Deucravacitinib for treating moderate to severe plaque psoriasis

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Technology appraisal committee B 14th December 2022

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NICE National Institute for Health and Care Excellence

Background on plaque psoriasis

Causes

- Inflammation of the skin caused by overactivity of parts of the immune system
- Causes accelerated rate of cell turnover and accumulation of skin cells on the epidermis (outer skin layer)
- These can be flaky, scaly, itchy and red and usually occur on the scalp, elbows, limbs and trunk and

Epidemiology

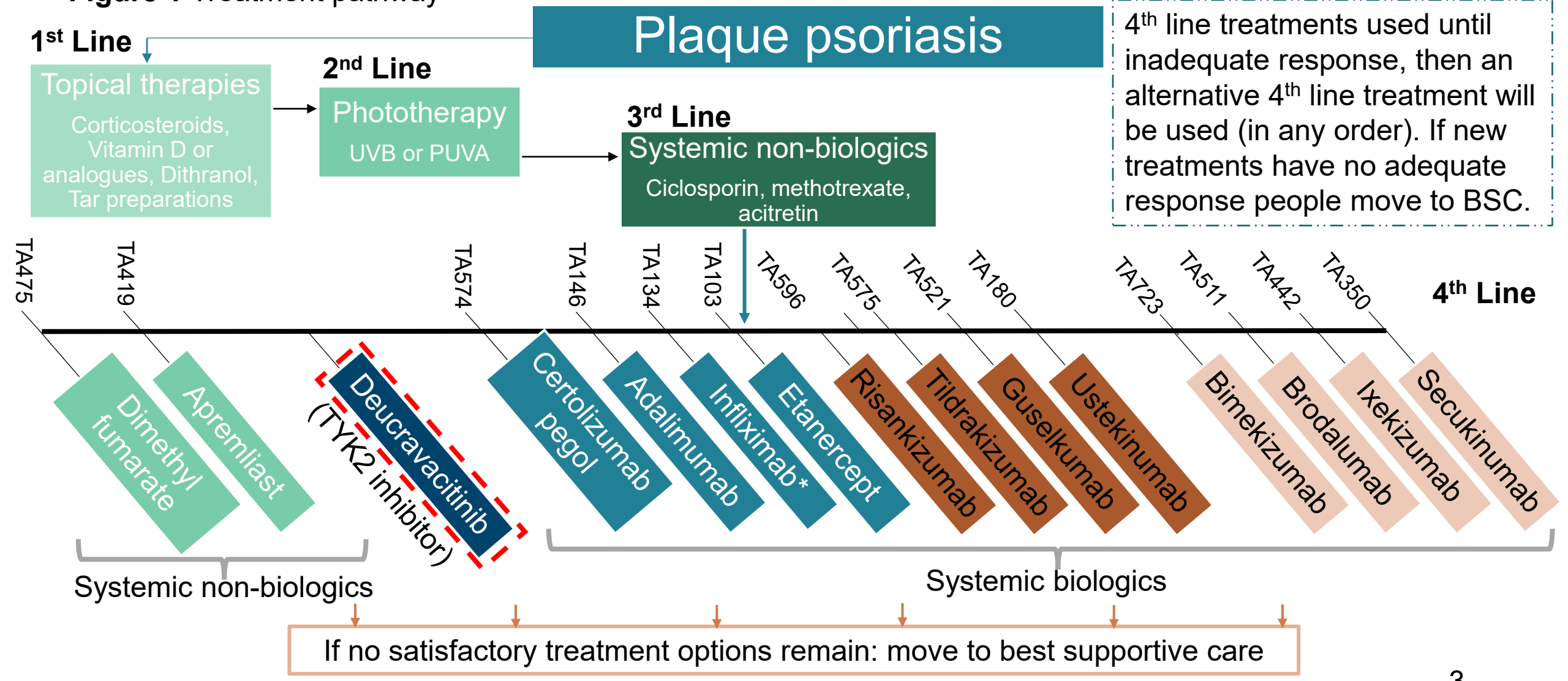
- Prevalence is thought to be between 1.3% and 2.2% in the United Kingdom
- About 20% of people with plaque psoriasis have moderate (15%) to severe (5%) disease equating to approximately 104,000 to 176,000 adults in the UK

Diagnosis and classification

- Plaque psoriasis is generally graded using the psoriasis area and severity index (PASI) which is a measure of skin redness, thickness and scaling as well as how much skin surface is affected *(scored 0 to 72)*
- Severe disease is usually classified as having a PASI score of 10 or more or sPGA 4-5
- The static physicians global assessment (sPGA) considers overall redness, thickness and scaling but does not take into account the extent of the affected skin surface *(scored 0 to 5)*
- The dermatology life quality index (DLQI) assesses the effect of psoriasis on quality of life *(0 to 30)*
- For the measures above, higher scores represent worse outcomes
- The PASI uses various response thresholds for example the “PASI75” is a 75% improvement in PASI score
- Adequate response to fourth line psoriasis treatments is generally defined as attainment of PASI75, or PASI50 with a 5 point reduction in DLQI

Plaque psoriasis treatment options in adults

Figure 1 Treatment pathway



Abbreviations: UVB, ultra-violet B therapy; PUVA, Psoralens and ultra-violet A therapy; TYK2, tyrosine kinase 2 *Infliximab only for v severe disease only Tumour necrosis factor alpha inhibitors Interleukin 23 inhibitors Interleukin 17 inhibitors

Patient perspectives

Submissions from Psoriasis and Psoriatic Arthritis Alliance (PAPAA) and Psoriasis Association

- Severe plaque psoriasis often impacts sleep, work and social aspects of life
- The highly visible nature of the disease can in particular affect social life and relationships and mental health
- People can develop coping mechanisms such as avoiding social situations
- The condition can be isolating and lonely which can in turn lead to habits such as alcohol and drug use or lack of exercise

"Whilst I was at college and university it really got me down and caused depression and made it difficult to focus"

- There is an increased positivity towards newer therapies however there is also anxiety about treatment failure and a lack of alternatives
- Initial elation when a new treatment works to reduce symptoms can give way to low emotions if treatment stops working
- People need access to a range of appropriate treatments that are reliable in the long term

"I've lost all confidence in myself and hate the skin I'm in, making intimacy too painful"

"adding an alternate targeted therapy is seen as an advantage and complements the existing treatment range. . . "

Clinical perspectives Submissions from British Association of Dermatologists

Unmet need

- Currently, biologic therapy is limited to those with a PASI score of 10 or more, this excludes those with moderate disease or those with severe disease in limited areas, both groups who have a substantial impact on their QoL.

