

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation document

XprESS multi-sinus dilation system for treating chronic sinusitis

The National Institute for Health and Care Excellence (NICE) is producing guidance on using the XprESS multi-sinus dilation system for treating chronic sinusitis in the NHS in England. The medical technologies advisory committee has considered the evidence submitted 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 draft recommendations made by the committee. NICE invites comments from the public. This document should be read along with the evidence base (see Sources of evidence considered by the committee).

The committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical effectiveness and resource savings reasonable interpretations of the evidence?
- Are the provisional 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 XprESS multi-sinus dilation system for treating chronic sinusitis. 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 public consultation. After considering these 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 guide](#) and [Medical Technologies Evaluation Programme methods guide](#).

Key dates:

- Closing time and date for comments: [00:00 Day Month Year]
- Second medical technologies advisory committee meeting: [Day month year]

NICE medical technologies guidance addresses specific technologies notified to NICE by sponsors. 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, then the technology has been found to offer advantages to patients and the NHS. The specific recommendations on individual technologies are not intended to limit use of other relevant technologies which may offer similar advantages.

1 Draft recommendations

- 1.1 Evidence supports the use of the XprESS multi-sinus dilation system for treating chronic sinusitis after medical treatment has failed. Treatment with XprESS leads to a rapid and sustained improvement in chronic symptoms, fewer acute episodes and improved quality of life which is comparable to functional endoscopic sinus surgery (FESS).
- 1.2 XprESS should only be used in patients with non-complex chronic sinusitis who do not have nasal polyps. In these patients, XprESS works as well as functional endoscopic sinus surgery, is associated with faster recovery times, and can more often be done under local anaesthetic.
- 1.3 Cost modelling indicates that savings are achievable as compared with FESS when XprESS treatment is performed under local anaesthetic in an office setting. If 80% of treatments are performed in this way, the estimated saving per patient is £152 with XprESS as compared with a 60 minute FESS procedure and assuming a cost for XprESS of £820.

2 The technology

Description of the technology

- 2.1 The XprESS multi-sinus dilation system (XprESS, Entellus Medical) is a sterile, single-use device for treating chronic sinusitis. The system comprises a balloon-tipped device with a reshapeable end that is inserted through the nose into the maxillary, frontal or sphenoidal sinuses. XprESS also includes an inflation syringe, bending tool and 2 extension lines to provide irrigation. The balloon is manipulated into the bony sinus outflow tracts (ostia) and inflated with saline. This reshapes and opens the ostia by displacing adjacent bone and paranasal sinus structures allowing the sinuses to drain more effectively
- 2.2 The system is available in 3 variants, XprESS Ultra, LoProfile and Pro, which differ in the dimensions of the suction tip and the balloon diameter and length. All suction tips and balloon lengths are appropriate for treating all sinuses; selection is based on clinician preference. The XprESS device, inflation syringe and bending tool are included in all variants. The Ultra and LoProfile (the version sold in the UK) systems also include an integrated PathAssist LED light fibre, which is available as an add-on for the Pro. XprESS can be used under local anaesthetic, once the surgeon has had sufficient experience of using the device.
- 2.3 According to the company's submission, the XprESS multi-sinus dilation system costs £900, with a reduction to £820 for centres that order 50 or more units in a year.
- 2.4 The claimed benefits of XprESS in the case for adoption presented by the company are:
- A minimally invasive alternative to functional endoscopic sinus surgery (FESS), offering equivalent efficacy and minimal acute inflammation while preserving more sinus tissue and mucosa.

- Reduction in risks associated with general anaesthetic and fewer staff resources needed, because the procedure is done while the patient is awake and under local anaesthetic.
- Faster recovery time with less nasal bleeding and a shorter duration of pain medication.
- Improved patient comfort and tolerance compared with other balloon technologies because XprESS allows more control of device placement.
- Easier to use than other balloon technologies, because XprESS is based on a sinus seeker and no guidewire is needed.
- More accurate cannulation of the maximally ostium.
- Reduction in theatre time compared with FESS.
- Reduction in length of stay in hospital.
- Reduction in duration of prescription pain medication.
- Reduction in post-operative nasal bleeding visits.
- Reduction in hospital readmissions.
- Potentially fewer patients waiting 18 weeks or longer for ear, nose and throat (ENT) surgery

Current management

- 2.5 Current treatment options for chronic sinusitis include nasal saline irrigation, intranasal corticosteroids, systemic antibiotics or topical drops, and functional endoscopic sinus surgery (FESS).
- 2.6 NICE's clinical knowledge summary on [chronic sinusitis](#) describes measures to relieve symptoms, particularly for acute episodes, that include analgesics for pain or fever, occasional intranasal decongestants and intranasal saline irrigation, and warm face packs. Patients should be offered advice about managing associated conditions (such as allergic rhinitis, asthma and dental infections), along with advice on smoking cessation and dental hygiene where appropriate. A short course of antibiotics may be prescribed for acute episodes, but longer-term courses are not

recommended without seeking specialist advice. A course of intranasal corticosteroids of up to 3 months may be considered, especially if there is a suspicion of an allergic cause (such as concomitant allergic rhinitis).

