reference no: 2423
Publication date: 16 July 2026

Clinical Commissioning Policy:

# Gemcitabine and paclitaxel albumin combination chemotherapy for the treatment of locally advanced non-metastatic pancreatic cancer (adults) [2423]

## Summary

Gemcitabine and paclitaxel albumin combination chemotherapy is recommended to be available as a routine commissioning treatment option for locally advanced non-metastatic pancreatic cancer within the criteria set out in this document.

The policy is restricted to adults (age ≥18 years) only as there is insufficient evidence to confirm safety for children (age <18 years).

## Committee discussion

Clinical Panel agreed with the policy and recommended that it progress as a routine commissioning policy. Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed here: Clinical Commissioning Policy: Gemcitabine and paclitaxel albumin combination chemotherapy for the treatment of locally advanced non-metastatic pancreatic cancer (adults)

## What we have decided

NHS England has carefully reviewed the evidence to treat locally advanced non-metastatic pancreatic cancer with gemcitabine and paclitaxel albumin combination chemotherapy. We have concluded that there is enough evidence to make the treatment available at this time.

The three-paper evidence summary which informs this commissioning position can be accessed here: Clinical Commissioning Policy: Gemcitabine and paclitaxel albumin combination chemotherapy for the treatment of locally advanced non-metastatic pancreatic cancer (adults)

## Links and updates to other policies

This document is linked to:

- National Institute for Health and Care Excellence (2017): Paclitaxel as albumin-bound nanoparticles with gemcitabine for untreated metastatic pancreatic cancer

## Plain language summary

## About locally advanced, non-metastatic pancreatic cancer

The pancreas is an organ in the abdomen that produces digestive enzymes, which help digest food and hormones, notably insulin which helps the body process sugar (glucose). Pancreatic cancer is the 10$^{th}$ most common cancer in the UK and is more common in older populations with 47% of new cases being diagnosed in people aged 75 years and over

(Cancer Research UK, n.d.). Other risk factors include deprivation, ethnicity (more common in Black patients compared to White patients), smoking and obesity (Cancer Research UK, 2023).

Unfortunately, pancreatic cancer has a poor prognosis, with one- and five-year survival being only 21% and 3.3% respectively. This is lower than the European and American average survival rates (Cancer Research UK, n.d; National Cancer Institute, 2024).

Pancreatic adenocarcinoma is the most common type of pancreatic cancer, and this arises from the cells that produce digestive enzymes (exocrine glands) (Rawla et al, 2019). Symptoms of pancreatic cancer include yellowing of the skin (jaundice), weight loss and abdominal pain. The onset of these is usually gradual and subtle as symptoms only become evident once the tumour is of significant size. As a result, patients usually present as an emergency or at an advanced state.

At presentation, 30-40% of pancreatic adenocarcinomas are locally advanced, inoperable and non-metastatic (Conroy et al, 2023). This is collectively referred to as locally, advanced non-metastatic pancreatic cancer (LANPC). These cancers spread in and around the pancreas, and may obstruct local vital structures, such as blood vessels.

## About current treatment

Patients with pancreatic cancer are referred to a tertiary (specialist) pancreatic multidisciplinary meeting where a decision about whether the tumour can be surgically removed is made. In LANPC, surgery is usually not possible due to the size and/or location of the tumour. Therefore, chemotherapy is the mainstay of treatment. This is mostly given for palliative intent (i.e. chemotherapy is unable to cure; however, for a minority of patients, chemotherapy may shrink their tumour enough to allow for surgery).