Benefits of deucravacitinib

- Deucravacitinib would offer another agent with a novel mode of action (TYK2 inhibitor), this would offer a new treatment option for when others have failed
- It could also provide motivation to drive down prices for biological drugs in general in this market, reducing costs to the NHS
- The tolerability and side effects profile based on phase 3 studies are reassuring and unlikely to impact drug use

*"Existing therapies, while effective for many, do not work for **all** those requiring treatment"*

Challenges with assessing psoriasis

- The PASI may underestimate disease severity in people with brown or black skin as redness may be less evident
- The DLQI underestimate the impact in people who are not sexually active, older or socially isolated

Abbreviations: PASI, psoriasis area severity index; DLQI, dermatology life quality index; TYK2, tyrosine-kinase 2; QoL, quality of life;

Key issues

The EAG identified three key issues in the submission

Table - Key issues and issues resolved at technical engagement

Issue	Resolved?	ICER impact
BSC and non-responder costs	No – for discussion	Moderate
Resolved Issues / Other uncertainties		
Application of drug acquisition costs	Partly	Small
Best supportive care (BSC) utility (baseline or response based)	Yes	Moderate
Pooling of PASI utility values from POETYK with those from previous appraisals	Yes	Small

 Abbreviations: EAG, external assessment group; ICER, incremental cost-effectiveness ratio; BSC, best supportive care

Deucravacitinib (Bristol Myers Squibb)

Table - Technology details

Marketing authorisation	• "[redacted]" • Not yet granted
Mechanism of action	• A small molecule allosteric inhibitor of the TYK2 enzyme • Reduces downstream pro-inflammatory signalling of IL-23, IL-12 receptors which in turn reduces inflammatory response which leads to psoriatic plaques
Administration	• Oral administration, 6mg taken once daily
Price	• List price [redacted] (28 tablets) • PAS discount results in a PAS price of [redacted]

NICE Abbreviations: TYK2, tyrosine-kinase 2; IL, interleukin; PAS, patient access scheme

Decision problem

Table - Population, intervention, comparators and outcomes from the scope

	Final scope	Company	EAG comments
Population	Adults with moderate-to-severe plaque psoriasis	Adults with moderate-to-severe plaque psoriasis for whom systemic non-biologic treatment or phototherapy is not an option	"Overall, the population addressed in the submission is considered appropriate"
Intervention	Deucravacitinib	As per scope	N/A
Comparators	- Systemic non-biological therapies - Phototherapy with or without psoralen - TNF alpha, IL-17, 23 and 12 inhibitors - Apremilast, dimethyl fumarate and BSC	Company compared against biologics, apremilast and dimethyl fumarate (excluded phototherapy, other non-biologics and BSC) Company stated infliximab was not a comparator, as only for very severe disease.	The EAG considered that deucravacitinib is likely to be used fourth line and that the comparators addressed by the company are appropriate.
Outcomes	Severity of psoriasis, psoriasis symptoms, mortality, response rate, relapse rate, adverse effects, HRQoL	Included all but relapse rate (not in trial) and mortality (not expected to be different to general population)	Considers the outcomes to be appropriate for addressing the topic of this appraisal.

NICE Abbreviations: TNF, tumour necrosis factor; IL, interleukin; HRQoL, health related quality of life; BSC, best supportive care

Clinical effectiveness

- POETYK-PSO-1
- POETYK-PSO-2
- POETYK-PSO-LTE

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Key clinical trials

Two randomised controlled trials followed by one open label extension

Table - Clinical trial designs and outcomes

	POETYK-PSO-1 & POETYK-PSO-2
Design	Double blind phase 3 RCTs
Population	People with moderate-to-severe plaque psoriasis (sPGA of 3 or more, BSA over 10% and PASI 12 or more) [Note, severe disease is classified as PASI 10 or more]
Intervention	Deucravacitinib 6mg daily
Comparator(s)	Placebo and apremilast (30mg twice daily)
Duration	52 weeks (16 weeks placebo controlled) + POETYK-PSO-LTE long term single arm rollover study
Primary outcome	PASI 75 response & sPGA response
Key secondary outcomes	Adverse effects, different PASI response thresholds, DLQI, EQ-5D-3L, PSSD score, ss-PGA, PGA-F
Locations	Multi-centre international
Used in model?	Yes POETYK-PSO-1 & 2 outcomes: PASI threshold response rates, AEs of interest and EQ-5D-3L

Abbreviations: RCT, randomised controlled trial; PASI, psoriasis area severity index; sPGA, static physicians global assessment; DLQI, dermatology life quality index; PSSD, psoriasis signs and symptoms diary; PGA-F, physicians global assessment of fingernail psoriasis AE, adverse events;

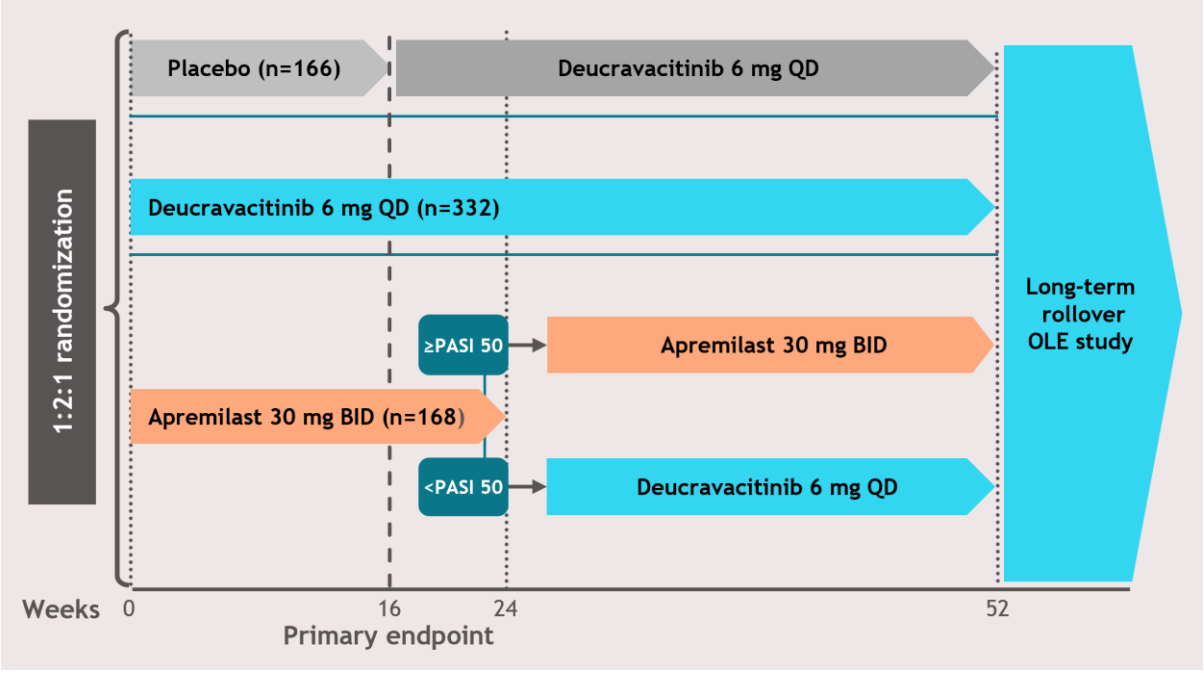
Trial study design
POETYK-PSO trials were placebo controlled for 16 weeks