- 2.7 A patient should be admitted to hospital if sinusitis is associated with a severe systemic infection, or a serious complication such as orbital or intracranial infection or inflammation. Referral to an ENT specialist should be considered for people with frequent recurrent episodes of acute sinusitis (for example more than 3 episodes requiring antibiotics in a year), unremitting or progressive facial pain (urgent referral for suspected malignancy), or nasal polyps that are causing significant nasal obstruction. Referral to an ENT specialist should also be considered if a person has taken intranasal corticosteroids for 3 months without effect.
- 2.8 FESS is currently the most common ENT surgery used to treat persistent and severe cases of chronic sinusitis. During FESS, the surgeon uses a magnifying endoscope inserted through the nostrils to identify and remove affected sinus tissue and bone. The aim is to clear the obstructed ostia and flush out infected material, but retain enough healthy tissue for normal nose and sinus function. FESS is usually done under general anaesthetic, but can also be done under local anaesthetic in the minority of cases. Scarring and adhesions can occur as a result of FESS, which may require post-operative removal of tissue, blood and bone (debridement). Other more serious risks occasionally associated with FESS include intraorbital and intracranial complications.
- 2.9 NICE interventional procedure guidance on [balloon catheter dilation of paranasal sinus ostia for chronic sinusitis](#) concluded that the current evidence on the procedure's short-term efficacy is adequate and raised no major safety concerns

3 Clinical evidence

Summary of clinical evidence

3.1 The key clinical outcomes presented in the decision problem were:

- change in sinusitis symptoms
- number of post-procedure sinusitis episodes needing medication
- number of post-operative debridements
- change in ostial patency (assessed by endoscopy or CT scan)
- number and types of sinus treated
- length of hospital stay
- procedure time and theatre/outpatient treatment room time
- rate of revision surgery
- number of sinus-related follow-up appointments
- rate of readmission
- rate and severity of nasal bleeding
- device-related adverse events.

3.2 The company conducted a literature search for evidence on XprESS and its predecessor device FinESS, which identified 11 published and 2 unpublished studies. The company did a meta-analysis including 6 of the 11 published studies

3.3 The external assessment centre (EAC) judged the company's search terms to be appropriate, but could not fully reproduce them because the search strategies for the Cochrane database of systematic reviews were not fully reported. The EAC reran the company's searches and conducted its own search, which identified no further evidence.

3.4 The EAC considered that 1 included study, Eloy et al. (2012), should be excluded from further assessment because the population (patients who had previously had a failed frontal sinustomy) was not consistent with the scope. The EAC therefore

assessed 12 publications, comprising 3 randomised clinical trials and 9 observational studies, 2 of which were unpublished.

Included studies: REMODEL

- 3.5 Three studies reported on the REMODEL study (Cutler et al. 2013, Bikhazi et al. 2014, Chandra et al. 2016) a prospective, multicentre, non-inferiority, parallel randomised clinical trial (the methodology is most comprehensively reported in Cutler et al. 2013). The trial compared FESS with balloon dilation systems (FinESS and XprESS) in adult patients with uncomplicated chronic sinusitis or recurrent acute sinusitis. The split between XprESS and FinESS was not reported in the papers but the company has indicated it was approximately 50:50. Patients and clinicians were blinded to their allocation. Blinding could not be maintained after treatment allocation, but some post-surgical assessments were done or audited by independent physicians. Following withdrawals after randomisation, there were 50 patients in the balloon arm and 42 in the FESS arm. A per-protocol analysis was done. The primary outcome measure was change in chronic sinusitis symptoms as measured by the Sino-Nasal Outcome Test-20 (SNOT-20) scores at 6 months from baseline (pre-procedure).
- 3.6 Cutler et al. (2013) reported outcomes up to 6 months after the procedure. At 1 week, the average change in SNOT-20 scores in the balloon arm was -1.49 (standard deviation [SD] ± 0.87), compared with -0.96 (SD ± 1.12) in the FESS arm. At 1 month, the average change was -1.70 (SD ± 0.98) for the balloon arm and -1.62 (SD ± 0.95) for FESS. At 6 months, the change was -1.67 (SD ± 1.10) for the balloon arm and -1.60 (SD ± 0.96) for FESS. The changes from baseline were significant ($p < 0.001$) in both groups at all time points, and because the changes exceeded 0.8 the differences were judged to be clinically meaningful. With the exception of the results at 1 week ($p = 0.014$), there was no statistically significant difference between the SNOT-20 scores in

the balloon dilation and FESS arms. This indicated non-inferiority of the balloon procedures in terms of symptom improvement, with a potentially significant short-term effect (at 1 week). The authors also reported significant ($p < 0.0001$) and clinically meaningful improvements in each of the subscales of the SNOT-20 at 6 months, with no statistically significant differences between the 2 arms. The same results were reported at 6 months for the subgroups that were considered: maxillary only or maxillary and anterior ethmoid, presence or absence of accessory ostia, presence or absence of septal deviation, and sinusitis diagnosis (chronic or recurrent acute). In the balloon arm, 92.0% (46/50) of patients did not need a postoperative debridement compared with 26.2% (11/42) of patients in the FESS arm. There was a mean of 0.1 ± 0.6 postoperative debridements per patient in the balloon arm compared with 1.2 ± 1.0 in the FESS arm ($p < 0.0001$). No statistically significant differences were found between balloon dilation and FESS in terms of post-discharge nausea and duration of over-the-counter pain medication. One patient in each arm had revision surgery.