The type of chemotherapy patients receive depends on functional status as measured by the Eastern Cooperative Oncology Group (ECOG) performance status. For patients with an ECOG performance status of 0 or 1 (i.e. they are physically fit), combination chemotherapy is offered. The combination chemotherapy used is most often a modified FOLFIRINOX regimen and this is made up of three different chemotherapy drugs (Macmillan Cancer Support, 2023):

- **FOL** - Folinic acid (this is not a chemotherapy drug – it is given to improve the efficacy of fluorouracil)
- **F** - Fluorouracil (5FU)
- **IRIN** - Irinotecan
- **OX** - Oxaliplatin

Irinotecan with folinic acid and 5FU and oxaliplatin with folinic acid and 5FU are licensed separately for advanced and metastatic colorectal cancer, however the use of modified FOLRINOX in LANPC is off-label. The modified FOLFIRINOX regimen is intensive for patients: they require central venous access (i.e. a line into a large vein, commonly in the neck, chest or arms), they must attend hospital frequently to connect and disconnect chemotherapy infusions[1], patients (or a trained relative/healthcare professional) must

[1] Patients attend hospital to receive folinic acid, irinotecan and oxaliplatin (this takes approximately 4 hours). They are then connected to an ambulatory pump which delivers 5FU over 48 hours. They then must return to hospital so that the ambulatory pump that delivered 5FU can be disconnected. As modified FOLFIRINOX is given every 14 days, patients must attend hospital 4 times every month during treatment.

administer filgrastim injections to prevent low white blood cell count (neutropenia), and there is a high toxicity. This high toxicity often results in hospital admissions, more frequent blood tests, and dose reductions or treatment cessation which can impact treatment efficacy and prognosis. As a result, modified FOLFIRINOX is only suitable for the fittest patients and tolerance can be an issue. Other less common regimens for patients with a good performance status include gemcitabine-capecitabine.

Patients may also have radiotherapy following chemotherapy (consolidation radiotherapy). In a small number of cases (i.e. frail or elderly patients), radiotherapy is given as an alternative to chemotherapy.

In patients with an ECOG performance status of 2, gemcitabine monotherapy is used and for patients with a poorer performance status (ECOG 3-4) only best supportive care is given.

## About gemcitabine and paclitaxel albumin

Like modified FOLFIRINOX, gemcitabine combined with paclitaxel albumin is a type of combination chemotherapy made up of two chemotherapy drugs that work together to stop cancer cells replicating and this blocks the growth of the cancer:

- **Gemcitabine** – this is a chemotherapy agent that works by entering cancer cells and stopping cancer cells from making DNA.

- **Paclitaxel albumin**– paclitaxel is a chemotherapy agent that is bound with a nanoparticle (albumin) to improve its uptake into cells. This version of the drug is often called nab-paclitaxel. Paclitaxel works by arresting cell division.

Both gemcitabine and paclitaxel albumin are given as a short intravenous (through a vein) infusion. It is usually given in a chemotherapy day unit. Compared to the modified FOLFIRINOX regimen, gemcitabine and paclitaxel albumin is associated with a lower toxicity, does not require central venous access and patients do not need to administer filgrastim injections. Moreover, there is no need for an ambulatory pump and the infusion can be given in a single, short (approximately 2 hours) visit. This means that patients have to attend hospital less frequently and for a shorter period. This both improves accessibility to treatment and is likely to require less NHS resources as there will be fewer and shorter attendances, patients do not require filgrastim injections and the treatment is considered to be less toxic, resulting in less monitoring and fewer hospital admissions to treat the complications (e.g. neutropenic sepsis) of chemotherapy.

Currently, this combination is only licensed to treat metastatic pancreatic cancer and NICE technology appraisal TA476 recommends that gemcitabine and paclitaxel albumin is given as an option for metastatic adenocarcinoma when other combination chemotherapies are unsuitable, and they would otherwise have gemcitabine monotherapy. Similar to modified FOLFIRINOX, the use of gemcitabine and paclitaxel albumin for LANPC as outlined in this policy is off-label.

# Epidemiology and needs assessment

There are approximately 10,800 new pancreatic cancer cases in the UK every year, and incidence rates are projected to rise (Cancer Research UK, n.d.). In 2021, the National Disease Registration Service recorded 517 patients with LANPC as being eligible to receive chemotherapy, with 267 patients receiving chemotherapy as their only treatment and for palliative intent. Assuming most patients have combination chemotherapy (i.e. they have an ECOG score of 0 or 1), it is estimated that half of patients would opt for gemcitabine and paclitaxel albumin over the modified FOLFIRINOX regimen, and therefore approximately 130 patients per year will be eligible for treatment under this policy. This policy has been restricted to adults only.

