NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

CAMBRIDGESHIRE AND PETERBOROUGH

JOINT PRESCRIBING GROUP

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What are we bringing to C&P CCG?

A discussion paper on the use of subcutaneous vedolizumab (Entyvio) for licensed indications and to support Recommendation 3 (see below) for the initiation of new patients and switching of existing patients to subcutaneous vedolizumab.

Why is this being brought to C&PCCG?

- Vedolizumab intravenous (IV) infusion is licensed and is recommended by NICE (TA 342 and TA 452) and is in use locally as a biologic used in the treatment of inflammatory bowel disease (IBD: Crohn's `disease (CD) and ulcerative colitis (UC)).
- The first subcutaneous (SC) preparation of vedolizumab (Entyvio® 108mg solution for injection) was authorised for use earlier in the year for been extended to the treatment of adults with Crohn's disease, and ulcerative colitis (the same indications as for intravenous vedolizumab. Entyvio is the only brand of SC vedolizumab currently available.
- Local specialists expressed an interest in using vedolizumab SC including switching existing patients, to avoid attendance at hospital during the COVID-19 pandemic.
- Following a request from CUH specialists, C&PCCG supported CUH undertaking restricted temporary switching of vedolizumab intravenous to subcutaneous in line with specified criteria. This was as an exception during the COVID-19 pandemic, with support for CUH claims for reimbursement from NHS England & NHS Improvement (NHSE/I) against the national COVID-19 funds. However due to the shortage of stock few patients could be switched. Due to a lack of resource, NWAFT, were not able to take part in this programme but are expecting this situation to be remedied in the future. The stock situation has now improved, and stock is now widely available and both CUH and NWAFT are both eager to utilise the new formulation as a means of both reducing the system costs and providing patients with their treatment in their homes thus relieving the hospital clinic burden and increasing patient safety.
- The evidence for SC use is not substantial. Limited trial data suggests that in the short term, efficacy, and safety for the two formulations are similar in the studied cohort for IBD.
  Efficacy outcomes are not available for all indications and use in practice, and extrapolation was used as part of marketing authorisation.

- Drug costs for Entyvio SC are the same as for IV vedolizumab (There is only one formulation available – Entyvio). Maintenance vedolizumab is given as IV infusions so there are both drug and administration activity costs. If administered via SC form, there will be no administration activity costs. The use of SC vedolizumab will result in no additional drug cost pressure but a reduction in overall cost as there will be a reduction and this needs to be considered when estimating the overall cost impact to the health economy.
  Given the desire to treat patients in their homes continues to be a priority for NHSE, then vedolizumab SC remains the most cost-effective option and will result in a cost saving to the system.

Background Information

- IV vedolizumab is given as infusions (300mg) at weeks 0, 2, 6 and then every 8 weeks.
- For new patients, following two IV infusions 2 weeks apart, the recommended dose for SC vedolizumab is 108mg once every 2 weeks starting 4 weeks after the 2nd IV dose.
- When switching from IV maintenance vedolizumab to SC vedolizumab the 1st dose may be administered 8 weeks after the last administration of the IV infusion.
- The only licensed dose for SC vedolizumab is 108mg every 2 weeks.
- Switching suitable patients to SC vedolizumab and starting in new patients who can self-inject could help
  - reduce unnecessary hospital attendances.
  - support capacity problems at providers
  - protect vulnerable individuals from the risk of infection during COVID pandemic (patients on vedolizumab may have been classified as shielders or recommended to self- isolate as a clinically vulnerable group)
  - reduce the risk of infection transmission between people attending clinical facilities.

Proposed Recommendation Options

1. To recommend the use of vedolizumab SC as an option when vedolizumab is indicated in new patients and to support switching of existing patients.
2. Not to recommend the use of vedolizumab SC as an option when vedolizumab is indicated in new patients and not to support switching of existing patients.
3. To recommend the use of vedolizumab SC as an option when vedolizumab is indicated in new patients and to support switching of existing patients from IV to SC.

Evidence of Clinical Effectiveness and Safety

Marketing authorisation for the s.c. formulation of vedolizumab was granted based on the data from two double-blind randomised phase three trials (VISIBLE1 and VISIBLE 2), and one open-label extension study (VISIBLE OLE)

In both double-blinded trials, patients with moderate to severe active disease received two induction doses of vedolizumab 300mg i.v. at weeks zero and two after which clinical response was assessed. Only patients who achieved a clinical response at week six were then randomised to receive s.c.

vedolizumab 108mg every two weeks, placebo or (for VISIBLE 1 only) i.v. vedolizumab 300mg every eight weeks. The total study period of both trials was 52 weeks.

In VISIBLE 1(ulcerative colitis), the primary efficacy endpoint (clinical remission at week 52) was met, with a rate of 14.3% for placebo compared with 46.2% and 42.6% for the s.c. vedolizumab and i.v. vedolizumab respectively (p<0.001).

In VISIBLE 2 (Crohn's disease), the primary endpoint was clinical remission (defined as Crohn's CDAI score ≤150 at week 52). At week 52, 48.0% of patients on vedolizumab versus 34.3% of patients with on placebo were in clinical remission (p=0.008).