- 3.7 Bikhazi et al. (2014) described 12-month results for 89 of the 92 patients reported by Cutler (2013) who completed 1-year follow-up (48 balloon, 41 FESS). Changes in SNOT-20 scores from baseline remained significant and clinically meaningful in both groups, and confirmed non-inferiority at 12 months between the 2 interventions on this measure (balloon arm: -1.64 ± 1.06 , FESS arm: -1.65 ± 0.94 ; $p < 0.0001$). In both arms patients reported significant reductions ($p < 0.0001$) in sinusitis episodes at 12 months following surgery compared with the year before (4.2 in the balloon arm, 3.5 in the FESS arm), although the comparison was not significant. Overall patency (maxillary ostia) in those with an evaluable CT scan at 12 months was 96.7% in the balloon arm and 98.7% in the FESS arm but this was not statistically significant. Both treatments had positive effects in all the domains of the Work Productivity and

Activity Impairment (WPAI) survey, except that FESS did not significantly improve the absenteeism domain ($p=0.169$).

- 3.8 Chandra et al. (2016) reported longer-term outcomes for patients from the original cohort who were not lost to follow-up, specifically at 18 months ($n=66$) and 24 months ($n=25$). The study also included an additional cohort of patients who had been subsequently randomised. This meant there was a total of 135 patients included at baseline, with results reported for 133 patients at 6 months and 130 patients at 12 months. Mean changes in SNOT-20 scores at 6 and 12 months were statistically significantly lower than baseline and clinically meaningful in both arms in this enlarged cohort (6 months, balloon arm -1.56 , FESS arm -1.60 ; 12 months, balloon arm -1.59 , FESS arm -1.60). Mean changes in SNOT-20 scores were also statistically significantly lower than baseline and clinically meaningful in the patients from the original cohort followed up at 24 months (balloon arm -1.65 , FESS arm -1.45). There were no statistically significant differences between the 2 arms. Overall revision rates at 18 months were 2.7% in the balloon arm and 6.9% in the FESS arm, which represents a non-statistically significant difference.

Included studies: others

- 3.9 The company and EAC identified a number of observational studies which compared balloon dilation (XprESS or FinESS) with baseline data. The EAC considered them to be of more limited relevance to the decision problem. Symptom improvement data from these studies were pooled in a meta-analysis reported in Chandra et al. (2016).
- 3.10 The XprESS Multi-Sinus Study (Gould et al. 2016) was a single-arm, prospective observational study which enrolled 82 adults with chronic sinusitis or acute recurrent sinusitis; the method of recruitment was not reported. Patients had to have maxillary sinus

disease as a minimum, although patients with additionally affected sinuses (frontal, sphenoid or ethmoid) were also included. The study found a significant and clinically meaningful improvement in the primary outcome, change in mean SNOT-20 score at 12 months, compared with baseline (-1.57 , $p < 0.0001$). At 12 months there were also statistically significant reductions in Rhinosinusitis Symptoms Inventory (RSI) major symptoms score, medication use, absenteeism, and acute sinus infection and sinus-related physician visits. The authors reported that the procedure was a technical success in 307 of 313 sinuses operated on (98.1%), with only 1 patient needing revision at 12 months (1.3%), with no serious device or procedural adverse events. The procedure appeared to be well tolerated (mean pain VAS 2.8 ± 2.2), with a high degree of patient satisfaction (87.8%).

- 3.11 The XprESS registry (Brodner et al. 2013) was the first full clinical study of XprESS. This was a single-arm, observational study that enrolled 175 patients needing treatment of the frontal recess and sphenoid sinus ostium, who had previously been scheduled for FESS. The primary outcome was safety, although effectiveness outcomes were also prespecified. Most (448 of 497) sinuses were treated using a hybrid procedure of FESS and XprESS (448/497); 31 had balloon-only surgery, in 4 the balloon did not inflate, and in 10 the ostia could not be accessed using XprESS so FESS was used instead. Because these results were not disaggregated, they were not included in the Chandra (2016) meta-analysis, and were considered to be of limited relevance by the EAC. Results were similar to the other observational studies employing standalone balloon dilation only, including statistically significant reductions at 3 months in SNOT-20 score (-1.1), medication use, work or school days missed and sinus-related physician visits. There was no statistically significant reduction in acute sinus infections reported after the procedure, and no serious adverse events reported

- 3.12 The XprESS Maxillary Pilot Study (Gould et al. 2012) was a single-arm, prospective observational study involving 21 adults with uncomplicated refractory chronic sinusitis or recurrent acute sinusitis of the maxillary or anterior ethmoid sinuses. All patients had the XprESS procedure under local anaesthetic, and the main outcome was change in SNOT-20 score from pre-procedure to up to 6-months post-procedure. The study was not peer reviewed.
- 3.13 The RELIEF study (Levine et al. 2013) was a single-arm, prospective observational study involving 74 adult patients with refractory chronic sinusitis or recurrent acute sinusitis of the maxillary and anterior ethmoid sinuses. The primary outcome was quality of life as measured by SNOT-20; this and most other outcomes were reported at 12 months. All patients had the procedure with FinESS, the predecessor device to XprESS. There was a statistically significant and clinically meaningful reduction in SNOT-20 score (-1.2) compared with baseline. Statistically significant reductions were also reported in RSI major symptoms, medication use (intranasal corticosteroids, antihistamines, antibiotics), absenteeism, sinus-related physician visits, and acute sinus infections. The procedure was reported as a technical success in 91.9% of sinuses operated on (124 of 135) with a revision surgery rate of 5.8% (4 of 69 patients). No serious adverse events were reported
- 3.14 The BREATHE study was published in 3 papers: Stankiewicz (2011 and 2012) and Cutler (2011). This was the first published study of an Entellus balloon product (FinESS) involving 71 patients with chronic sinusitis of the maxillary or ethmoid sinuses. The study was a single-arm, prospective study. Follow-up was 2 years with the primary outcome of quality of life improvement measured using SNOT-20. There was a statistically significant and clinically meaningful improvement compared with baseline in SNOT-20 at 1 year (-1.80) and 2 year (-1.86) follow-up. At 1 year there was also

