NICE advice

Actim Pancreatitis for diagnosing acute pancreatitis

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is the Actim Pancreatitis rapid test. It is to diagnose acute pancreatitis in people presenting to emergency departments with acute abdominal pain or in people who have had endoscopic retrograde cholangiopancreatography (ERCP).
- The **innovative aspects** are that it is a urine dipstick test which means the likelihood of pancreatitis can be rapidly assessed. It does not need processing in a laboratory.
- The intended **place in therapy** would be instead of amylase or lipase blood tests to diagnose acute pancreatitis.
- The **main points from the evidence** summarised in this briefing are from 6 studies including 3,134 patients in a meta-analysis and 5 observational studies. They show that Actim Pancreatitis could be a reliable way to diagnose or rule out acute pancreatitis. Results from the meta-analysis showed a pooled sensitivity of 82.3% and specificity of 93.5% for diagnosing acute pancreatitis in people presenting to emergency departments with acute abdominal pain.
- **Key uncertainties** around the evidence or technology are that there are no data from the UK.
- The **cost** of Actim Pancreatitis is £4.50 per test (excluding VAT). The cost of standard care is £1.10 to £4.81 for serum amylase or lipase tests.

The technology

Actim Pancreatitis (Medix Biochemica) is a point-of-care test to diagnose acute pancreatitis. The test works by detecting levels of trypsinogen-2 (from approximately 50 micrograms/L up to 100,000 micrograms/L) in urine, based on immunochromatography. Trypsinogen-2 is a pancreatic enzyme, which is elevated in the urine of patients with acute pancreatitis. The dipstick should be placed in a urine sample (minimum volume of 500 microlitres). Trypsinogen-2 in the sample will bind to monoclonal antibodies in the test strip. If levels exceed the cut-off value for the test, a positive blue line (test line) will appear in the result area. A second blue line confirms the test has worked properly. A negative test result should be confirmed at 5 minutes. The Actim Pancreatitis test kit contains all necessary materials and can be stored at room temperature (2°C to 25°C).

Innovations

Actim Pancreatitis is a dipstick test which allows relatively rapid assessment of the likelihood of acute pancreatitis in emergency situations, without the need for processing in a laboratory.

Current care pathway

People with acute pancreatitis usually have sudden-onset upper abdominal pain and are referred to emergency medicine. Other symptoms may be present, including feeling or being sick, diarrhoea, indigestion, fever, jaundice, tenderness or swelling of the abdomen and a fast heartbeat. People may also have a history of gallstones or excessive alcohol intake, although it should not be assumed the cause is alcohol-related if the person drinks alcohol. Diagnosis is usually made through physical examination and confirmed using blood tests for lipase or amylase levels, which are usually elevated in acute pancreatitis. If elevated lipase and amylase levels in the blood are not detected, abdominal CT may be done to confirm pancreas inflammation.

NICE's guideline on pancreatitis is relevant to this care pathway.

Population, setting and intended user

Actim Pancreatitis is intended to be used in emergency medicine to help diagnose acute pancreatitis in people with suspected symptoms. The most common presenting symptom of acute pancreatitis is upper abdominal pain which steadily gets worse and may move to the back. The company states that the test can also be used in people who have had endoscopic retrograde cholangiopancreatography (ERCP). ERCP is a test to examine and diagnose conditions of the liver, bile ducts, pancreas or gallbladder. It is associated with a 5% to 10% increase in the risk of

pancreatitis (The National Pancreas Foundation, 2019).

Acute pancreatitis is a condition in which the pancreas becomes inflamed over a short period of time. It can develop quickly and can be mild or life threatening. For most people with acute pancreatitis, the condition settles over a few days. In 25% of cases however, it is severe and associated with complications such as respiratory or kidney failure, or the development of abdominal fluid collections. These people often need critical care and a prolonged hospital stay. Overall the mortality rate in acute pancreatitis is approximately 5% but can be up to 25% in severe cases. People who are aged over 70, obese, have 2 or more alcoholic drinks a day, smoke or have a family history of pancreatitis are more likely to develop severe pancreatitis. The incidence of acute pancreatitis in the UK is approximately 56 cases per 100,000 people every year. The condition is commonly caused by gallstones (around 50% of cases) or drinking too much alcohol (25% of cases), but in some cases no cause can be found.