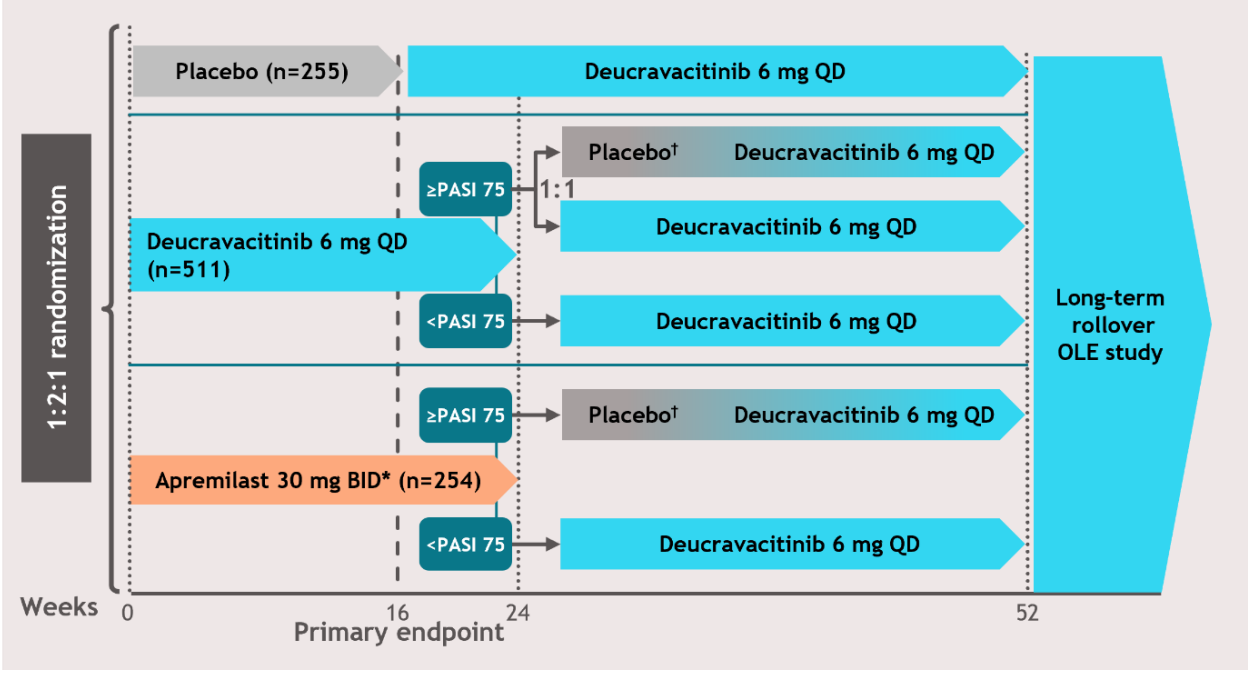
POETYK-PSO-1 trial design (N= 666)

- Placebo controlled to week 16 (then switch to deucravacitinib)
- Apremilast controlled to week 24 when those with PASI below 50 switch to deucravacitinib
- Those with PASI above 50 stay on apremilast

POETYK-PSO-2 trial design (N=1020)

- Placebo controlled until week 16 (then switch to deucravacitinib
- Apremilast controlled to week 24 when those with PASI below 75 switch to deucravacitinib
- Those with PASI 75 or above move to placebo before being phased onto deucravacitinib





Abbreviations: OLE, open label extension; PASI, psoriasis area severity index; QD, daily; BID, twice daily

Clinical trial results – POETYK-PSO-1 and 2 pooled efficacy results

Table – Clinical trials primary results (efficacy)

Outcome		Deucravacitinib (N=843)	Placebo (N=421)	Apremilast (N=422)
PASI75 (week 16)	n, %	[redacted]	[redacted]	[redacted]
	Odds Ratio	-	[redacted]	[redacted]
sPGA 0/1 (week 16)	n, %	[redacted]	[redacted]	[redacted]
	Odds Ratio	[redacted]	[redacted]	[redacted]

Pooled PASI75 response

Pooled sPGA 0/1 response

Deucravacitinib (n=843) Placebo (n=421) Apremilast (n=422)

NICE Abbreviations: PASI, psoriasis area severity index; sPGA, static physician's global assessment

Clinical trial results – POETYK-PSO-1 and 2 pooled efficacy results

Table – Clinical trials key secondary efficacy results

Type	Outcome	Odds ratio (95%CI) versus placebo	Odds ratio (95%CI) versus apremilast
Secondary outcomes	PASI90 (week 16)	[redacted]	[redacted]
	PASI90 (week 24)	n/a	[redacted]
	PASI100 (week 16)	[redacted]	[redacted]
	PASI100 (week 24)	n/a	[redacted]
	sPGA 0 (week 16)	[redacted]	[redacted]
	sPGA 0 (week 24)	n/a	[redacted]