a statistically significant reduction in WPAI survey score and on the Work Limitation Questionnaire (WLQ) compared with baseline. The technical success rate was reported as 97.7% (129 of 132 sinuses). Procedures were well tolerated with a mean pain VAS of 2.7, and 88% of patients were reported to have recovered within 2 days. Patient satisfaction rates were 89% after 1 year and 91.5% after 2 years. After 2 years, 4 of 59 patients (6.8%) needed revision surgery. One patient was reported as having suffered a serious procedure-related adverse event following balloon dilation (subcutaneous emphysema).

- 3.15 The FinESS registry study was published as a protocol on ClinicalTrials.gov. However, it has not been subsequently published or peer reviewed, and was provided to the EAC in abstract form only. Because the EAC could not appraise this study, and only limited outcomes were reported, it did not consider it further. Data from the FinESS registry did contribute to the meta-analysis by Chandra et al. (2016).
- 3.16 Soler et al. (2016) is a single-arm, prospective observational study (n=50) expected to be published in 2016. It was provided to the EAC as an abstract that did not allow for critical appraisal, and only limited results were reported as academic in confidence. This was the only study that was reported on children. Although children were included the scope of the decision problem as a subgroup, the EAC understands through discussion with clinical experts that sinus surgery is rarely performed on children in England. Because of this, the EAC did not consider the study any further.
- 3.17 Chandra et al. (2016) undertook a meta-analysis of the observational studies to compare their results on SNOT-20, RSI scores and short-term outcomes with those reported in the REMODEL study. These are reported in detail on pages 37 to 39 of the company's submission, and critiqued on pages 81 to 84 of the

assessment report. The authors had access to individual patient data so the EAC could not replicate the meta-analyses. The authors reported that there was no statistical difference in SNOT-20 outcomes between studies (REMODEL FESS arm, REMODEL balloon dilation arm or pooled observational studies), measured at 6, 12 and 24 months. There were significant reductions ($p < 0.0001$) from baseline to 12 months in the stand-alone balloon dilation studies in absenteeism ($5.0 \text{ days} \pm 9.5$), homebound due to nasal problems ($6.3 \text{ days} \pm 11.3$), number of physician/nurse visits due to nasal problems (4.5 ± 11.5), number of infections of nose/sinuses (3.9 ± 4.5), and number of antibiotic courses (2.9 ± 3.1).

- 3.18 Changes in WLQ score over 1 week, 1 month, 3 months, 6 months, 12 months, 18 months and 24 months compared with baseline were presented as a longitudinal graph. There were statistically significant and immediate reductions in several domains, which appeared maximal at 1 month before plateauing over 2 years. Revision rates at 12 months were 1.7% for the FESS arm of the REMODEL trial, 1.4% for the balloon dilation arm of the REMODEL trial and 3.2% for the pooled analysis ($p = 0.628$). However, this analysis was based on very low event numbers (a single patient in each of the REMODEL arms).

Adverse events

- 3.19 The company performed a limited search for adverse events and identified 5 case reports of adverse events with a different balloon technology and 3 that did not specify which device was used (see page 36 of the company's clinical submission). The EAC searched the FDA MAUDE database for Entellus and identified 12 reports, of which 8 involved XprESS. Of the reports, 6 described cerebral spinal fluid leak in balloon-only procedures ($n = 2$), balloon with septoplasty ($n = 2$), or hybrid endoscopic sinus surgery (ESS) procedures ($n = 2$). None noted any long-term adverse health effects as a consequence. One report was a case of orbital wall damage

identified by the company in its clinical evidence submission, which was reported to have had no long-term adverse effect on the patient's vision. The eighth reported case was a death from massive intracranial bleed, shortly after successful completion of a bilateral maxillary balloon procedure. This was reported by the clinicians involved as unrelated to the device or procedure.

EAC's analysis

3.20 The EAC considered the best evidence on the technology to be the papers arising from the REMODEL trial. This study design was assessed as being of high methodological quality, and internal validity was generally good. However, the EAC noted concerns about the high initial attrition rates in the FESS arm immediately following randomisation, and the subsequent need for per-protocol rather than intention-to-treat analysis. The EAC was satisfied that the evidence showed balloon dilation to be non-inferior to FESS in terms of the primary outcome (SNOT-20) for up to 2 years post-procedure. The EAC also judged that the evidence demonstrated that balloon dilation was equivalent to FESS over this time frame in terms of the secondary outcomes measured, such as maintaining ostia patency, reducing future episodes of sinusitis, and improving work and productivity. However, it noted that long-term outcomes were assessed on small patient numbers. The EAC considered that there was evidence that balloon dilation with XprESS offers advantages over conventional FESS by speeding recovery, reducing post-operative pain and reducing the need for nasal debridement.

