National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Ertugliflozin combination therapy for treating type 2 diabetes

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	AstraZeneca	Yes.	Comment noted
	Janssen	This topic is appropriate	Comment noted
	MSD	Yes	Comment noted
	Novo Nordisk	Whilst we understand that NICE does not want to create differential access and funding requirements for products within the SGLT2 class, it should be considered whether a full appraisal is needed given this is a 4th in class SGLT2, and whether there may be abbreviated methods of appraisal that may be more appropriate.	Thank you for your comment. NICE agrees that a cost comparison for monotherapy and dual therapy would be appropriate.
Wording	AstraZeneca	Yes.	Comment noted
	Janssen	Wording is appropriate	Comment noted

Section	Consultee/ Commentator	Comments [sic]	Action
	MSD	No, dual therapy should be appraised as a fast track appraisal (FTA) and not a single technology appraisal (STA). Ertugliflozin in dual therapy fulfils the criteria for an FTA: • It provides similar or greater health benefit to NICE approved treatments for the same indication. • It has similar or lower costs compared to NICE approved treatments for the same indication. • It can be compared to the treatments approved in NICE TAs 288, 315 and 336. Ertugliflozin dual therapy should be appraised under the new FTA cost comparison process.	Thank you for your comment. NICE agrees that a cost comparison for monotherapy and dual therapy would be appropriate.
Timing Issues	AstraZeneca	We believe that ertugliflozin will be available in early 2018.	Comment noted
	Janssen	No Comments	Noted

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AstraZeneca	It is adequate.	Comment noted
	Janssen	No Comments	Noted
	MSD	It is accurate	Comment noted
	AstraZeneca	No. Having searched the clinicaltrials.gov website, there are no trials, ongoing or completed, which examine the use of ertugliflozin	The scope has been updated.

Section	Consultee/ Commentator	Comments [sic]	Action
The technology/ intervention		in combination with insulin. The "…and/or insulin" should be deleted from the end of the sentence regarding the technology	
	Janssen	No Comments	Noted
Population	AstraZeneca	The "…with or without insulin" would need to be removed from the population for the same reason as stated above in the technology/intervention section.	The scope has been updated.
	Janssen	No Comments	Noted
	MSD	Yes, the dual therapy (Metformin with Ertugliflozin) and triple therapy (Metformin with dipeptidyl peptidase-4 (DPP-4) and Ertugliflozin) have been defined appropriately. There are no groups within the dual and triple therapy populations that should be considered separately	Comments noted
Comparators	AstraZeneca	Yes.	Comment noted
	Janssen	**Dual Therapy** In dual therapy for the combination of ertugliflozin and metformin, the comparators should be expanded to include: • GLP-1 analogues (with metformin) This would be consistent with other scopes for SGLT-2 inhibitors, namely, TA 288, 315 and 336. In dual therapy for the combination of ertugliflozin and sulfonylurea, the comparators should be expanded to include: • GLP-1 analogues (with sulfonylurea)	Comments noted. The comparators listed in the draft scope are based on the recommendations in NG28 Type 2 diabetes in adults: management. The recommendations for pharmacological management of blood glucose levels have been updated since the publication of other scopes for SGLT-2 inhibitors such as TA288, TA315

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		This would be consistent with other scopes for SGLT-2 inhibitors, namely, TA 288, 315 and 336. **Triple therapy** In triple therapy, for the combination of ertugliflozin, metformin and a sulfonylurea, the comparators should be expanded to include: • insulin (with metformin and a sulfonylurea) This would be consistent with other scopes for SGLT-2 inhibitors, namely, TA 288, 315, 336 and 418. For the combination of ertugliflozin, metformin and a pioglitazone, the comparators should be expanded to include: • DPP-4 inhibitors (with metformin and pioglitazone) • GLP-1 analogues (with metformin and pioglitazone) • insulin (with metformin and pioglitazone). This would be consistent with other scopes for SGLT-2 inhibitors, namely, TA 288, 315, 336 and 418. Please note that the individual SGLT-2 inhibitors have different contraindication profiles with pioglitazone. Triple therapy should also include the use of ertugliflozin in any other triple therapy regimen and the comparator should be: • Insulin (alone or in combination with one or more oral anti-diabetic agents) This would be consistent with other scopes for SGLT-2 inhibitors, namely, TA 288, 315, 336 and 418.	and TA336, therefore the comparators will differ.

