AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Rituximab as second- or third-line treatment of fibrotic interstitial lung disease (not idiopathic pulmonary fibrosis) associated with connective tissue disease or idiopathic fibrotic non-specific interstitial pneumonia

August 2019

ONE WALES INTERIM COMMISSIONING DECISION

Rituximab as second- or third-line treatment of fibrotic interstitial lung disease (not idiopathic pulmonary fibrosis) associated with connective tissue disease or idiopathic fibrotic non-specific interstitial pneumonia

Date of advice: August 2019

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

Using the agreed starting and stopping criteria, rituximab can be made available within NHS Wales for the second- or third-line treatment of fibrotic interstitial lung disease (not idiopathic pulmonary fibrosis) associated with connective tissue disease or idiopathic fibrotic non-specific interstitial pneumonia.

The rituximab product with the lowest acquisition cost should be chosen for newly initiated patients.

The risks and benefits of the off-label use of rituximab for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the General Medical Council Guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Interim Commissioning decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Interim Commissioning decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice assists consistency of access across NHS Wales.

Start and stop criteria for rituximab as second- or third-line treatment of fibrotic interstitial lung disease (not idiopathic pulmonary fibrosis) associated with connective tissue disease or idiopathic fibrotic non-specific interstitial pneumonia

Start criteria:
Rituximab may be commenced after evidence of progression on azathioprine and/or mycophenlate mofetil following regional interstitial lung disease multi-disciplinary team diagnosis review and treatment recommendation.

Progression is defined as:

- > 10% decline percent predicted forced vital capacity (FVC) on first- or second-line therapy within 12 months; or
- > 15% decline percent predicted transfer factor for carbon monoxide (TLCO) on first- or second-line therapy within 12 months; or
- significant radiological evidence of progression whilst on first- or second-line therapy within 12 months.

Patients who satisfy the start criteria will be prescribed rituximab following consultation with the patient and/or carer taking into account potential adverse effects, cautions and contraindications. This consultation should be recorded in the patient's notes.

The recommended rituximab treatment dose regimen is 1,000 mg rituximab followed by a second 1,000 mg dose two weeks later administered by intravenous infusion. A further 1 g may be offered within the first 12 months and then annually, according to response.

Monitoring:

- Pulmonary function tests every 4–6 months.
- Repeat high resolution CT scan in event of physiological decline.

Stop criteria:
Treatment with rituximab should be discontinued according to one or more of the following definitions of disease progression:

- > 10% decline percent predicted FVC on rituximab therapy within 12 months; or
- > 15% decline percent predicted TLCO on rituximab therapy within 12 months; or
- significant radiological evidence of progression whilst on rituximab therapy within 12 months.

One Wales Interim Commissioning Process
Interim Pathways Commissioning Group (IPCG) summary of decision rationale

Medicine: **rituximab**
Indication: **second- or third-line treatment of fibrotic interstitial lung disease (not idiopathic pulmonary fibrosis) associated with connective tissue disease or idiopathic fibrotic non-specific interstitial pneumonia**
Meeting date: **29 April 2019**

Criteria	IPCG opinion
Clinical effectiveness	IPCG notes that the clinical effectiveness evidence is from open-label controlled studies, a phase II study and retrospective case studies. There are no studies of rituximab to treat idiopathic fibrotic non-specific interstitial pneumonia. IPCG considers that the evidence provided demonstrated clinical effectiveness. IPCG considers that the place in therapy will be for patients with fibrotic interstitial lung disease or idiopathic fibrotic non-specific interstitial pneumonia which does not respond to treatment with conventional corticosteroid and immunosuppressant therapy. Current treatment options for second- and third-line treatment are treatment with cyclophosphamide followed by palliative care. Lung transplant is rarely an option for these patients due to co-morbidities.
Cost-effectiveness	IPCG notes that no cost effectiveness studies have been undertaken. There is insufficient information on resource use and quality of life data to provide cost effectiveness analyses.
Budget impact	IPCG considers that the clinical estimate of patient numbers reported is reasonably accurate. IPCG acknowledges that budget impact estimates are subject to uncertainty. The budget impact is accepted based on the agreed dosing regimen and start/stop criteria. IPCG considers that treatment costs are subject to uncertainty.
Other factors	IPCG accepts that the pathology and treatment of idiopathic fibrotic non-specific interstitial pneumonia are similar to that of fibrotic interstitial lung disease and treatments are likely to be similar.
Final recommendation	IPCG recommends that rituximab is made available for the second- or third-line treatment of fibrotic interstitial lung disease (not idiopathic pulmonary fibrosis) associated with connective tissue disease or idiopathic fibrotic non-specific interstitial pneumonia. This recommendation is subject to the development of appropriate start/stop criteria, using an agreed dosing regimen and choosing a rituximab product with the lowest acquisition cost for newly initiated patients.
Summary of rationale	Although limited, evidence suggests that rituximab is clinically effective in the treatment of interstitial lung disease associated with connective tissue disorders. Due to the similar aetiology and treatment of non-specific interstitial pneumonia, in the absence of direct evidence of efficacy, rituximab is expected to also be of benefit in this patient group.