3.21 The observational studies supplemented the evidence from REMODEL and were supportive of its results. However, the EAC noted a number of methodological weaknesses in all the observational studies which led it to conclude that the evidence from these studies is of limited use to the decision problem. Although the studies matched the scope, the EAC was concerned

about extrapolating the results from selected patient cohorts enrolled in trials in the US to the wider population of patients in the NHS. The EAC assumed equivalence between the FinESS and XprESS systems but considered there was only weak, indirect evidence to substantiate this assumption

Committee considerations

- 3.22 The committee considered that the evidence from REMODEL demonstrated that balloon dilation (with either XprESS or FinESS) is clinically non-inferior to FESS in regard to symptom alleviation in patients with chronic sinusitis
- 3.23 The committee considered that although the single-arm observational studies were of lower quality, the results were consistent with the findings of the REMODEL study. It considered that these studies provide evidence that balloon dilation is effective in regard to improving other clinical outcomes including post-operative debridements, ostial patency, use of analgesic medication, time of recovery, and time taken to return to work.
- 3.24 The committee heard from the company that FinESS and XprESS both function in the same way once inflated within the sinus ostia. However, it was informed that the trans-nasal approach used for XprESS allows more sinuses to be treated, than does the FINESS, which is introduced with a trans-antral approach.
- 3.25 The committee heard from experts that XprESS can be undertaken as a local anaesthetic procedure and therefore allows patients to return to work on the same day. It further heard that balloon dilation reduces post-operative pain, preserves mucosa and bony structures, reduces scarring in the sinuses, and reduces nasal bleeding and the risk of damage to the ethmoidal artery.

- 3.26 The committee noted that the REMODEL study excluded patients with severe nasal polyposis, and it was advised by experts that balloon dilation is not suitable in these patients.

4 NHS considerations

System impact

- 4.1 The company presented a number of claimed system benefits for Xpress in its submission (see section 2.4).

Committee considerations

- 4.2 The committee accepted expert advice that outpatient XprESS is more easily deliverable than FESS within the NHS. This potentially allows improvements in patient throughput and the treatment of more patients at an earlier stage in their disease course.
- 4.3 The committee was advised by experts that adoption of the XprESS balloon dilatation system involves an inevitable period of learning and experience acquisition. In the early stages this may be gained by performing the procedure in a theatre environment using general anaesthesia, but that a transition to an outpatient setting can usually be undertaken at a later stage. The experts added that there has been some professional resistance to switching from FESS to balloon dilatation in UK clinical practice and that this has been driven by a number of factors including the price of the technology as well as a lack of surgical familiarity with the new technique.

5 Cost considerations

Cost evidence

- 5.1 The company conducted a search of the health economics literature on balloon sinus dilation using XprESS or equivalent systems, and functional endoscopic sinus surgery (FESS). This

identified 134 articles, 6 of which were included in the company's economic analysis.

- 5.2 The external assessment centre (EAC) judged the company's search terms to be appropriate. However, it noted: inconsistencies in the search terms across the databases searched; that the company's submissions did not provide search terms for its searches of the Cochrane database or the NHS Economic Evaluation Database; and it considered that the company's searches would have benefited from the inclusion of a wider range of databases, such as the cost-effectiveness registry. The EAC reran the company's searches where details were provided, and conducted additional searches. The EAC concluded that none of the economic studies identified by the company was relevant to the decision problem, and identified no additional relevant studies.

Economic model

Model design

- 5.3 The company presented a decision tree model to capture costs and outcomes in the first year following sinus surgery and a Markov model to capture costs and outcomes out to 5 years after sinus surgery, applying a 1-year cycle length.
- 5.4 Patients entered the model needing sinus surgery, and could be routed to either FESS or XprESS. The model base case used a theoretical patient who had multiple sinuses treated in a single episode of care. The first phase of the decision tree captures differences in treatment costs. The next stage covers the first 3 months following surgery, during which patients either have a sustained recovery or need 1 or more GP visits, and in both scenarios could require a re-admission into secondary care. Surgical re-interventions and GP visits are also included from 3 months to 12 months. Irrespective of those outcomes, patients then

enter a Markov model to capture outcomes out to 5 years using yearly cycle lengths. The Markov model consists of 2 mutually exclusive states, surgery revision or sustained recovery. Surgery revision is an absorbent state, meaning that patients cannot leave it, so it is assumed that patients could have only 1 revision surgery over the study period. Death, a common absorbent state in Markov models, is not included because it was expected to be a very rare outcome over the time horizon modelled

- 5.5 Figures for clinical parameters were obtained from published literature, expert opinion and UK audit data. The company relied heavily on UK audit data published by Brown et al. (2003) to determine the base values for FESS. It then used US data reported in Chandra et al. (2016) to determine the relative values for XprESS in relation to FESS.

Model costs

- 5.6 The cost for FESS and XprESS surgery under general anaesthetic was based on staff costs for a nurse and surgeon, bed day costs, theatre time, device and surgical consumable costs. The total cost for a FESS surgery under general anaesthetic (including equipment costs of £300) was calculated to be £2,894. The total cost for XprESS surgery (including equipment costs of £900) was calculated to be £1,884. The equivalent costs under local anaesthetic were calculated by applying a ratio of 0.631 to the surgical costs under general anaesthetic reported in Zilvetti et al. (2009), providing costs for FESS of £2,536 and for XprESS of £1,524. These costs were also used in the model if the patient had a revision surgery.
- 5.7 The company reported a base-case per-patient cost of £2,679 for XprESS and £3,981 for FESS, representing an average saving of £1,302 per patient.