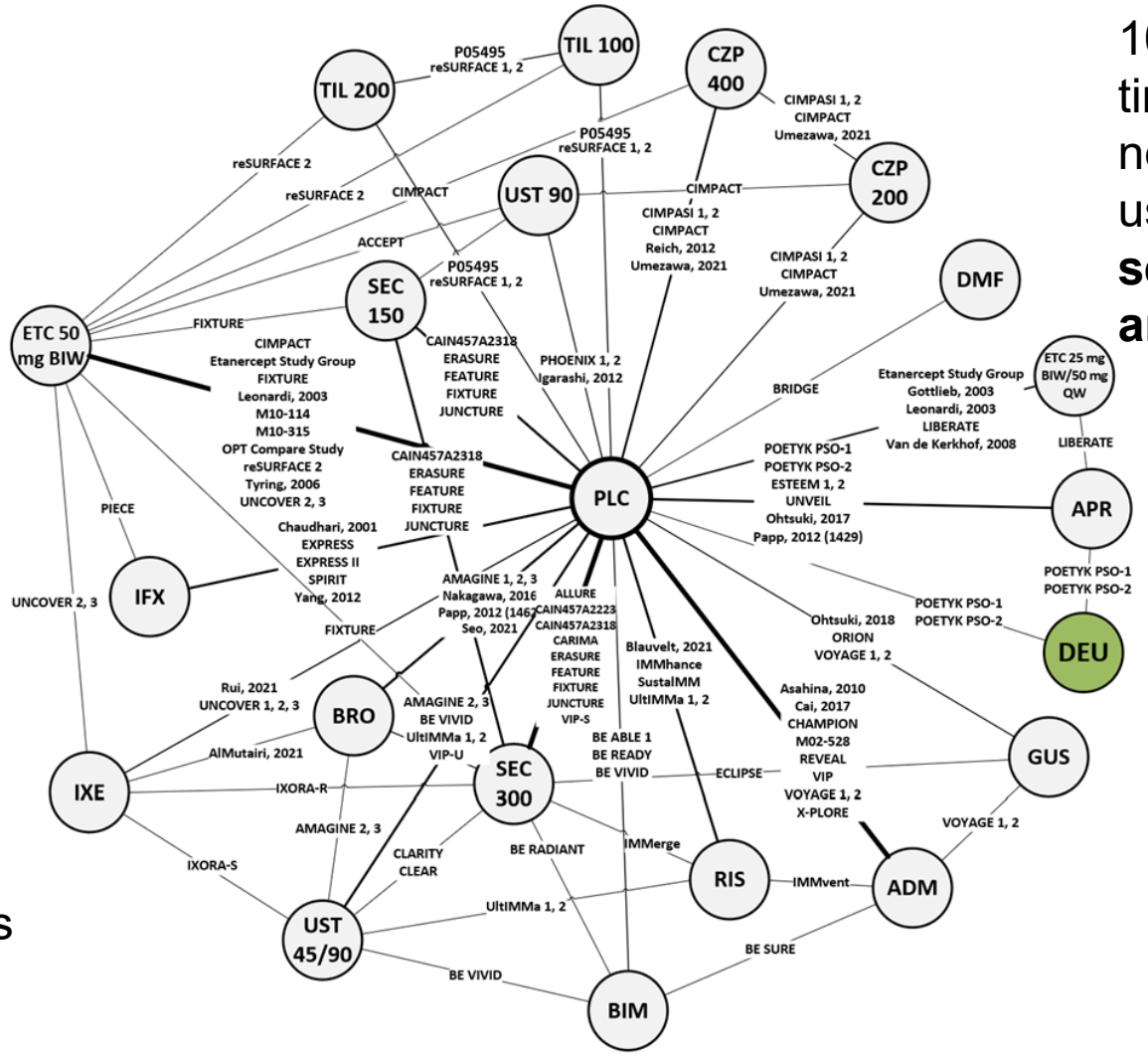
- Adverse events were [redacted] between the deucravacitinib and apremilast groups at 16 weeks in a controlled safety pool
- A "phase 3 safety pool" showed that adverse events for deucravacitinib at 52 weeks were similar to those observed at 16 weeks.

NICE Abbreviations: PASI, psoriasis area severity index; sPGA, static physician's global assessment

NMA/ITC network diagram(s) – 10 – 16 week time point

- Multinomial model NMAs on categories of 50%, 75% 90% and 100% PASI responses
- These responses were analysed at three different timepoints: (10-16 weeks, 24-28 weeks and 44-60 weeks)
- Both fixed and random effect models were fitted with adjustment for baseline risk

EAG: The model is appropriate and is consistent with either the models used or the EAG preferred models in five previous cost-utility analyses in this disease area



10-16 week timepoint network (as used in **sensitivity analysis 1**)

Abbreviations: ADM = adalimumab; APR = apremilast; BIM = bimekizumab; BIW = twice weekly; BRO = brodalumab; CZP = certolizumab pegol; DEU = deucravacitinib; DMF = dimethyl fumarate; ETC = etanercept; GUS = guselkumab; IFX = infliximab; IXE = ixekizumab; PLC = placebo; Q2W = every two weeks; QW = once weekly; RIS = risankizumab; SEC = secukinumab; TIL = tildrakizumab; UST = ustekinumab

NMA/ITC results – Tables

"deucravacitinib is.."

+	Statistically significantly superior
0	No significant differences detected
-	Statistically significantly inferior
	No data

Sensitivity analysis 1: [redacted], 28 week data for tildrakizumab, 10-16 week data for all other comparators **(used in base case)**

Sensitivity analysis 2: [redacted], 10-16 week data for all other comparators

 Abbreviations: PASI, psoriasis area severity index; QW, per week; ***Full results available on slides 34-38**

