NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Consideration of consultation responses on review proposal

Review of TA211; Prucalopride for the treatment of chronic constipation in women

This guidance was issued December 2010 with a review date of October 2013.

Background

At the GE meeting of 22 October 2013 it was agreed we would consult on the review plans for this guidance. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

Proposal put to consultees:	TA211 guidance for women should be placed on the static list. We should consult on this proposal. An appraisal in men should be considered in topic selection for referral as an STA.
Rationale for selecting this proposal	The few new studies available on the long-term safety and efficacy of prucalopride in women will not change the recommendations. The TA211 guidance should therefore be transferred to the static list. The remit of TA211 is for chronic constipation in women, and would need to be expanded to include the planned marketing authorisation extension for prucalopride [redacted] should be considered in topic selection for referral as an STA.

GE is asked to consider the original proposal in the light of the comments received from consultees and commentators, together with any responses from the appraisal team. It is asked to agree on the final course of action for the review.

Recommendation post consultation:	TA211 guidance for women should be placed on the static list. An appraisal in men should be considered in topic selection for referral as an STA.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
British Society of Gastroenterology	Agree	1. The literature identified since TA2011 is appropriate. 2. The decision to move prucalopride to the static list is supported by the data presented. 3. The last line of page 2 is a bit confusing: the efficacy of prucalopride vs placebo is in chronic constipation: it is in the next sentence after opioid induced constipation (OIC) and can be misread as prucalopride being indicated for OIC. 4. There is no mention of the overlap between chronic constipation and IBS-C: I think it would be important to state that there is no evidence to support the use of prucalopride in IBS-C. Otherwise I think the document is reasonable.	Comments noted.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Bladder and Bowel Foundation	Disagree	The Bladder & Bowel Foundation are aware of callers to our clinical helpline reporting feelings of frustration because they cannot access Prucalopride without first failing 6 months of treatment on at least two alternative first line laxatives. Many long term sufferers have been on numerous laxatives for years (over the counter and prescription) and would deem that they have failed to restore their bowel function. Sadly in practice the recommendation above results in GP's re-prescribing two alternative laxatives for 6 months prior to reassessing suitability for Prucalopride – this is very difficult for those who have been 'off laxatives' for a period of time as 'nothing worked' or that 'the side effects of high doses were intolerable'. The thought of repeating the medication for 6 months in order to be considered for Prucalopride is off-putting. Could the wording of the recommendation be altered to highlight that an individual must have been prescribed two alternative first line treatments from different classes before being considered for Prucalopride.	Comment noted. This was considered by the Committee in sections 4.3 and 4.4 of the final guidance: "4.3. ….The Committee heard from the clinical specialists that it is often difficult to differentiate between people for whom laxatives do not provide adequate relief and those who no longer want to use laxatives because of the side effects, despite any treatment benefit they may achieve. Based on advice from the clinical specialists, the Committee concluded that inadequate relief from previous laxative treatments could be defined by duration of follow-up and by the number of laxatives previously used." "4.4 …..The Committee also heard from the clinical specialists that people whose constipation has not responded adequately to laxatives would usually be encouraged to stop all current treatments and then restart their laxative regimen in a stepwise manner." No changes to the TA211 guidance required
Association for Continence Advice	Agree	Having reviewed your proposal ACA agree that this would be appropriate.	Comment noted.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
United Kingdom Clinical Pharmacy Association	Agree	The UKCPA supports the decision to move this guidance to the static list till further evidence is available particularly for the use in the male populations. No additional evidence not mentioned has been identified by the UKCPA.	Comment noted.
Association of Coloproctology of Great Britain and Ireland	Agree	**Comments on the guidance** The review of the current guidance is accurate. The current recommendations have been in place for nearly three years and seem to be working in clinical practice. There is continued uncertainty amongst the medical community relating to the phrasing in section 1.3 of the guidance which states that “Prucalopride should only be prescribed by a clinician with experience of treating chronic constipation….” It is unclear whether this statement suggests someone with specialist secondary care expertise, or whether a GP who has treated numerous patients with constipation would also fulfil these criteria. I doubt however that there is an urgent need to produce clarification on this at this point. With regard to new data, I am aware of three studies conducted which have yet to report. Study 401 is a longer term study looking at 24 week use. There is also a paediatric study which is also mentioned in your report. I would agree	Comments noted.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
		with the conclusions of your report that neither of these studies is likely to change the current recommendations. I believe the findings of the male study are important and could lead to a change in the licence application. Certainly, as a clinician, it seems incongruous to me that I can prescribe the drug to one patient but not to another just because of gender. The mechanism of constipation is likely to be the same as is the mechanism of action of the drug. Having said that, the analysis of this trial is not expected until the spring 2014 and the license application will go to the EMA and take several months to process. Taking all the above into account, I would feel that it is quite reasonable for this guidance to be moved to the static list as suggested.	