## Implementation

### Inclusion criteria

Patients aged ≥ 18 years with pancreatic cancer who meet the following criteria:

- Histologically or cytologically confirmed pancreatic adenocarcinoma

**AND**

- Locally advanced, non-metastatic disease (i.e. unresectable disease)

**AND**

- Have an ECOG performance status of 0 or 1

**AND 1 of the following:**

- The patient is either completely treatment naive for systemic therapy for pancreatic cancer

  **OR**

- The patient has received prior systemic anti-cancer therapy (SACT) as neoadjuvant, or adjuvant therapy and this treatment was completed at least 6 months previously

### Exclusion criteria

Patients who meet **any** of the following criteria are not eligible for treatment with gemcitabine and paclitaxel albumin under this policy:

- Non-adenocarcinoma pancreatic cancer (this includes pancreatic cancers where there is malignant change in another tissue type in addition to glandular tissue, e.g. adenosquamous carcinoma)
- The tumour can be resected with curative intent
- ECOG performance status of ≥ 2
- Metastatic pancreatic cancer
- Previous SACT for pancreatic cancer within the last 6 months

- Individuals with contraindications to gemcitabine, as described by the Summary of Product of Characteristics: Gemcitabine 10 mg/ml, solution for infusion - Summary of Product Characteristics (SmPC) - (emc)
- Individuals with contraindications to paclitaxel albumin[2], as described by:
    - Abraxane 5 mg/ml powder for dispersion for infusion - Summary of Product Characteristics (SmPC) - (emc)
    - Paclitaxel (Pazenir) 5 mg/ml Powder for Dispersion for Infusion - Summary of Product Characteristics (SmPC) - (emc)

## Starting criteria

Gemcitabine and paclitaxel albumin should only be prescribed by an oncologist with experience in the treatment of pancreatic cancer and the use of SACT and/or an appropriately delegated healthcare professional working with a hepatobiliary oncologist. Once treatment has been initiated by an oncologist, gemcitabine and paclitaxel albumin can be administered at a community chemotherapy unit depending on local networks[1]. Patients should have a baseline full blood count (FBC), and liver function test (LFT) performed.

## Stopping criteria

Gemcitabine and paclitaxel albumin should be stopped if one of the following criteria is met:

- Disease progression whilst on treatment
- Symptomatic deterioration (where dose reduction is not suitable or has failed)
- Unacceptable toxicity
- Patient decision to stop treatment
- Complete surgical resection of the tumour performed on or following treatment
- Starting other anti-cancer treatment for pancreatic cancer (e.g. radiotherapy)

## Dosing

The use of gemcitabine with paclitaxel albumin is off-label and Trust policy regarding off-label use of medicines should apply. Gemcitabine with paclitaxel albumin should be given on days 1, 8 and 15 of each 28-day cycle as follows:

- Paclitaxel albumin should be administered first. It is given as an IV infusion over 30 minutes, at a dose of 125mg/m$^2$
- Gemcitabine should be given immediately after paclitaxel albumin. It is given as an IV infusion over 30 minutes, at a dose of 1000mg/m$^2$

[2] Please note that other brands of gemcitabine and paclitaxel albumin are available and can be used within the criteria set out in this clinical commissioning policy. Please refer to each specific SmPC for guidance on the use of each product.

[1] There should be appropriate shared-care agreements in place between local and specialist centres when patients are receiving treatment at local centres, including a point of contact when there are clinical queries or escalation to specialist input is required.