Actim Pancreatitis would be used in secondary care by clinicians or nurses working in emergency medicine. It may also be used by gastroenterologists.

Costs

Technology costs

The cost per test for Actim Pancreatitis is £4.50 (excluding VAT). The company states that this cost includes all necessary materials and consumables and that no other purchases are needed.

Costs of standard care

Average laboratory costs for serum amylase and lipase tests are £1.10 for an inpatient serum amylase or lipase test blood test or £4.81 for an outpatient blood test (includes £1.10 for biochemical test and an additional £3.71 for the phlebotomy costs; NHS reference costs 2018/19).

Resource consequences

The technology could be resource releasing if it leads to a reduced risk of misdiagnosing acute pancreatitis or reduces the delay to diagnosis and treatment. However, this is not supported by the available evidence. The technology is a simple dipstick test with all necessary materials that can be stored at room temperature. Adopting the technology will not need any changes to facilities or infrastructure, and little to no staff training will be needed to use the test.

Regulatory information

Actim Pancreatitis is a CE mark class I (IVDD general category) medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

No equality issues were identified.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Six studies are summarised in this briefing including 3,134 patients who had either come to hospital with acute abdominal pain or who have had endoscopic retrograde cholangiopancreatography (ERCP).

The clinical evidence and its strengths and limitations are summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The evidence suggests that the Actim Pancreatitis rapid test may be a reliable method for diagnosing acute pancreatitis. Included studies consist of 1 meta-analysis and 5 prospective observational studies. Most of the evidence base for the technology was on patients coming to hospital with acute abdominal pain (patients with susceptive acute pancreatitis). Three prospective single centre studies investigated the diagnostic accuracy in patients after ERCP.

Results from the meta-analysis, which involved 13 studies on patients with suspected acute pancreatitis, showed a pooled sensitivity of 82.3% and specificity of 93.5% in these patients. This

indicated that the test may result in 17.7% false negative and 6.5% false positive results. Two multicentre prospective observational studies also assessed diagnostic accuracy for this clinical situation and showed sensitivities of 73.1% and 68.6%, and specificities of 62.5% and 87.1%. The sensitivity and specificity for detecting post-ERCP ranged from 81% to 100% and 96% to 97.1%, respectively.

All studies had a urinary trypsinogen-2 cut-off value of 50 micrograms/L. Of the studies that reported on the severity of disease, the proportion of severe pancreatitis patients was between 13% and 40%, which may be reflective of the patient population (approximately 25% of acute pancreatitis cases are severe). Most of the individual studies compared the test with serum or urine amylase measurements; 4 studies used serum lipase as a reference standard. Some of the studies may have been underpowered to detect diagnostic accuracy because of their small sample size. None of the studies were done in the UK, limiting the generalisability of results to the NHS. Available evidence reports on the diagnostic accuracy of the test only. There are no data on the effect of the test on clinical outcomes or healthcare resource use.

Yasuda et al. (2019)

Study size, design and location

Prospective multicentre observational study on 94 patients with acute abdominal pain, from 17 centres in Japan between April 2009 and December 2012.

Intervention and comparators

Urinary trypsinogen-2 dipstick test (Actim Pancreatitis).

Key outcomes

Of the 78 patients with acute pancreatitis, 57 had a positive trypsinogen-2 dipstick test result. The test had a sensitivity of 73.1% and specificity of 62.5%. The positive and negative predictive values of test for diagnosing acute pancreatitis were 90.5% and 32.3%, respectively. The median levels of urinary trypsinogen-2 were 2.87 mg/dL and 6.49 mg/dL in patients with mild and severe pancreatitis and the area under the curve (AUC) score was 0.704. This was numerically higher than that of other pancreatic enzymes tested which included urinary and serum amylase, creatine and lipase, and urinary trypsinogen activation peptide.

Strengths and limitations

Small sample size and indirect comparisons with other pancreatic enzyme tests. The study was

done in Japan, so the relevance to the NHS is limited.

Mayumi et al. (2012)

Study size, design and location

Prospective multicentre observational study on 412 patients with acute abdominal pain, from 21 centres in Japan between September 2008 and April 2009.

