Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Eflornithine with sulindac for treating familial adenomatous polyposis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of eflornithine with sulindac within its marketing authorisation for treating familial adenomatous polyposis.

Background

Familial adenomatous polyposis (FAP) is a rare condition that can often run in families, but it can also develop in people who do not have a family history of the condition. FAP causes hundreds or thousands of small growths called polyps to develop in the large bowel. These polyps are not cancerous, but if they are not treated some of them are likely to develop into cancer. If there is a family history of FAP, people will have regular screening from a young age, usually done as a colonoscopy. Classical FAP is characterised by the presence of more than 100 colorectal polyps, while people with attenuated FAP have fewer than 100.[1] Polyps usually appear in people in their teenage years if they have classic FAP, and around 15 years later if they have attenuated FAP.[2] For people with classic FAP, there is a nearly a 100% risk of progression to colorectal cancer by 40 years of age if no treatment has been given.[1] People with FAP may have symptoms including blood or mucus in their stools, diarrhoea or constipation, pain in the abdomen or rectum, and unexplained weight loss.[3]

The estimated prevalence of FAP is around 3 people per 100,000 in England.[4] Based on current population estimates for England and Wales (2019) this equates to a population size of 1784.[5] It is estimated that 1% of bowel cancers are linked to FAP.[3] There were 23,243 registrations of newly diagnosed cases of bowel cancer in England in 2017, which would equate to around 233 cases linked to FAP.[6]

The only preventative treatment available for FAP is surgery to remove the colon and sometimes the rectum. After surgery, people may need to go to the toilet more often, and may need to have a stoma (an opening in the abdomen allowing faeces to be collected in a bag). NICE clinical guideline 118 recommends colonoscopic surveillance for people who have had adenomas removed. It suggests that the surveillance strategy (time delay until a colonoscopy is offered) should depend on the risk of developing colorectal cancer as determined by the number and size of adenomas initially removed.

The technology

Eflornithine in combination with sulindac (CPP-1X/sul, Cancer Prevention Pharmaceuticals) comprises of a difluoromethylated ornithine compound,

eflornithine, and a sulfinylindene derivative prodrug, sulindac. Eflornithine inhibits an enzyme called ornithine decarboxylase, slowing the growth of polyp cells and the formation and spread of tumour cells. Sulindac works by activating the spermidine/spermine N(1)-acetyltransferase (SSAT) enzyme that is expected to reduce polyamine levels in the intestine, reducing cell growth and improving symptoms. Both eflornithine and sulindac are administered orally.

Eflornithine in combination with sulindac does not currently have a marketing authorisation in the UK for treating familial adenomatous polyposis. It has been studied in clinical trials in combination with sulindac compared with both eflornithine and sulindac monotherapy in adults with classical FAP with disease involvement of the duodenum and/or colon/rectum/pouch. It has also been studied in combination with sulindac compared with placebo for the prevention of colorectal cancer in people with colon polyps aged between 40 and 80 years.

Intervention(s)	Eflornithine in combination with sulindac
Population(s)	People with familial adenomatous polyposis who have an intact colon, rectum or pouch
Comparators	Established clinical practice without eflornithine in combination with sulindac including: • best supportive care.
Outcomes	The outcome measures to be considered include: • time to FAP-related event • reduction in surgery • change in bowel habit • mortality • pain • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

Appendix B

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Guidelines: 'Colorectal cancer prevention: colonoscopic surveillance in adults with ulcerative colitis, Crohn's disease or adenomas' (2011) NICE clinical guideline 118. Review date TBC. Related Interventional Procedures: 'Combined endoscopic and laparoscopic removal of colonic polyps' (2014) NICE interventional procedures guidance 503 'Computed tomographic colonography (virtual colonoscopy)' (2005) NICE interventional procedures guidance 129 'Endoscopic full thickness removal of non-lifting colonic polyps' (2017) NICE interventional procedures guidance 580 Related Diagnostics Guidance: 'Virtual chromoendoscopy to assess colorectal polyps during colonoscopy' (2017) NICE diagnostics guidance 28
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) (chapter 110, Specialist gastroenterology, hepatology and nutritional support services for children) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Appendix B

Questions for consultation

How is familial adenomatous polyposis diagnosed in clinical practice? Which treatments are considered to be established clinical practice in the NHS for familial adenomatous polyposis?

Is eflornithine or sulindac monotherapy used off-label in the NHS to treat familial adenomatous polyposis in clinical practice?

Where does eflornithine with sulindac fit in the treatment pathway for familial adenomatous polyposis? How are treatment decisions affected by the stage of familial adenomatous polyposis?

In clinical practice what is considered to be a FAP-related event? How does this relate to treatment decisions?

Should best supportive care be included as a comparator? If so, how would best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom eflornithine with sulindac is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Will people aged under the age of 18 years be treated with eflornithine with sulindac? Is there any evidence to suggest its efficacy in people aged under 18 years?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for whom eflornithine will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Appendix B

Do you consider eflornithine with sulindac to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of eflornithine with sulindac can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. BMJ Best Practice. Familial adenomatous polyposis syndromes. Accessed: July 2020
2. Genetics Home Reference. Familial Adenomatous Polyposis. Access: July 2020
3. Macmillan Cancer Support. Familial Adenomatous Polyposis (FAP). Accessed: July 2020
4. Genomics Education Programme. Familial Adenomatous Polyposis. Accessed: July 2020
5. Office for National Statistics. Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2019. Accessed: July 2020
6. Office for National Statistics. Cancer Registration Statistics, England, 2017. Accessed: July 2020