Sensitivity and scenario analyses

- 5.8 The company presented one-way deterministic sensitivity analyses varying the model parameters from their base-case level by 20%. The parameters with the biggest effect on the level of cost saving were equipment costs and procedure time for XprESS. The results of these analyses provided a range of cost savings, from £1,044 to £1,559.
- 5.9 Scenario analyses were performed by changing parameter values to those reported in other sources. The parameters that were changed were type of anaesthetic (from general only to include local), the percentage having revision surgery each year, procedure time, length of hospital stay, and unit cost of theatre time. None of these altered the direction of the cost saving for XprESS, and at worst reduced it to £367, when a unit cost for theatre time of £6.40 per minute was used.
- 5.10 Break-even analyses were conducted varying the procedure time with XprESS and FESS. The company reported that XprESS was cost neutral when the XprESS procedure time was 80 minutes or cost saving when the FESS procedure time was greater than 41 minutes.

EAC's comments on the model

- 5.11 The EAC noted the assumptions in the company's model and considered them to be largely appropriate. It did note some important omissions in the model tornado diagram, such as the unit cost of a FESS procedure. The EAC was also unable to replicate results in the tornado diagram for the monthly rate of GP visits beyond 3 months with FESS. The EAC considered the company's analyses of the structural uncertainties to be limited. It judged that it would have been appropriate to run the model assuming that there was no difference in GP visits and readmission in the first 3 months following surgery.

EAC's changes to the model

- 5.12 The EAC revised the company's relative risk estimates for revision surgery, based on their limited numbers in the REMODEL study. It consulted experts and considered published evidence. It judged the estimates for the values up to 12 months provided in the REMODEL trial to be more appropriate. Based on expert opinion and Philpott et al. (2015), the EAC considered that the evidence did not show any difference in revision surgery rates between FESS and XprESS beyond 12 months.
- 5.13 Based on expert opinion, the EAC judged the company's base-case estimate of 0% for the proportion of XprESS procedures done under local anaesthetic to be conservative, and revised it up to 10%. It also revised the estimate for FESS procedures done under local anaesthetic to 2%, noting that this was consistent with the company's scenario analysis.
- 5.14 The EAC conducted a bottom-up approach to determine the costs of FESS and XprESS surgery. In the absence of published data, the EAC consulted experts to determine the duration of surgery for FESS in the patient population eligible for XprESS. Based on the average of their responses, the EAC estimated procedure times for FESS of 42.5 minutes and for XprESS of 26.7 minutes. The figure for FESS was consistent with figures quoted in a national audit and a health technology assessment report. The EAC revised the cost of operating time to £13.65 per minute based on data for ENT surgery (2014/15) reported by the Information Services Division Scotland. It also revised the length of stay in hospital following FESS to under 5 hours (0.208 days), and for XprESS to 4.17 hours (0.174 days) based on expert responses. The EAC revised the cost per day in hospital to £370 using a weighted average of 2014/15 NHS reference costs for elective inpatient excess bed days for minor sinus procedures (CA29Z), intermediate sinus procedures (CA28Z), major sinus procedures (CA23Z) and complex sinus

procedures (CA26Z). Based on these figures, the EAC revised the cost of FESS under general anaesthetic to £657, and the cost of XprESS under general anaesthetic to £428. None of these figures includes equipment costs.

- 5.15 The EAC also revised the cost of FESS and XprESS under local anaesthetic using a similar bottom-up approach. Using averages based on expert advice, it estimated procedure lengths of 30 minutes for FESS and 31.7 minutes for XprESS, and in-hospital stay of 3.00 hours for FESS and 2.17 hours for XprESS. Information Services Division Scotland operating theatre costs of £13.65 a minute were used to calculate operation costs. The hospital bed cost of FESS was calculated using the same methodology.
- 5.16 The EAC revised the cost of revision surgery for FESS and XprESS by applying weightings to the cost per procedure figures. The weightings applied for FESS were 98% general anaesthetic and 2% local anaesthetic. The weightings applied for XprESS were 90% general anaesthetic and 10% local anaesthetic. These changes provided a cost per revision surgery for FESS of £653 and for XprESS of £432.
- 5.17 The EAC revised the cost of a GP visit based on expert advice, the British National Formulary and data from the Personal Social Services Research Unit. It used a value of £37.00 per GP visit, and added drug prescription costs according to the clinical indication for the visit, leading to the following total costs per visit for a blocked nose (£48.91), infection (£38.97 to £39.64), and blocked nose and infection (£50.00). The mean value of these figures produced an estimate of £46.00.
- 5.18 The company did not include any training costs for XprESS because the company provides training at no extra cost, but the EAC judged that the costs for the staff time spent on training should

be included in the model. It concluded that this amounted to 7 hours of a surgeon time at a cost of £106 an hour, leading to a total of £742 per surgeon. Over the duration of the economic model this was estimated to add £5.50 to the cost of each procedure.