Cost effectiveness

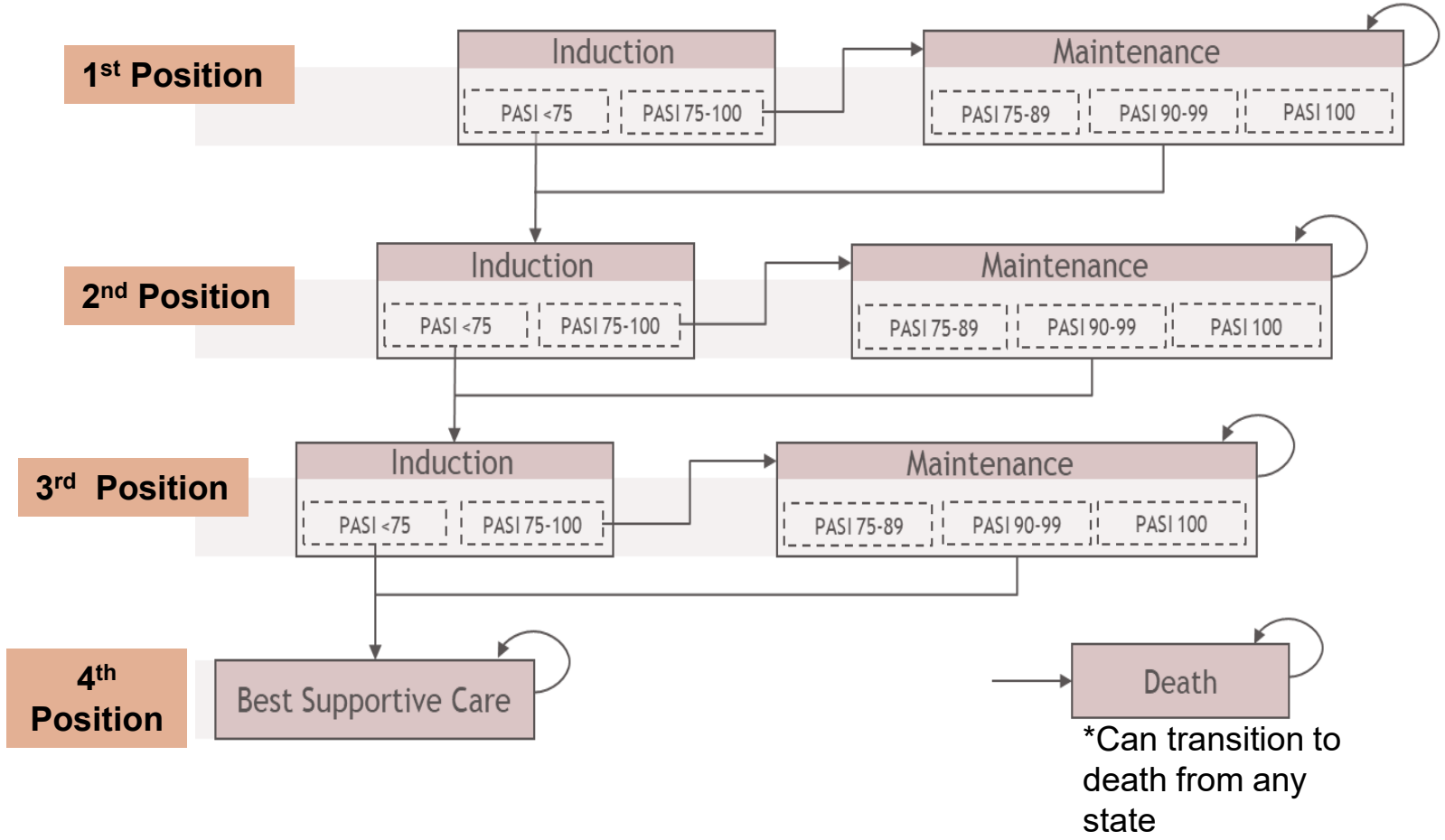
Deucravacitinib was compared with 14 comparators as first treatment in a sequence of three treatments followed by best-standard care.

Company's model overview

Markov model with 8 health states over four positions of 4th line of treatment

- Technology affects **costs** by: having different acquisition costs, AE specific costs and PASI75 response which determines progression through the treatment pathway and subsequent treatment and BSC specific costs.
- Technology affects **QALYs** by: having different AE incidences, PASI75 responses determining progression through pathway and different PASI responses to determine the utility accrued in each health state

Figure - Model structure



*Can transition to death from any state

Abbreviations: AE, adverse events; PASI, psoriasis area severity index; QALY, quality adjusted life year; BSC, best supportive care

Company's model overview

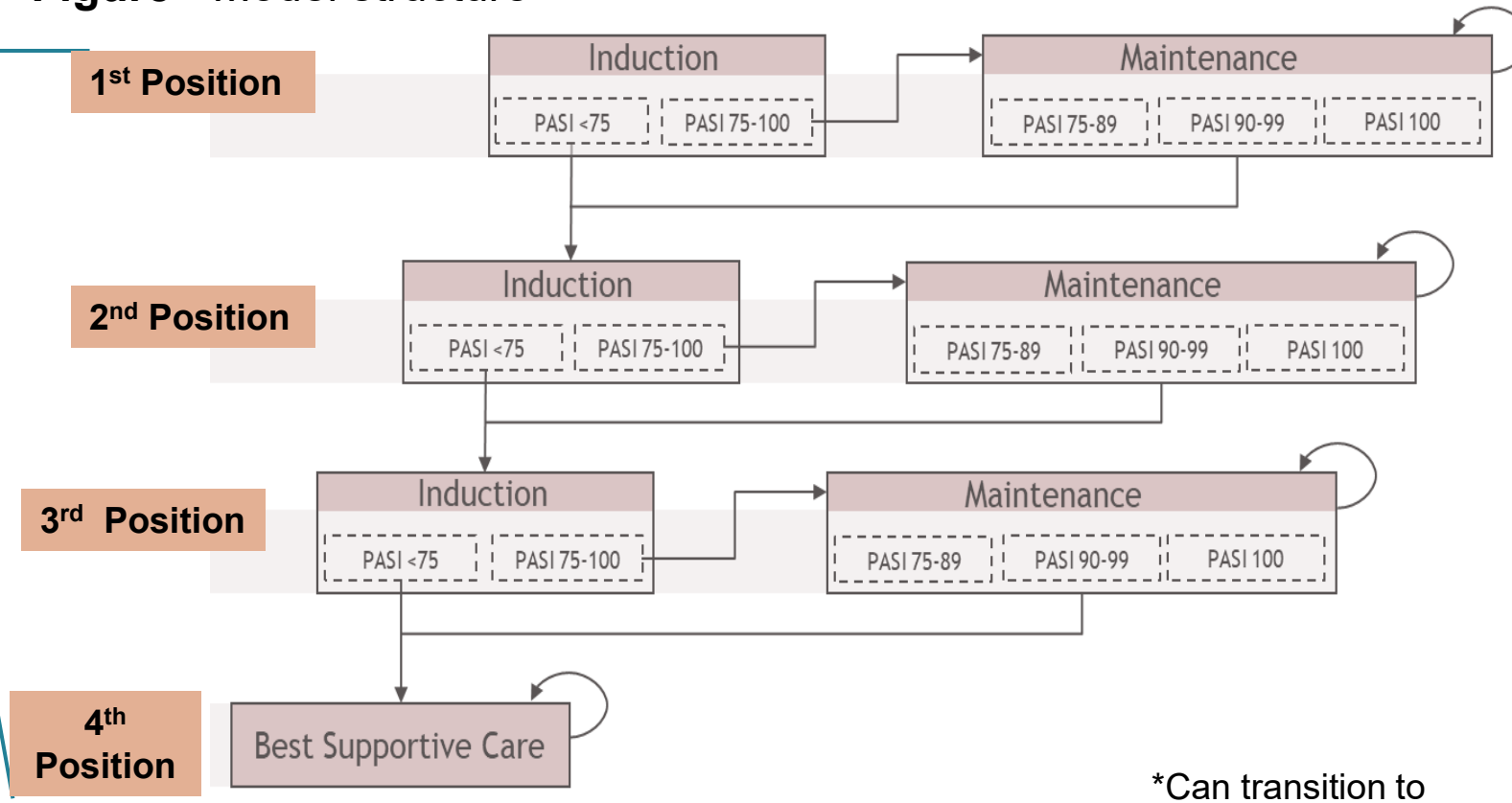
Markov model with 8 health states over four lines of treatment