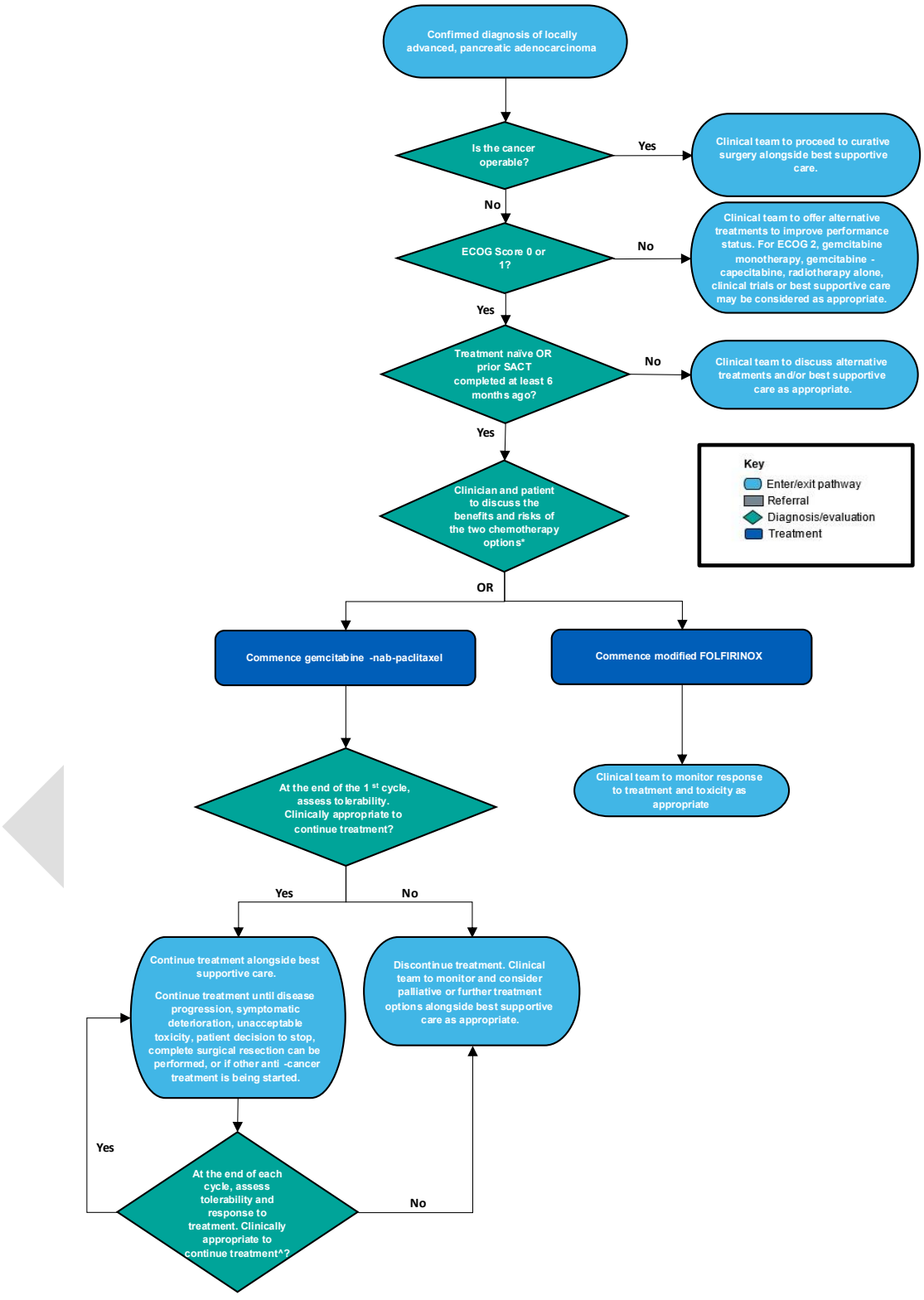
Prescribing clinicians should be aware of dosing considerations as outlined in the respective gemcitabine and paclitaxel albumin Summary of Product Characteristics (SmPC)), including dose reductions for adverse events (e.g. sensory neuropathy).

## Monitoring

A formal medical review to assess the tolerability of treatment should occur at the end of the first cycle and before the subsequent cycle at approximately 28 days by the patient's oncology team. Following this, reviews should occur at a minimum of at the end of every cycle (i.e. every 28 days) to assess both the tolerability and response to treatment (assessed clinically and with imaging) to determine whether it is suitable to continue gemcitabine with paclitaxel albumin.

Before each infusion, patients should have their full blood count (FBC) and liver function test (LFT) monitored.