5.19 The EAC used a bottom-up approach to estimate the unit cost of XprESS performed in an office setting. Based on expert advice it used a length of a procedure of 31.7 minutes, and a length of stay in hospital of 2.17 hours. It used NHS reference costs of £370 for a hospital bed day, the Personal Social Services Research Unit for the costs of surgeon time and nurse time, and applied £115 for the costs of gown and a tray to produce estimate total estimate of £251.

5.20 The analysis based on the EAC's revised parameters found that XprESS was cost incurring by £330 compared with FESS (average per-patient costs: XprESS £1,694, FESS £1,364). The EAC conducted univariate analyses on all the model parameters, varying their value by 20%. None of these analyses changed the direction of the results, and XprESS remained cost incurring. The key drivers were the equipment cost of XprESS and the unit costs of a FESS and XprESS procedure under general anaesthetic. This was consistent with the company's analysis.

EAC sensitivity and scenario analyses

5.21 The EAC conducted a series of univariate sensitivity analyses on the main model parameters. Sensitivity analysis on the length of FESS procedure performed under general anaesthetic demonstrated that XprESS became cost saving when the duration of FESS exceeded 66.0 minutes, compared with the EAC base case of 42.5 minutes. Analysis on the length of stay in hospital after FESS found that XprESS became cost saving when hospital stay was longer than 1 day. Further analyses showed that length of XprESS procedure under general anaesthetic had to be as low as 0

before XprESS became cost saving, and that no value for length of stay in hospital after XprESS under general anaesthesia changed the direction of the result. Analysis on the unit cost of theatre time demonstrated that XprESS became cost incurring when the unit cost exceeded £34 per minute (£2,040 per hour). Varying the unit cost of hospital stay had very little effect on the results, and the cost would have to reach an unreasonably high level for XprESS to become cost saving

5.22 The EAC performed a number of scenario analyses. In the first of these, the EAC used hospital episode statistics data for length of stay, as per the company's model, of 0.97 days. In this scenario, XprESS remained cost incurring but by a smaller margin of £136 per patient. The EAC considered a scenario in which XprESS was performed in an office setting, so there were no theatre costs. This provided a total procedure cost of £251 (see table 4.20, page 158 of the assessment report). The proportion of procedures performed in an office setting under local anaesthetic was varied between 0% and 100%, and the results showed that XprESS remained cost incurring even at 100%. The EAC also conducted scenario analyses in which:

- it used a cost ratio of 0.631 between general and local anaesthetic (as used in the company's submission)
- it used an annual revision rate of 3.5% between years 2 and 5, based on figures reported by Hopkins et al. (2009)
- the cost of a hospital appointment for debridement of £162 (NHS reference cost, 2014/15) was added to each FESS procedure
- It used a consistent proportion of 42% for patients visiting the GP in the first 90 days after the procedure for both treatments
- It varied the rate of revision surgery for XprESS at 2 to 5 years after surgery.

- 5.23 In all cases, XprESS remained cost incurring. The EAC considered a scenario that included an additional appointment for debridement after FESS, and in which the rate of XprESS procedures performed in an office setting under local anaesthesia was varied. In this scenario, XprESS was cost saving when over 80% of procedures were performed in an office setting under local anaesthesia and when every FESS procedure required a single additional hospital appointment for debridement.
- 5.24 At the request of NICE, the EAC did additional sensitivity analyses on the price of the XprESS device and FESS consumables. XprESS became cost saving when the price of the device is less than £586 per patient, and the cost of FESS consumables is more than £614 per patient. The EAC did a 2-way sensitivity analysis varying the price of XprESS and the length of a FESS procedure. XprESS was only cost saving when the device cost £800 or less and the FESS procedure takes more than 60 minutes. At prices above £800, the EAC stated that the length of time the FESS procedure would need to take in order for XprESS to be cost saving was increasingly implausible.

Committee considerations

- 5.25 The committee considered the price of the XprESS device to be the main factor influencing the economic model, and that this should also be its main consideration in the case for adoption. It heard from experts that the cost of the technology was a barrier to current adoption in the NHS. It heard from the company that the price of the technology is negotiable on the basis of the volume of products used. For example, the XprESS is available at a lower price of £820 per unit for centres that order 50 or more units in a year.
- 5.26 The committee considered that the duration of the XprESS procedure and its comparator FESS was integral to the outcome of the cost modelling calculations. Expert advice indicated that the

duration of both procedures should be estimated by including the time involved in the administration of the anaesthesia as well as in undertaking the procedure itself. Experts indicated that for the FESS procedure, this will usually be the composite of the time taken to administer general anaesthesia as well as to undertake the surgery. For the XprESS procedure, experts indicated that this will usually be the composite of the time taken to administer and wait for local anaesthetic to take effect as well as performing the balloon dilatation.

- 5.27 The committee heard from experts that the greater use of XprESS has the potential to change the care pathway, by allowing chronic sinusitis to be treated at an earlier stage and potentially avoiding the need for FESS. Patients who have the XprESS procedure are also able to return to work on the same day. The committee heard from the experts that these factors may result in additional cost savings that were not considered in the model.
- 5.28 The committee carefully considered the plausibility of the EAC scenario in which XprESS is cost saving when more than 80% of procedures are performed in an office setting under local anaesthesia and assuming that every FESS procedure requires an extra appointment for debridement. The committee was advised by experts that patients treated in the NHS do not usually have a follow-up debridement appointment after FESS and therefore concluded that this scenario is unlikely to be widely applicable.
- 5.29 The committee heard from experts that if XprESS was more widely adopted, at least 70%, and potentially 90%, of patients currently treated with FESS, could receive XprESS instead.
- 5.30 The committee considered the cost case for XprESS to be uncertain. It concluded that any cost savings were dependent on the length of FESS, the cost of the device, and the proportion of

XprESS procedures that are performed in an office setting under local anaesthesia.