Figure - Model structure

#	Intervention sequence	Comparator sequences
1	Deucravacitinib	[Comparator]
2	Secukinumab	Secukinumab*
3	Risankizumab	Risankizumab*
4	BSC	BSC

*When secukinumab or risankizumab are in comparator position they are replaced by ustekinumab at second or third line.

Figure - Model structure



*Can transition to death from any state

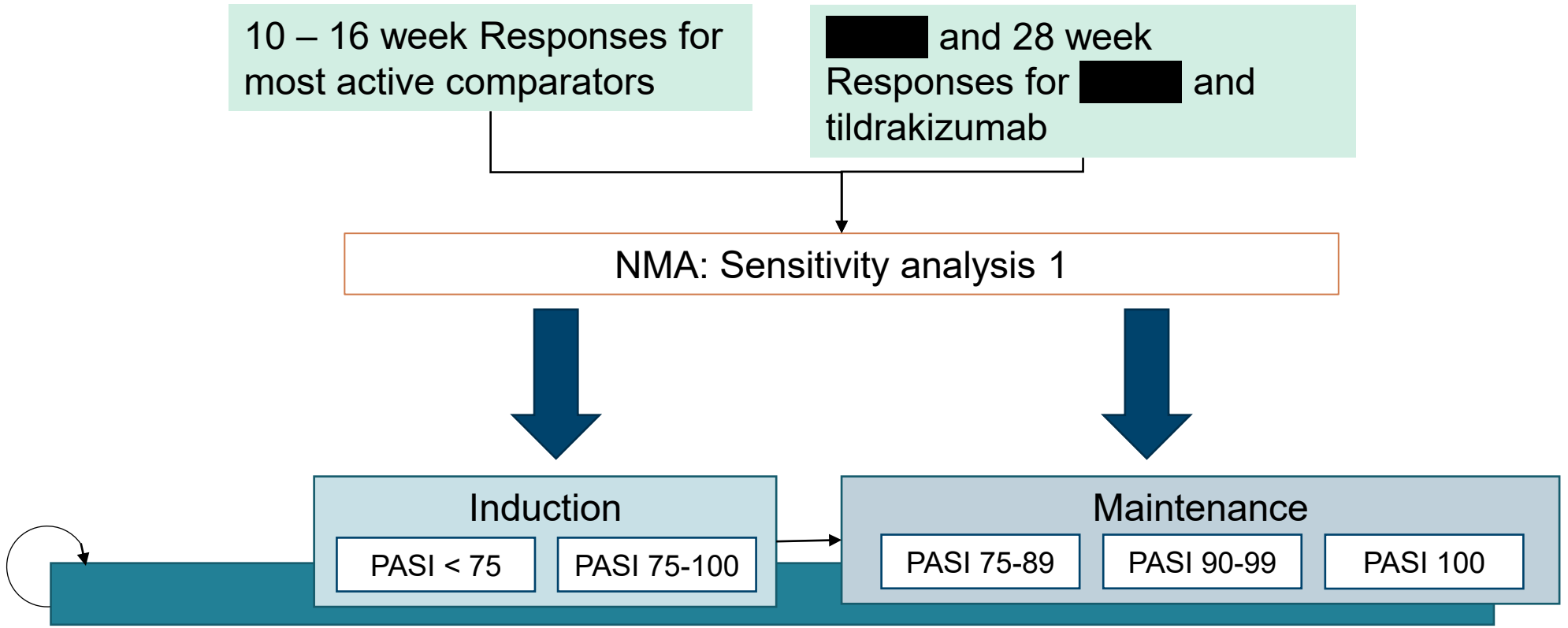
Abbreviations: AE, adverse events; PASI, psoriasis area severity index; QALY, quality adjusted life year; BSC, best supportive care

How company incorporated evidence into model

How the NMA informed the model *(company and EAG base case)*

Effectiveness evidence

Modelling



Company: used sensitivity analysis 1 to inform the transition probabilities in the base case of the model.

EAG: Reliance on NMA sensitivity analysis 1 is justified as these are likely to be the chosen timepoints for assessing response in clinical practice.

NICE

How company incorporated evidence into model (i)

Table Input and evidence sources

Input	Assumption and evidence source	EAG comments
Model structure	Based on previous psoriasis appraisal models and the York model from TA103.	Consistent with previous appraisals. Use of only 3 lines a simplification but consistent with previous appraisals.
Intervention efficacy	POETYK-PSO 1 and 2 trials, and their long term extension. PASI responses at [redacted] weeks used to inform NMA and sensitivity analysis 1 and model.	
Comparator efficacy	Systematic literature review to inform NMA sensitivity analysis 1 PASI responses at 10-16 weeks, except for Tildrakizumab (28 weeks)	
Utilities*	POETYK trial EQ-5D-3D data used and pooled with weighted utility value from previous appraisals (TA511 & TA350) to generate utility values for each PASI category. Utility is health state specific only, **not** modified by treatment.	Accept the company's approach of pooling utility estimates.
Costs	Drug costs, BNF; support costs, NHS reference costs (20/21)	Considers costs adequately dealt with. With exception to drug acquisition costs (see key issue)

Abbreviations: BNF, British National Formulary; TA, technology appraisals; NMA, network meta-analysis

How company incorporated evidence into model (ii)

Table Input and evidence sources

Input	Assumption and evidence source	EAG comments
Resource use	DISCOVER study (non-interventional, retrospective cohort), used to inform resource use for costings in base case. AE frequency derived from POETYK trials. (In line with TA442). Scenario with costs from Fonia et al study, (somewhat higher than DISCOVER) provided for consistency with previous appraisals.	Would not capture all long term costs (e.g cancer events) but accepts simplifying approach. Noted that the scenario using the Fonia costs had little effect on cost-effectiveness.
Treatment discontinuation	Fixed all cause discontinuation rate applied to those on all maintenance treatments each cycle. In the base case this is not drug specific.	Satisfied that the final discontinuation rates are credible
Adverse events	Severe infections, non-melanoma skin cancer and other malignancies modelled on a one off basis in first cycle.	Notes simplifying approaches like this can be used as per TA633. Considered there were limitations but unlikely to be an important driver of cost-effectiveness.
Subsequent treatments	Secukinumab and risankizumab second and third line as determined by market share.	Accept simplification of assuming only three active lines of treatment. Considered guselkumab may also be relevant at second line and included scenario.

