.

Endovascular treatment for descending thoracic aorta diseases is an alternative to surgical treatment.
RELAY has a benefit, because of its therapeutic effect, in the treatment of the main diseases of the descending thoracic aorta.

2. Expected public health benefit

2.1 Seriousness of the condition

Aneurysms and dissections are the two main diseases that can affect the thoracic aorta (TA). These two degenerative processes have multiple aetiologies, and without treatment are very often fatal.
An aneurysm is an irreversible dilatation of the aorta. The natural history of the condition is an increase in the calibre of the aneurysm, which inevitably ruptures.
Dissection is defined as an infiltration of the media of the aortic wall by extraluminal blood, leading to a split in the media, creating a false lumen. It is a medical and surgical emergency, with high rates of mortality and morbidity.
Ulcers are rare atheromatous lesions, which carry a risk of progression to rupture, dissection or aneurysm.
Rupture of the isthmus arises as a result of violent trauma and is a serious emergency.

The main diseases of the descending thoracic aorta cause disability and a marked degradation of quality of life. They are life-threatening.

2.2 Epidemiology of the condition

The annual incidence of thoracic aortic aneurysms is estimated to be 6 cases per 100,000 people, and the risk of rupture is between 50% and 75%. Aneurysms involve the descending aorta in around 38% of cases and the abdominal aorta in around 25% of cases.

The mean annual prevalence of aortic dissection is between 0.5 and 2.95/100,000 people. The annual incidence is not known precisely, but is estimated at around 10/100,000 people. Annual mortality is between 3.25 and 3.6/100,000 people.
Dissections in the ascending aorta are the most common (60%). 25% affect the descending aorta[3].

2.3 Impact

Endovascular treatment of thoracic aorta disease, including aneurysm, dissection and rupture of the isthmus, appears to provide a significant benefit in terms of operative mortality and major morbidity (e.g. paraplegia: mean rate is 2.1% for thoracic aortic stent-grafts, versus 5% for surgery).

For patients for whom surgery is contraindicated, thoracic aortic stent-grafts are the only treatment alternative.

Several thoracic aortic stent-grafts are available to healthcare professionals. Just one stent-graft is currently included on the LPPR.

The RELAY thoracic aortic stent-graft provides a public health benefit, given the seriousness of diseases of the descending thoracic aorta and the existence of a treatment need if conventional surgery is contraindicated.

In conclusion, the National Committee for the Evaluation of Medical Devices and Health Technologies considers that the Actual Benefit of the RELAY thoracic aortic stent-graft is sufficient to allow it to be included on the List of Products and Services qualifying for reimbursement (LPPR) mentioned under article L. 165-1 of the French Social Security Code, for the following diseases of the descending thoracic aorta:

- ***Aneurysms greater than 6 cm in diameter;***
- ***Acute dissections if surgery is indicated;***
- ***Penetrating ulcers, if there are complications;***
- ***Traumatic rupture of the isthmus in the context of multiple trauma.***

Factors determining the Actual Benefit

- Minimum technical specifications

Not applicable

- Conditions for prescription and use

Implantation of the RELAY thoracic aortic stent-graft must be done in compliance with the guidelines issued by the Haute Autorité de Santé (HAS), which include the following:

- Implantation must be done in centres that have expertise in both types of treatment (endovascular and surgical), and that have suitable technical capability.
- There must be a multidisciplinary discussion process, particularly concerning the risks of conversion to surgery and possible use of cardiovascular bypass.
- There must be a proximal section of aorta of at least 2 cm in length, which will enable the stent-graft to be inserted.
- Patients must be informed of the advantages and drawbacks of the available repair techniques, i.e. open surgery and endovascular sent grafting.
- There must be annual monitoring using CT scan, or MRI + X-ray.

Implantation of RELAY must lead to the use of one or two devices. In exceptional cases, a maximum of 3 devices may be implanted. The various devices are connected to the SAFEX end configuration, which enables the stent-graft to be extended.

The Committee requests that patients be included in a prospective registry of all implantations of thoracic aortic stent-grafts, and that patients be followed up.

Added clinical value (ACV)

There are no randomised prospective studies comparing open surgery with endovascular treatment. The results that were observed in these two studies were variable.

The National Committee for the Evaluation of Medical Devices and Health Technologies considers that the RELAY thoracic aortic stent-graft provides no improvement in Added clinical value (level V) in comparison with other thoracic aortic stent-grafts.

Renewal conditions and duration of inclusion

- **Renewal conditions:**

Implantation and follow-up data in the registry will be requested when renewal of inclusion is applied for.

- **Proposed duration of inclusion:**

3 years

Target Population

There are no epidemiological data that enable an estimation of the target population for thoracic aortic stent-grafts. The number of patients admitted to hospital because of thoracic aortic disease each year enables an approximation of the population involved.
In 2009, according to the French clinical information systems programme (PMSI), the number of stays in a healthcare facility involving the main diagnoses was as follows:

- 2386 aortic dissections (all sites)
- 3456 thoracic aortic aneurysms, with no mention of rupture
- 225 ruptured thoracic aortic aneurysms
- 423 thoracic/abdominal aortic aneurysms, with no mention of rupture
- 87 ruptured thoracic/abdominal aortic aneurysms

Given the epidemiological data mentioned above, the following estimations can be made:
- there are around 1600 aneurysms of the descending thoracic aorta per year in France. Experts estimate that around 1000 aneurysms of the thoracic aorta are operated on each year.
- there are around 1500 dissections of the descending thoracic aorta per year in France.
Around 40% of patients with type B dissections must undergo surgical treatment sooner or later because of complications, i.e. around 600 patients.

In total, the number of patients with aneurysm or dissection of the thoracic aorta and who undergo surgery is estimated at 1600. The percentage of patients who could benefit from endovascular treatment is not known.

The number of patients undergoing endovascular treatment who have a disease of the descending aorta other than aneurysm or dissection is low and difficult to estimate, and is therefore not taken into account when calculating the target population.

According to an analysis of PMSI 2009 data broken down by classification of procedure, the number of hospital stays for insertion of a covered stent-graft into the thoracic aorta via percutaneous arterial route was 595 (procedure code DGLF003/0).
It should be noted that the ZENITH thoracic aortic stent-graft is the only thoracic aortic stent-graft that is included on the LPPR, following the decree dated 29 June 2007 (Journal Official of 6 July 2007).

The Committee considers that the number of patients with aneurysm or dissection of the thoracic aorta and who undergo surgery is 1600.