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Health Technology Briefing
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Catumaxomab for treating malignant ascites in epithelial cellular adhesion molecule (EpCAM)-positive carcinomas

Company/Developer	Pharmanovia

☒ New Active Substance ☐ Significant Licence Extension (SLE)

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Licensing and Market Availability Plans

Catumaxomab received a positive opinion from the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) October 2024, and was granted EMA marketing authorisation February 2025 for the intraperitoneal treatment of malignant ascites in adults with EpCAM-positive carcinomas, who are not eligible for further systemic anticancer therapy.

Summary

Catumaxomab is currently in development for the treatment of malignant ascites (a build-up of fluid in the abdomen) caused by cancers that are EpCAM-positive (meaning that the cancer cells have a molecule on their surface called epithelial cellular adhesion molecule). Catumaxomab is used in patients who cannot have any further cancer treatment. Symptoms include bloating, abdominal pain, loss of appetite and breathlessness, which can have a detrimental impact on physical and mental health along with a reduction in overall quality of life. Standard-of-care for malignant ascites is a medical procedure, called paracenteses, in which a tube drains the fluid. Patients with large-volume ascites often have limited mobility and can negatively affect quality of life.

The active substance in catumaxomab, is a monoclonal antibody. A monoclonal antibody is an antibody (a type of protein) that has been designed to recognise and attach to a specific structure (called an antigen) that is found on certain cells in the body. Catumaxomab has been designed to attach to two antigens: EpCAM and CD3. By attaching to these two antigens, catumaxomab forms a bridge between the cancer cells and the T-cells. This brings the cells close together so that the T-cells can kill the cancer cells. Catumaxomab is administered directly into the peritoneal cavity. The benefit of catumaxomab is its ability to reduce the need for, or lengthen the time between, paracenteses in patients with malignant ascites. If licensed, catumaxomab will offer an additional treatment option for malignant ascites in adults with EpCAM-positive carcinomas who are not eligible for further systemic anticancer therapy.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

The intraperitoneal treatment of malignant ascites in adults with epithelial cellular adhesion molecule (EpCAM)-positive carcinomas, who are not eligible for further systemic anticancer therapy.[1]

Technology

Description

Catumaxomab (Korjuny) is a monoclonal antibody that targets the epithelial cell adhesion molecule (EpCAM), which is found in high levels on some types of cancer cells, and CD3 antigen on T-cells, inducing an immunoreaction against EpCAM expressing tumour cells. By bringing cancer cells and T cells close together, catumaxomab promotes the killing of cancer cells by T cells. Catumaxomab also attaches to a third protein called Fc-gamma receptor which helps the cells of the immune system to attack cancer cells. All these actions cause the death of cancer cells in the abdomen, removing a major cause of excessive abdominal fluid.[1]

Catumaxomab is currently in development for the intraperitoneal treatment of malignant ascites in adults with EpCAM-positive carcinomas, who are not eligible for further systemic anticancer therapy.[1] In the Phase II/III pivotal trial (NCT00836654), the effectiveness of catumaxomab is being assessed for symptomatic malignant ascites versus an untreated control group.[2]

Key Innovation

Malignant ascites are often treated by physically draining the fluid (this is called paracentesis or an ascitic drain), however the fluid may build up again.[3,4] Catumaxomab combined with drainage is more effective at treating malignant ascites than drainage alone. On average, patients who received catumaxomab lived for 46 days without the need for further drainage. This is compared with 11 days for patients who were treated with drainage alone.[1] Patients with large-volume ascites often have limited mobility. These symptoms can be debilitating and have been shown to negatively affect quality of life.[5] Deterioration in quality of life was delayed by treatment with catumaxomab in patients suffering from malignant ascites, compared with drainage alone. Catumaxomab thus enables patients to benefit from better health-related quality of life during a prolonged survival period.[6]

If licensed, catumaxomab will offer an additional treatment option for malignant ascites in adults with EpCAM-positive carcinomas, who currently have only a single effective therapy available