Abbreviations: BNF, British National Formulary; TA, technology appraisals; NMA, network meta-analysis

Key issue: BSC and non-responder costs

Background

- In DISCOVER, costs were estimated in the 12 months following discontinuation; unclear if these can be extrapolated to lifetime time horizon
- Secondary care costs and non-responder costs are averaged and applied to those in the BSC state only
- It is unclear whether these costs can be solely attributed to those discontinuing or whose disease does not respond to active therapy.

Company

- Applying these costs to the lifetime horizon is in line with previous appraisals, to explicitly model these costs over lifetime horizon would be complex
- Provided a breakdown of the individual components of secondary care costs

EAG comments

- Cost breakdown does not explain proportion of costs that may be applicable to those on active treatments
- Considers that the impact on costs from transitioning from treatment to BSC are not well informed
- Submitted scenarios reducing both BSC and non-responder costs by fixed percentages
- Reducing these costs benefits less effective active treatments with deucravacitinib seeing increased ICERs against less effective comparators but lower ICERs against superior comparators.

Are BSC and non-responder costs modelled in an appropriate way?

NICE Abbreviations: BSC; best-supportive care; ICER, incremental cost effectiveness ratio

Key issue: BSC utility returns to baseline

Background

- In the model when people move into the BSC state after a third treatment they return to baseline utility, instead of having utility gains in line with the PASI responses from the placebo group in the NMA
- If the response in the trial placebo group reflected natural improvement in the disease then using baseline utility for BSC could overestimate the health benefits of the active comparators.

Company

- This approach is consistent with TA575; whose committee concluded BSC utility should return to baseline
- Clinical experts stated that the PASI responses seen in the trial placebo arm were likely due to the trial (placebo effect, caregiver setting) and that baseline utility would better reflect BSC in a non-trial setting

EAG comments [mention tech team considerations if relevant]

- Acknowledges consistency with TA575; "It may be reasonable to assume baseline utility for those on BSC in routine practice"
- Acknowledged PASI responses in trial likely driven by trial setting, (does not rule out natural disease history) and considered that any trial effect could also affect active comparators
- Proposed two scenarios to explore uncertainty around this issue
  - 1. Apply PASI response based utilities to BSC state according to the responses in the NMA placebo arm
  - 2. Apply PASI responses to portion of BSC state that achieves PASI50 or more, but baseline to the rest

Is it appropriate to use baseline utility to inform BSC health state utility?

Abbreviations: BSC, best supportive care; PASI, psoriasis activity severity index; NMA, network meta-analysis

Resolved issues / other uncertainties

Pooled utility values

- The baseline utility value from the pooled POETYK trials was higher than similar previous appraisals' trials
- This created a ceiling effect which reduced the amount that utility improved between PASI categories and meant that PASI category utility gains in this model would be smaller than in previous appraisal's models
- Company pooled POETYK utility values with values (weighted by sample size) from previous trials (pivotal trials from TA350 and TA511) to provide utility values for the base case (as recommended in DSU TSD 12)
- EAG was concerned about the magnitude of the difference in baseline utility as it suggests differences in trial population. However, no reason for the baseline utility differences was found by EAG or company.
- The EAG considered that the company's approach to pooling utility estimates across the available trials was appropriate and resulted in better consistency with previous appraisals.

Drug acquisition costs

- Average drug costs are applied every two weeks, this does not always align with induction period length
- This can result in over or underestimation of drug costs for drugs. For example a drug where the first dose is due 12 weeks into maintenance may overestimate drug costs.
- Company acknowledged the model does not fully reflect treatment costs, however there is no systematic bias and very complex modelling would be required to achieve this.
- EAG acknowledges the complexity required to model drug costs in a more accurate way
- "The EAG is generally satisfied with the company's response"
- Two scenarios provided to assess potential impacts of drug acquisition cost modelling on the ICERs

 Abbreviations: BSC, best supportive care; EAG, external assessment group; ICER, incremental cost effectiveness ratio

Other considerations

Equality considerations

- The PASI, which uses skin redness as a key measure, can underestimate disease severity in those with black or brown skin
- The DLQI can have limited validity in some people and may also miss anxiety and depression

Abbreviations: PASI, psoriasis area severity index; DLQI, dermatology life quality index

Summary of company and EAG base cases and scenarios for consideration

EAG base case incorporates only two changes

Table – Key EAG provided scenarios

#	Scenario
1	BSC utility based on placebo PASI response
2	BSC utility based on PASI response (baseline for PASI <50)
3a/b/c	10/25/50% reduction in BSC costs
4a/b/c	10/25/50% reduction in non-responder costs
5a	Adjustment to 1st line acquisition costs
5b	Adjustment to 1-3rd line acquisition costs
6	Replace secukinumab with guselkumab
7	Age adjusted utilities

- Company base case compares sequence deucravacitinib at first line, with 14 other comparators at first line.
- The EAG base case incorporates scenario 5b and scenario 7

Abbreviations: EAG, external assessment group; BSC, best supportive care; PASI, psoriasis area severity index;

Impact of EAG preferred assumptions on base case NHB

Table Impact of individual assumptions on NHB compared with company corrected base case

Scenario	What was done	Effect on results
Scenario 5b	Pack/dose costs are applied to the proportion of cohort remaining on first line at the start of each cycle. The over/under estimate per patient then applied to second and third line treatments.	• Minor effect on most ICERs and NHBs (slight reduction in ICERs against some comparators). • Does not change the decision in terms of which comparators deucravacitinib is cost effective against.
Scenario 7	Utilities accrued in the model were age adjusted.	• Slightly increases ICERs and NHB for comparisons in the NE and SW quadrants
EAG Base case (scenario 5b and 7)	Combination of scenario 5 and 7	• Slightly higher ICERs versus clinically inferior comparators • Slightly higher SW quadrant ICERs versus clinically superior comparators

Results do not include confidential commercial discounts for comparators

NICE Abbreviations: ICER, incremental cost effectiveness ratio; NHB, net health benefit; NE, north east; SW, south west

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS discounts

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Thank you.