Intervention and comparators

Urinary trypsinogen-2 dipstick test and quantitative trypsinogen-2 assay (Actim Pancreatitis) compared with serum amylase and lipase tests.

Key outcomes

The trypsinogen-2 dipstick test had a sensitivity of 68.6% and a specificity of 87.1%. The sensitivity of the dipstick test for pancreatitis caused by alcohol and gallstones was 72.2% and 81.8%, respectively, which was much higher compared with amylase testing. Changing the cut-off point to include positive (+) and very positive (++) results only, increased the specificity to 92.2%, and the positive likelihood ratio was 7.63.

Strengths and limitations

Useful real-world data on patients presenting as an emergency with acute abdominal pain. The study was done in Japan, so the relevance to the NHS is limited. Study enrolment was done by gastroenterologists and surgeons and it involved a high proportion of patients with mild pancreatitis, which may not reflect standard clinical practice or typical patient population in the UK.

Chang et al. (2012)

Study size, design and location

Meta-analysis including 13 studies and a total of 2,342 patients presenting to hospital with acute abdominal pain.

Intervention and comparators

Urinary trypsinogen-2 test (Actim Pancreatitis).

Key outcomes

The pooled sensitivity was 82.3% and the specificity was 93.5%. The diagnostic odds ratios for the test was 85.23 and the AUC was 0.9673.

Strengths and limitations

Included 13 studies that the authors judged as generally high quality. In total, involved a large number of patients, but some of the included studies had a small sample size and may not have been adequately powered to estimate diagnostic accuracy. There could have been publication bias. Only 1 of the studies used a serum lipase test as a reference standard. None of the included studies were done in the UK.

Tseng et al. (2011)

Study size, design and location

Prospective single centre observational study on 150 patients having ERCP between March 2006 and July 2008 in Taiwan.

Intervention and comparators

Urinary trypsinogen-2 dipstick test (Actim Pancreatitis) compared with serum amylase and lipase tests.

Key outcomes

Of the 13 patients with post-ERCP pancreatitis, 11 (84.6%) had a positive dipstick test result 3 hours after ERCP. All 13 patients with post-ERCP pancreatitis showed a positive test result 24 hours after ERCP. Three hours after ERCP, the dipstick test had a sensitivity for diagnosing post-ERCP pancreatitis of 84.6% and a specificity of 97.1%. The positive and negative predictive values for the test were 73.3% and 98.5%, respectively. The test showed numerically higher positive predictive values compared with the serum amylase test (42.9%) and lipase tests (36.4% and 42.3% at the cut-off level of 3 and 5 times the upper reference, respectively) 3 hours after ERCP.

Strengths and limitations

The study was done in Taiwan, so the relevance to the NHS is limited. The definition of post-ERCP pancreatitis is not consistent in the literature, the study used a definition from a consensus in 1991. The study excluded patients who had a positive urinary trypsinogen-2 dipstick test result before

ERCP.

Sankaralingam et al. (2007)

Study size, design and location

Prospective single centre observational study on 30 patients having ERCP in the US.

Intervention and comparators

Urinary trypsinogen-2 dipstick test (Actim Pancreatitis).

Key outcomes

One patient with a history of pancreatic adenocarcinoma was excluded because the pre-ERCP test results were positive. One of the patients was unable to give a urine sample for the 1-hour test. Five of the 29 patients developed post-ERCP pancreatitis, diagnosed by the gastroenterologist. Six out of 28 patients had positive results in 1 hour and 6 of 29 patients had positive results in 4 hours. One hour after ERCP, the dipstick test had a sensitivity for diagnosing post-ERCP pancreatitis of 1.0 and a specificity of 0.91. The positive predictive value was 0.66, and the negative predictive value was 1.0. Four hours after ERCP, the test had a sensitivity of 1.0 and a specificity of 0.96. The positive predictive value was 0.8, and negative predictive value was 1.0.

Strengths and limitations

All ERCPs were done by 1 gastroenterologist using the same preoperative preparation. The treating physician was blinded to the urinary trypsinogen-2 results. The study was a pilot study with a small sample size. It was done in the US, so the relevance to the NHS is limited.

Kemppainen et al. (1997)

Study size, design and location

Prospective single centre observational study on 106 patients having ERCP between November 1994 and December 1995 in Finland.