Regulatory & Development Status

Catumaxomab received a positive opinion from the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) October 2024, and was granted EMA marketing authorisation February 2025 for the intraperitoneal treatment of malignant ascites in adults with EpCAM-positive carcinomas, who are not eligible for further systemic anticancer therapy.[1]

Catumaxomab is in phase III/II development for the treatment of gastric adenocarcinoma, ovarian cancer and peritoneal carcinomatosis in patients with gastric adenocarcinomas.[7]

Patient Group

Disease Area and Clinical Need

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Ascites is a build-up of fluid in the lining of the abdomen (peritoneum), which can be caused by cancer (malignant ascites), or other conditions, such as advanced liver disease and heart failure. Malignant ascites is often caused by cancers originating from organs in the abdomen (such as stomach, liver and pancreatic cancers), or mesothelioma in the peritoneum. Ascites may develop when cancer cells irritate the lining of the abdomen, causing it to make too much fluid. Additionally, lymph nodes in the abdomen become blocked and the fluid cannot drain properly. If cancer spreads to the liver, it raises the pressure in nearby blood vessels, which forces fluid out. Furthermore, liver damage can impair the production of blood proteins, leading to fluid leakage from the veins. The main symptom of ascites is bloating and a swollen stomach; other symptoms include pain or discomfort in the abdomen or back, nausea, loss of appetite, indigestion, fatigue, constipation, increased urination, breathlessness, and difficulty sitting comfortably and moving around.[4,8]

Malignant ascites are associated with poor prognosis and deterioration in quality of life (QoL).[9] The occurrence of malignant ascites results in considerable morbidity for patients due to its high symptom burden impeding patients physical and mental well-being. It does not only cause considerable morbidity but is also associated with impeded survival. Survival times after ascites diagnosis vary, ranging from few weeks to months.[10] In one retrospective analysis, patients with EpCAM-positive malignant ascites showed significantly poorer overall survival ($p = 0.028$) compared to EpCAM-negative.[11] Another study has found that higher concentration of EpCAM-positive tumour-derived extracellular vesicles in ascites is associated with shorter progression-free survival, regardless of treatment strategy.[12]

In England 2023-24, there were 11,594 finished consultant episodes (FCE) and 8,671 admissions for ascites (ICD-10 code R18), of which malignant ascites makes up around 10% of all ascites, which resulted in 19,893 FCE bed days and 3,611 day cases.[13,14]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends the PeritX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites.[15] To date, treatment of malignant ascites still focusses on symptomatic treatment with no standardised treatment guidelines as evidence is lacking. These treatments include paracentesis, diuretics and systemic treatment of the underlying malignancy.[10] There are no recommendations or approved pharmacological options specifically for the treatment of malignant ascites with EpCAM-positive carcinomas.

Clinical Trial Information

Trial	**IP-REM-AC-01** (Pivotal trial), NCT00836654, EudraCT 2004-000723-15; Two-Arm, Randomized (2:1), Open-Label Phase II/III Study in EpCAM Positive Cancer Patients With Symptomatic Malignant Ascites Using the Trifuncitonal Bispecific Antibody Catumaxomab (Anti-EpCAM x Anti-CD3) Versus an Untreated Control Group. **Phase III** – Completed **Location(s):** No location data **Actual study completion date:** November 2006
Trial Design	Randomised, crossover assignment, open label
Population	N (actual) = 258; EpCAM positive cancer patients with symptomatic malignant ascites; 18 years and older.