Overall, 86.2% of ulcerative colitis patients and 82.6% of Crohn's Disease patients achieved a clinical response after two or three vedolizumab intravenous infusion.

Cost of treatment and Cost Effectiveness

Currently maintenance vedolizumab is given as IV infusions every 8 weeks so there are both drug and administration activity costs. If administered via SC form then patients will be able to receive supplies via homecare arrangements and self-administer, there will be no administration activity costs and the drug cost will remain the same. This amounts to a substantial cost saving for the healthcare system.

Current estimated <u>existing</u> patients:

Trust	No of patients on IV vedolizumab (8 weekly)
CUHFT	75
NWAFT	60
Totals	135

- For any patients switching, additional patient contact (and activity costs) would likely be required in the interim to train on use and monitor tolerance / effectiveness. It is possible that patient reviews are currently undertaken while patients are having IV vedolizumab administered. There may be some costs associated with additional outpatient appointments to undertake reviews of patients on SC treatment.

Current estimated <u>new patients</u> per annum:

Trust	Estimated No of new patients requiring vedolizumab
CUHFT	20
NWAFT	25
Totals	45

Estimate based on GPA's approved between 2018/19 and 2019/20

The needs of the population

- The needs of the population may be high as use of a SC formulation will avoid regular attendance at hospital for repeat infusions and the associated risks during the COVID-19 pandemic (patients on vedolizumab may have been classified as shielders or recommended to self-isolate as a clinically vulnerable group) and reduce the risk of infection transmission between people attending clinical facilities.
- Some patients may prefer self-administering a SC version. Other treatments are available as SC formulations. However, some patients may not be able to administer SC injections.
- Some stable patients may have reservations concerning the risk of switching and potential for destabilising disease control and the limited efficacy and safety data.
- Switching would only occur with the consent of the patient.

The needs of the community

Not all existing patients may be appropriate for, or consent to, a switch and/or patients/carers may be unable to self-administer which will affect cost impact.

The availability of a SC formulation may allow for reduced staffing and healthcare resources associated with infusion clinics and support any capacity problems at providers. This may be particularly relevant during the COVID pandemic. And subsequent continued impact on providers. However, providers would also no longer receive activity costs associated with IV administration.

- For any patients switching, additional patient contact (and activity costs) would likely be required in the interim to train on use and monitor tolerance / effectiveness.
- There may be some costs associated with additional outpatient appointments to undertake reviews of patients on SC treatment.

Equity and Equality

No impact anticipated. Treatment recommendations apply to all adult patients. No differential impact on people with protected characteristics is anticipated. A switch to a SC formulation could be an option for all patients. Some patients could be considered to be disabled and therefore members of a protected equality group under the Equality Act 2010. Approval of vedolizumab SC as an option may have a positive impact for this group. However, some patients/carers may not be able to self-inject due to disability. Appropriateness of medicines for individual patients is a clinical decision by the prescribing clinician. There are many considerations concerning appropriate and safe drug use in pregnancy / breast feeding and standard drug choices may need to be amended depending on the risk/benefit and safety information available. NHS England is the responsible commissioner for children.

Policy Drivers

- All areas considered introducing SC vedolizumab at the start of the pandemic and this has been revisited due to the increase availability of stock

COVID-19 rapid guideline: Rheumatological autoimmune, inflammatory, and metabolic bone disorders - NG167 supports switching patients and states:

Assess whether patients having intravenous treatment can be switched to the same treatment in subcutaneous form.

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COVID-19 rapid guideline: gastrointestinal and liver conditions treated with drugs affecting the immune response - NICE guideline NG172 includes the following:

- When deciding whether to start a new treatment with a drug that affects the immune response, discuss the risks and benefits with the patient or their parents or carers, and
  consider the following in the context of COVID-19:
  - Is it essential to start this drug immediately?
  - If treatment is needed, is there an alternative with a better risk profile?
  - Is the required monitoring and review feasible?
  - Can monitoring be done remotely or at a frequency that minimises the risk to the patient's safety and wellbeing?
  - Is there a route of administration that could make hospital attendance or admission less likely?
- For patients who are already taking drugs that affect the immune response, continue with existing courses of treatment to minimise the risk of a flare-up. Think about whether any changes are needed to minimise face-to-face contact during the COVID-19 pandemic, including:
  - dosage
  - route of administration
  - mode of delivery.

Implementation

Switching would need to be undertaken by the specialist team in consultation with the patient. Implementation would be dependent on adequate homecare capacity.

Comments Received

This paper has been developed with the gastroenterology department at CUH who approve the recommendation.

Conversations have taken place with the pharmacy department at NWAFT who again support the recommendation.

References

NICE COVID-19 rapid guideline: Rheumatological autoimmune, inflammatory and metabolic bone disorders - NG167 , April 2020

NICE COVID-19 rapid guideline: Gastrointestinal and liver conditions treated with drugs affecting the immune response - NG172 , August 2020

Summary of Product Characteristics: Entyvio 108mg solution for injection in pre-filled pen
``https://www.medicines.org.uk/emc/product/11361/smpc

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