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	MSD	In technology appraisals 288, 315, 336 and TA418, it was concluded that the most appropriate comparators for sodium-glucose cotransporter-2 (SGLT-2s) were other SGLT-2s and DPP-4s. The list of comparators should reflect this.	Comment noted. The comparators listed in the draft scope are based on the recommendations in NG28 Type 2 diabetes in adults: management. The recommendations for pharmacological management of blood glucose levels have been updated since the publication of other scopes for SGLT-2 inhibitors such as TA288, TA315 and TA336, therefore the comparators will differ. The SGLT-2 and DPP-4 inhibitors are currently included as part of the listed comparators.
Outcomes	AstraZeneca	We do not believe that currently available data for this technology will be able to inform on the outcome measures of mortality or complications of diabetes including cardiovascular, renal and eye.	Comment noted. The outcomes listed include longer term outcomes such as mortality and complications as these are listed as secondary outcomes in some trials (for example the VERTIS CV study includes time to cardiovascular death and time to stroke as secondary outcome measures). The outcomes listed in the scope are examples of clinically relevant outcomes but

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			analysis of these will depend on the availability of data.
	Janssen	For consistency with previous scopes for SGLT-2 inhibitors, outcomes to be measured should include weight change and if evidence allows baseline HbA1c.	Comment noted. Change in weight is included as part of the outcome 'body mass index' and is in line with outcomes listed in more recent scopes for other SGLT-2 inhibitors (for example TA390 and TA418).
	MSD	Yes	Comment noted
Economic analysis	Janssen	No Comments	Noted
	MSD	For dual therapy a cost comparison analysis should be conducted as part of a fast track appraisal (FTA) rather than a cost-utility analysis as part of a single technology appraisal (STA). Ertugliflozin is likely to provide similar or greater health benefits at similar or lower cost than the other SGLT-2s already recommended in technology appraisal (TA) 288, 315 and 336 for the same indication. We propose that triple therapy (metformin with DPP-4 and Ertugliflozin) should be assessed by an STA.	Thank you for your comment. NICE agrees that a cost comparison for monotherapy and dual therapy would be appropriate.
Equality	MSD	We have not identified any equality issues	Comment noted
Innovation	AstraZeneca	Three other SGLT-2 inhibitors are currently available and recommended by NICE.	Comment noted

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		We are not aware of benefits beyond the QALY calculation for this technology.	
	Janssen	No Comments	Noted
	MSD	Ertugliflozin adds an additional treatment choice in the SGLT-2 inhibitor class. The SGLT2 inhibitor class provides adults with type 2 diabetes with an additional oral treatment option. The SGLT2 mechanism of action removes excess glucose, providing clinically significant glucose reduction alongside decrease in blood pressure and weight loss.	Comment noted
Other considerations	Janssen	No Comments	Noted
	MSD	None	Noted
Questions for consultation	Janssen	No Comments	Noted
	MSD	As noted above MSD feels that dual therapy should be assessed via the new fast track appraisal (FTA) process. Ertugliflozin fulfils the criteria for an FTA of being likely to provide similar or greater health benefits at similar or lower cost than the other SGLT-2s already recommended in TA 288, 315 and 336 for the same indication.	Thank you for your comment. NICE agrees that a cost comparison for monotherapy and dual therapy would be appropriate.
Additional comments on the draft scope	Janssen	No Comments	Noted

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Department of Health and Social Care, Sanofi, Pfizer