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Royal College of Nursing	Agree	The RCN notes the proposal to move the guidance to the static list because no new evidence has been identified that would lead to a change in the existing recommendations. . We have also been unable to find any new in vivo studies of prucalopride but found a study of in vitro synergistic effects of prucalopride and Cholinesterase inhibitors. We therefore, support the proposal to move the existing guidance to the static list of technology appraisals.	Comments noted.
Shire	Agree	We agree that there is currently no new or clinically meaningful evidence that would lead to a material change to the current recommendation so the move to the static list is supported by Shire. We would however want to initiate a discussion with your team once we have the male study data available and may seek at that time to transfer TA211 back to the active list.	Comments noted. Guidance placed on the 'static guidance list' remains in place. The guidance can be considered for review at any point if NICE becomes aware of substantive information which would make it reconsider.
Medicines and Healthcare Products Regulatory Agency	No comment	We are not aware of any new information that impinges on NICE recommendations issued in December 2010.	Comment noted.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Royal College of Physicians	Agree	The RCP wishes to endorse the comments submitted by the BSG.	Comment noted.

No response received from:

Patient/carer groups

- Action on Pain
- Afiya Trust
- Black Health Agency
- Equalities National Council
- Men's Health Forum
- Muslim Council of Britain
- Muslim Health Network
- Pain Concern
- Pain Relief Foundation
- Pain UK
- PromoCon
- South Asian Health Foundation
- Specialised Healthcare Alliance
- The IBS Network
- Wellbeing of Women
- Women's Health Concern

Professional groups

- British Geriatrics Society
- Primary Care Society for Gastroenterology

General

- Allied Health Professionals Federation
- Board of Community Health Councils in Wales
- British National Formulary
- Care Quality Commission
- Commissioning Support Appraisals Service
- Department of Health, Social Services and Public Safety for Northern Ireland
- Healthcare Improvement Scotland
- National Association of Primary Care
- National Pharmacy Association
- NHS Alliance
- NHS Commercial Medicines Unit
- NHS Confederation
- Scottish Medicines Consortium

Comparator manufacturers

- Abbot Laboratories UK (lactulose)
- Actavis UK (glycerol suppositories)
- Almirall (linaclotide)
- Bio-Health (psyllium husk)

• Royal College of General Practitioners • Royal College of Pathologists • Royal Pharmaceutical Society • Royal Society of Medicine <u>Others</u> • Department of Health • NHS Bromley CCG • NHS England • Powys Teaching Health Board • Welsh Government	• Boehringer Ingelheim (bisacodyl suppositories and tablets, docusate, macrogol, sodium picosulfate) • B R Pharmaceuticals (senna) • Cardinal Health Martindale Products (glycerol suppositories, bisacodyl suppositories) • Casen Fleet Laboratories (sodium dihydrogen phosphate dihydrate/disodium hydrogen phosphate dodecahydrate enema) • Chanelle Medical (biscodyl, macrogol) • Dr. Reddy's Laboratories UK (bisacodyl) • Forest Laboratories (phosphates enema, arachis oil enema, docusate enema) • Galen (macrogol, dantron, dantron/docusate sodium, senna) • Hermal (formerly Reckitt Benckiser) (ispaghula husk, glycerol suppositories, senna) • Intrapharm Laboratories (lactulose) • Kent Pharmaceuticals (glycerol suppositories, bisacodyl suppositories and tablets, lactulose, dantron, senna, dantron/docusate sodium) • Lanes Health (senna) • Manx healthcare (ispaghula husk) • Meda Pharmaceuticals (macrogol) • Merck Consumer Healthcare (senna) • Mylan (lactulose) • Napp Pharmaceuticals (dantron) • Norgine Pharmaceuticals (sterculia/frangula, macrogol, docusate sodium enema) • Novartis Consumer Health UK (lactulose, senna) • Perrigo (bisacodyl, senna) • Pinewood Healthcare (sodium citrate enema, dantron)

	• Potter's Herbal Medicines UK (psyllium husk, senna) • Procter & Gamble Health and Beauty Care (ispaghula husk) • Sandoz (lactulose) • Solvay Healthcare (lactulose) • Teva UK (glycerol suppositories, lactulose, senna, dantron, docusate sodium) • Thornton & Ross (glycerol suppositories, macrogol, magnesium hydroxide, senna) • Typharm (docusate) • UCB Pharma (sodium citrate enema, docusate) <u>Relevant research groups</u> • CORE (Digestive Disorders Foundation) • Health Research Authority • MRC Clinical Trials Unit • National Institute for Health Research • Research Institute for the Care of Older People <u>Assessment Group</u> • Assessment Group tbc • National Institute for Health Research Health Technology Assessment Programme <u>Associated Guideline Groups</u> • None <u>Associated Public Health Groups</u> • Public Health England • Public Health Wales NHS Trust

GE paper sign-off: Frances Sutcliffe, Associate Director – Technology Appraisals Programme

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6 December 2013