# Patient pathway




*Modified FOLFIRINOX and gemcitabine -nab-paclitaxel are considered equivalent in their clinical efficacy (progression -free survival, overall survival, distant metastasis-free survival, response to treatment). The decision to commence modified FOLFIRINOX or gemcitabine-nab-paclitaxel should be made considering patient characteristics and patient choice.

^ Clinicians should refer to the stopping criteria when making decisions about continuing or stopping treatment.

## Governance arrangements

This policy should be used in conjunction with the following service specifications:

- Cancer: Chemotherapy (Adult)

Any provider organisation treating patients with this intervention will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process.

Gemcitabine and paclitaxel albumin must only be used for treatment in specialised centres or in collaboration with specialised centres under the supervision of a multi-disciplinary team.

Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

# Mechanism for funding

Initiation and maintenance of gemcitabine with paclitaxel albumin within the criteria set out in this document will be commissioned and funded by NHS England under existing arrangements for the provision of specialised services.

# Audit requirements

Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined. This information is collected to inform future policy revisions.

## Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

## Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations

between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and

- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

## Definitions

| | |
|---|---|
| Adenocarcinoma | A type of cancer that affects the organs and tissues (glands) that produce hormones and digestive juices. |
| Cancer | Abnormal cells that divide in an uncontrolled way. |
| Central venous access | A thin, soft flexible tube that is placed into a vein in the neck, chest, groin or arms that leads into a blood vessel (vein) in the heart. This is often done to deliver fluids, nutrition and medications, notably chemotherapy. |
| Chemotherapy | A type of cancer treatment where medication is used to kill the cancer cells. Chemotherapy also affects healthy cells and this can cause side-effects, which will vary depending on the type of cell affected. |
| Exocrine glands | Organs that release substances into organs or body surfaces. |
| Jaundice | Yellowing of the skin or the whites of the eyes caused by excess pigment (bilirubin). It is typically caused by disease in the liver, bile duct or excessive breakdown of the red blood cells. |
| Pancreatic cancer | A cancer that starts in the pancreas. The pancreas is part of the digestive system and is a large gland that produces digestive juices, insulin and other hormones to do with digestion. |
| Palliative intent | Treatment that is given to relieve symptoms, rather than targeting the cause of the condition. |
| Performance status | A measure used to quantify patients' general wellbeing and ability to perform activities of daily living. This is used to determine whether it is appropriate certain treatments. |
| Radiotherapy | A treatment where radiation is used to kill cancer cells. There are many different ways radiotherapy can be given, but they all work in a similar way. They damage cancer cells and stop them from growing or spreading in the body. |
| Unresectable | A situation where the tumour or cancer is not able to be removed using surgery |

## References

Cancer Research UK (2023). Pancreatic cancer risks and causes. Available at: https://www.cancerresearchuk.org/about-cancer/pancreatic-cancer/risks-causes. (Accessed 1 November 2024)

Cancer Research UK (no date). Pancreatic cancer statistics. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/pancreatic-cancer#heading-Zero. (Accessed 1 November 2024)

Conroy T, Pfeiffer P, Vilgrain V, et al. (2023). 'Pancreatic Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up,' Annals of Oncology, 34(11), pp. 987-1002. https://doi.org/10.1016/j.annonc.2023.08.009

Macmillan Cancer Support (2023). FOLFIRINOX (or FOLFOXIRI). Available at: https://www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/folfirinox. (Accessed 1 November 2024)

National Cancer Institute: Surveillance, Epidemiology, and End Results Program (2024). Cancer Stat Facts: Pancreatic Cancer. Available at: https://seer.cancer.gov/statfacts/html/pancreas.html. (Accessed 1 November 2024)

Rawla P, Sunkara T, Gaduputi V. (2019). 'Epidemiology of Pancreatic Cancer: global trends, etiology and risk factors,' World Journal of Oncology, 10(1), pp. 10–27. https://doi.org/10.14740/wjon1166.

Tempero M, Malafa MP, Al-Hawary M, et al. (2021). 'Pancreatic Adenocarcinoma, Version 2.2021,' NCCN Clinical Practice Guidelines in Oncology, 19(4), pp. 439-457. doi: 10.6004/jnccn.2021.0017