Intervention and comparators

Urinary trypsinogen-2 dipstick test (Actim Pancreatitis) compared with serum and urine amylase measurements.

Key outcomes

Post-ERCP pancreatitis developed in 11 of the 106 patients studied. At 6 hours, the test was positive in 9 of these patients and in 9 of the 97 patients without post-ERCP pancreatitis. The sensitivity of the dipstick test for diagnosing post-ERCP pancreatitis was 81% and the specificity was 90%. When asymptomatic patients were excluded the specificity was 97%. The dipstick test showed a good correlation with quantitative trypsinogen-2 assays (0.75). The sensitivities of serum and urine amylase measurements were 91% and 81%, respectively. The specificities were 96% and 95%, respectively.

Strengths and limitations

Patients were recruited consecutively. All ERCPs were done by a single experienced clinician. Patients were not tested with the dipstick test before the ERCP procedure. The study was done in Finland, so the relevance to the NHS is limited.

Sustainability

The company did not provide any sustainability claims for the technology.

Recent and ongoing studies

Urine trypsinogen 2 dipstick for the early detection of post-ERCP pancreatitis. ClinicalTrials.gov identifier: NCT03098082. Status: recruiting. Indication: post-ERCP acute pancreatitis. Devices: Actim Pancreatitis. Study completion date: August 2021. US.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

None of the experts were familiar with or had used this technology before.

Level of innovation

Most experts thought Actim Pancreatitis was a novel way to diagnose acute pancreatitis because it does not need blood sample collection and can be done at the bedside with fairly rapid test results.

The current standard of care involves blood tests to rule disease in or out, no urinary dipstick assay is currently used for acute pancreatitis. Most of the experts felt the test would be used in addition to standard care.

Potential patient impact

Reduction in delays to diagnosis and treatment, reduced need for hospital admission for further investigations and quicker discharge from hospital were some of the main potential benefits identified by experts. One expert noted that published studies seem to have promising results. Another expert explained that the clinical advantage of urinary dipstick testing is that the test results can be available within minutes compared with hours using conventional laboratory testing. People who have had endoscopic retrograde cholangiopancreatography (ERCP) and people who present to primary or secondary care with acute abdominal pain when acute pancreatitis is suspected were identified by experts as people who would particularly benefit from Actim Pancreatitis testing. One of the experts said the test could be used for acute pancreatitis in all clinical settings. One of the experts did not think there would be any patient benefits in an emergency setting but it could help rule acute pancreatitis in or out in primary care. One expert thought that the test could change the current care pathway and clinical outcomes for post-ERCP patients. Another expert noted that the test was unlikely to change the current care pathway in emergency departments where blood tests are available and commonly used.

Potential system impact

Potential system benefits identified by experts included avoiding further admissions or tests by helping to triage patients. One expert said that the test could help to streamline the patient care pathway from primary to secondary care and that this may improve system performance with regards to the 4-hour access standard for patients attending emergency departments. Another expert thought that the test was unlikely to have a substantial effect on the healthcare system. Two of the experts thought the technology would cost more than standard care and the other expert said that it was difficult to say without further data. Most of the experts felt that adopting the technology would have little effect on staffing needs and resource. All experts said that no changes to facilities or infrastructure, or any specific training would be needed to use the technology. None of the experts were aware of any safety concerns surrounding this technology.

General comments

Experts were not aware of the technology being used in the NHS. One expert commented that a positive test result would not avoid the need for further confirmatory tests. Patients with a positive

test would still need a CT scan to confirm the diagnosis of pancreatitis, assess its severity and the presence of local complications. Another expert said that they did not see a place for the technology in emergency care. One expert highlighted that the prevalence of acute pancreatitis is variable across different care settings and a better understanding of risk in these patients would be helpful.

Expert commentators

The following clinicians contributed to this briefing:

- Dr Peter Hampshire, consultant in intensive care medicine and anaesthesia, Royal Liverpool Hospital, Liverpool University Hospitals NHS Foundation Trust, did not declare any interests.
- Dr Steve Jones, consultant in emergency and intensive care medicine, Manchester University NHS Foundation Trust, did not declare any interests.
- Dr Sharan Shetty, consultant gastroenterologist, Russells Hall Hospital, Dudley, did not declare any interests.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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