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Intervention(s)	Catumaxomab and paracentesis
Comparator(s)	Paracentesis alone
Outcome(s)	The primary efficacy endpoint was puncture-free survival. Secondary efficacy parameters included time to next paracentesis, ascites signs and symptoms and overall survival (OS).[16]
Results (efficacy)	Puncture-free survival was significantly longer in the catumaxomab group (median 46 days) than the control group (median 11 days) (hazard ratio = 0.254: p<0.0001) as was median time to next paracentesis (77 versus 13 days; p<0.0001). In addition, catumaxomab patients had fewer signs and symptoms of ascites than control patients. OS showed a positive trend for the catumaxomab group and, in a prospectively planned analysis, was significantly prolonged in patients with gastric cancer (n = 66; 71 versus 44 days; p = 0.0313).[16] Treatment with catumaxomab delayed deterioration in QoL in the study population. Compared with paracentesis alone, catumaxomab enabled patients to benefit from better QoL for a prolonged survival period as deterioration in QoL scores appeared more rapidly in the control than in the catumaxomab group: median 19-26 days versus 47-49 days (difference between the groups was statistically significant for all scores, p<0.01).[6]
Results (safety)	The most commonly reported catumaxomab-related adverse events in both the ovarian and nonovarian groups were cytokine release–related symptoms (pyrexia, nausea and vomiting) and abdominal pain. These events were generally mild to moderate in intensity and reversible.[16] The hazard ratios ranged from 0.08 for nausea and vomiting score to 0.24 for emotional functioning score.[6]

Trial	**STP-REM-01** (Supportive study)[17] **Phase II** – Completed
Trial Design	Non-randomised, multi-centre, dose-escalation study
Population	N (actual) = 23; patients with malignant ascites due to ovarian carcinoma.
Intervention(s)	Catumaxomab
Comparator(s)	-
Outcome(s)	
Results (efficacy)	The median decrease was 52 ml/h from 105 ml/h at baseline to 23 ml/h on day 1 after the 4th infusion.
Results (safety)	

Trial	**IP-REM-PK-01-EU** (Supportive study), Eudra-CT 2005-001700-39; Determination of systemic exposure and characterization of pharmacokinetics of the tri-functional antibody catumaxomab (anti-EpCAM X anti-CD3) administered intraperitoneally in EpCAM positive cancer patients with malignant ascites.[17,18]

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	Phase II – Completed **Locations:** 2 EU countries
Trial Design	Multi-centre, open-label, non-randomised
Population	N (actual)= 13; EpCAM expressing tumours in patients with malignant ascites requiring therapeutic ascites puncture; adults.
Intervention(s)	Catumaxomab
Comparator(s)	-
Outcome(s)	Primary outcomes: • Determination of systemic exposure of catumaxomab during and after four intraperitoneal infusions with increasing doses • Characterisation of pharmacokinetics of catumaxomab after the second, the third and the fourth intraperitoneal infusion See trial record for full list of other outcomes
Results (efficacy)	The efficacy value of this study is limited. Although tumour cells have been reduced, no reduction in ascites volume has been shown here.
Results (safety)	

Trial	**IP-REM-AC-02-US** (completed after the original MA)[17] **Phase II** – Completed **Location:** USA
Trial Design	Multi-centre, open-label, single arm
Population	N (actual) = 32; patients with recurrent symptomatic malignant ascites due to ovarian cancer.
Intervention(s)	Catumaxomab
Comparator(s)	-
Outcome(s)	Primary outcome: the proportion of patients who achieved at least a 4-fold increase in their puncture/paracentesis-free interval following catumaxomab.
Results (efficacy)	Interpretation of efficacy is very limited due to lack of comparator and subjective indication for paracentesis (patient's request) after administration of catumaxomab. EpCAM positivity was not required. Puncture-free interval was longer after catumaxomab treatment. However, the pre-defined threshold of study success >60% has not been achieved. Moreover, only 28% of patients achieved a 4-fold prolongation interval, this is lower than 30% which was considered the limit to assess the efficacy as low. Although the study formally failed, the mean and median value of the punction-free interval was prolonged, which supports the efficacy of catumaxomab and is considered supportive for the conclusion of the pivotal study.
Results (safety)	

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Estimated Cost

Cost of catumaxomab was confidential at the time of producing this briefing.

Relevant Guidance

NICE Guidance

- NICE technologies guidance. PeritX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites (MTG9). July 2022.

NHS England (Policy/Commissioning) Guidance

No relevant guidance found.

Other Guidance

- Shaw L, Mclintock S, Scott A, Fradsham S, Corrigan M, Tobin L, et al. 165 A NICE accredited guideline for the management of malignant ascites. 2023.[19]
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