- 5.31 The committee considered that further research on the cost consequences of using Xpress for treating chronic sinusitis should be carried out.

6 Conclusions

- 6.1 The committee concluded from the evidence presented that XprESS provides a clinically non-inferior but less invasive treatment alternative to FESS in patients with non-complex chronic sinusitis but with the prospect of a quicker recovery time and a lower risk of some complications.
- 6.2 The Committee concluded that cost savings are plausible. These are dependent on the cost of the technology, the length of a FESS procedure and proportion of XprESS procedures that can be done in an office setting using local anaesthetic. For example, if 80% of XprESS treatments are performed in an office setting using local anaesthesia, savings of £152 per patient are achievable with Xpress assuming a 60 minute FESS procedure and a cost for XprESS of £820.
- 6.3 The Committee concluded that XprESS has the potential to treat patients at an earlier stage in the disease process within the NHS and therefore has the potential to improve quality of life and clinical outcomes as well as reduce surgical waiting lists.

Peter Groves
Chairman, medical technologies advisory committee
June 2016

7 Committee members and NICE lead team

Medical technologies advisory committee members

The medical technologies advisory committee is a standing advisory committee of NICE. A list of the committee members who took part in the discussions for this guidance appears below.

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

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

Dr Peter Groves (Chair)

Consultant Cardiologist, Cardiff and Vale University Health Board

Dr Fiona Denison (Vice-chair)

Reader/Honorary Consultant in Maternal and Fetal Health, University of Edinburgh

Ms Susan Bennett

Lay member

Mr Matthew Campbell-Hill

Lay member

Professor Daniel Clark

Head of Clinical Engineering, Nottingham University Hospitals NHS Trust

Mr Steven Fearn

Market Access & Reimbursement Manager, St. Jude Medical UK

Professor Tony Freemont

Professor of Osteoarticular Pathology, University of Manchester

Professor Shaheen Hamdy

Professor of Neurogastroenterology, University of Manchester

Dr Cynthia Iglesias

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Professor Mohammad Ilyas

Professor of Pathology, University of Nottingham

Dr Greg Irving

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Dr Paul Knox

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Professor Rory O'Connor

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Dr Jai V Patel

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Mr John Wilkinson

Director of Devices, Medicines and Healthcare Products Regulatory Agency

Mr Alun Williams

Consultant Paediatric Urologist & Transplant Surgeon
Nottingham University Hospitals

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Lecturer and Researcher in Nursing, University of Manchester

Dr Amber Young

Consultant Paediatric Anaesthetist, Bristol Royal Hospital for Children

NICE lead team

Each medical technology assessment is assigned a lead team of a NICE technical analyst and technical adviser, an expert adviser, a technical expert, a patient expert, a non-expert member of the medical technologies advisory committee and a representative of the external assessment centre.

Neil Hewitt

Technical Analyst

Paul Dimmock

Technical Adviser

Mr Atef El Kholy

Lead Expert Adviser

Mr John de Carpentier

Lead Expert Adviser

Professor Daniel Clark

Non-Expert MTAC Member

Dr Joyce Craig

External Assessment Centre Representative

Ms Michelle Jenks

External Assessment Centre Representative

8 Sources of evidence considered by the Committee

The External Assessment Centre report for this assessment was prepared by Newcastle and York:

- Jenks M, Willits I, Eaton Turner E, The XprESS Multi-Sinus Dilation System for the treatment of chronic rhinosinusitis, April 2016

Submissions from the following sponsor:

- Entellus Medical

The following individuals gave their expert personal view on The XprESS MSDS by providing their expert comments on the draft scope and assessment report.

- Mr Andrew Swift, ratified by British Rhinological Society – clinical expert
- Mr Paul Chatrath, ratified by British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK) – clinical expert
- Professor Valerie Lund, ratified by British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK) – clinical expert
- Mr Carl Philpott, nominated by British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK) – clinical expert
- Mr Hesham Saleh, nominated by British Society for Allergy & Clinical Immunology – clinical expert
- Mr Rajiv Bhalla, nominated by British Rhinological Society – clinical expert
- Mr Atef El Kholy, ratified by British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK) – clinical expert
- Mr Peter de Carpentier, ratified by British Association of Otorhinolaryngologists, Head and Neck Surgeons (ENT UK) – clinical expert

About this guidance [NICE to complete on publication]

This guidance was developed using the NICE [medical technologies guidance process](#).

It updates and replaces NICE medical technology guidance XXX (published [month year]). [Amend as necessary. Delete if not relevant.]

It has been incorporated into the NICE pathway on XXX, along with other related guidance and products. [Amend as necessary. Hyperlink to pathway from pathway name. Delete if not relevant.]

We have produced a summary of this guidance for the public [add hyperlink to the UNG page]. Tools [add hyperlink to the guidance summary page] to help you put the guidance into practice and information about the evidence it is based on are also available. [delete any wording that isn't relevant]

Related NICE guidance

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