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Adverse events
Controlled safety pool showed

- Controlled safety pool was pooled population from periods of POETYK-PSO 1 and 2 which were placebo and apremilast controlled
- Proportion of AEs and severe AEs in deucravacitinib group was comparable to apremilast
- A “Phase 3 safety pool” contains data only from deucravacitinib patients from both randomised trials and the long term extension. The deucravacitinib AEs profile in the phase 3 pool was consistent with the controlled safety pool

Table – Controlled safety pool adverse events

AE category	Deucravacitinib, n (%)	Placebo, n (%)	Apremilast, n (%)
All adverse events	995 (72.9)	347 (52.1)	299 (70.9)
Drug-related AEs	[redacted]	[redacted]	[redacted]
Severe AEs	[redacted]	[redacted]	[redacted]

Abbreviations: AE, adverse events;

Clinical trial results – Pooled QoL data and 52 week efficacy

Table – POETYK-PSO-1 & 2 Pooled quality of life results

Outcome	Odds ratio (95%CI) versus placebo	Odds ratio (95%CI) versus apremilast
DLQI 0/1 (week 16)	[redacted]	[redacted]
PSSD score 0 (week 16)	[redacted]	[redacted]
PSSD score 0 (week 24)	n/a	[redacted]
Outcomes	**Change from baseline placebo (SE)**	**Change from baseline apremilast**
PSSD cfb (week 16)	-3.8 (1.4)	-19.3 (1.4)
PSSD cfb (week 24)	n/a	-21.4 (1.6)

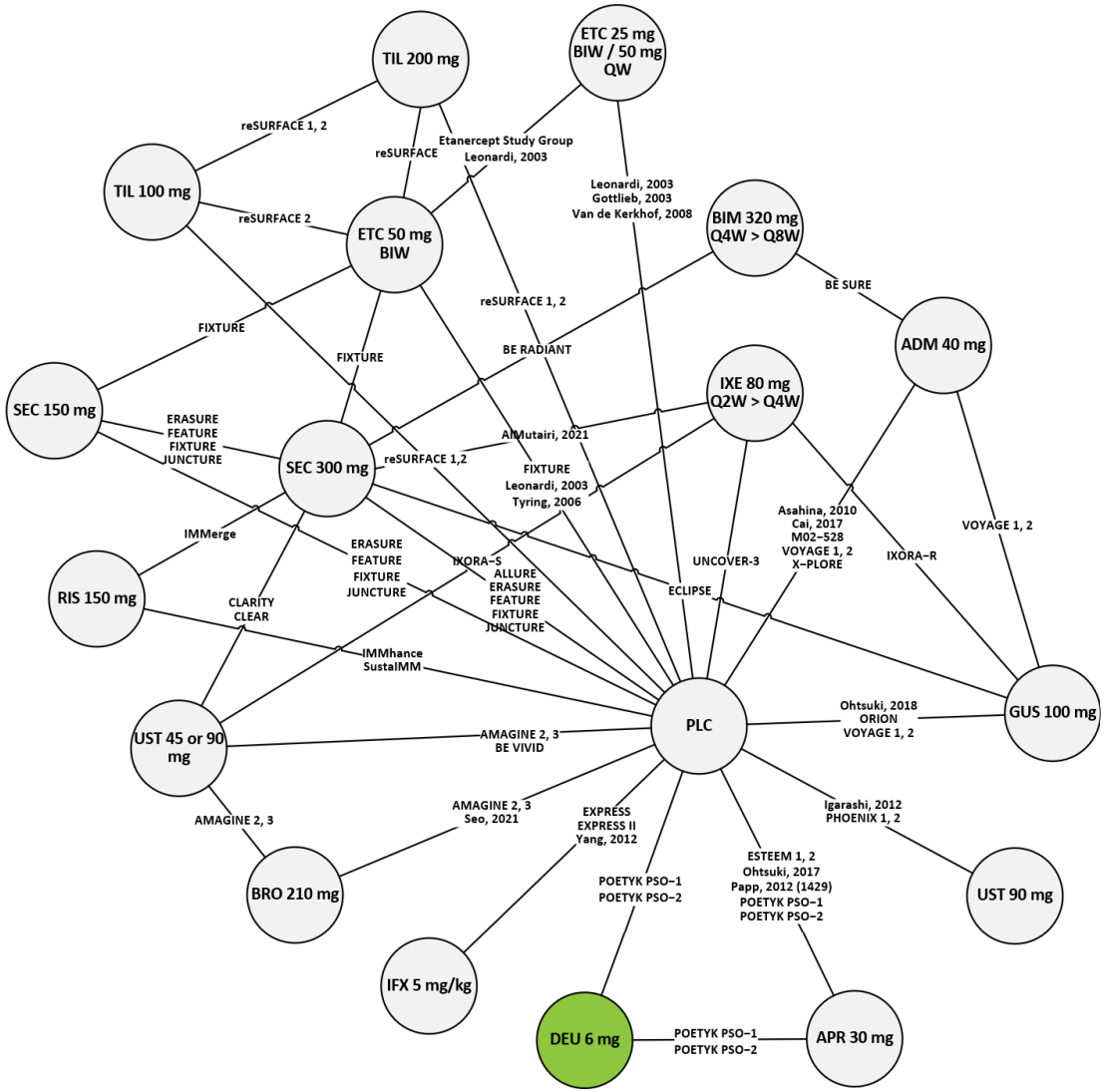
Table – Numbers of responders maintaining their response at 52 weeks (reported separately for each trial)

Outcome (52 week)	POETYK-PSO-1	POETYK-PSO-2
PASI75 responders, n (%)	[redacted]	[redacted]
PASI90 responders, n (%)	[redacted]	[redacted]
PASI100 responders, n (%)	[redacted]	[redacted]
sPGA 0/1 responders, n (%)	[redacted]	[redacted]

- Interim results from POETYK-PSO-LTE suggest that PASI 75 responses are maintained for up to 60 weeks after the end of the initial studies.

NICE Abbreviations: PASI, psoriasis area severity index; sPGA, static physician's global assessment; QoL, quality of life

NMA/ITC network diagram(s) – 24 – 28 week time point



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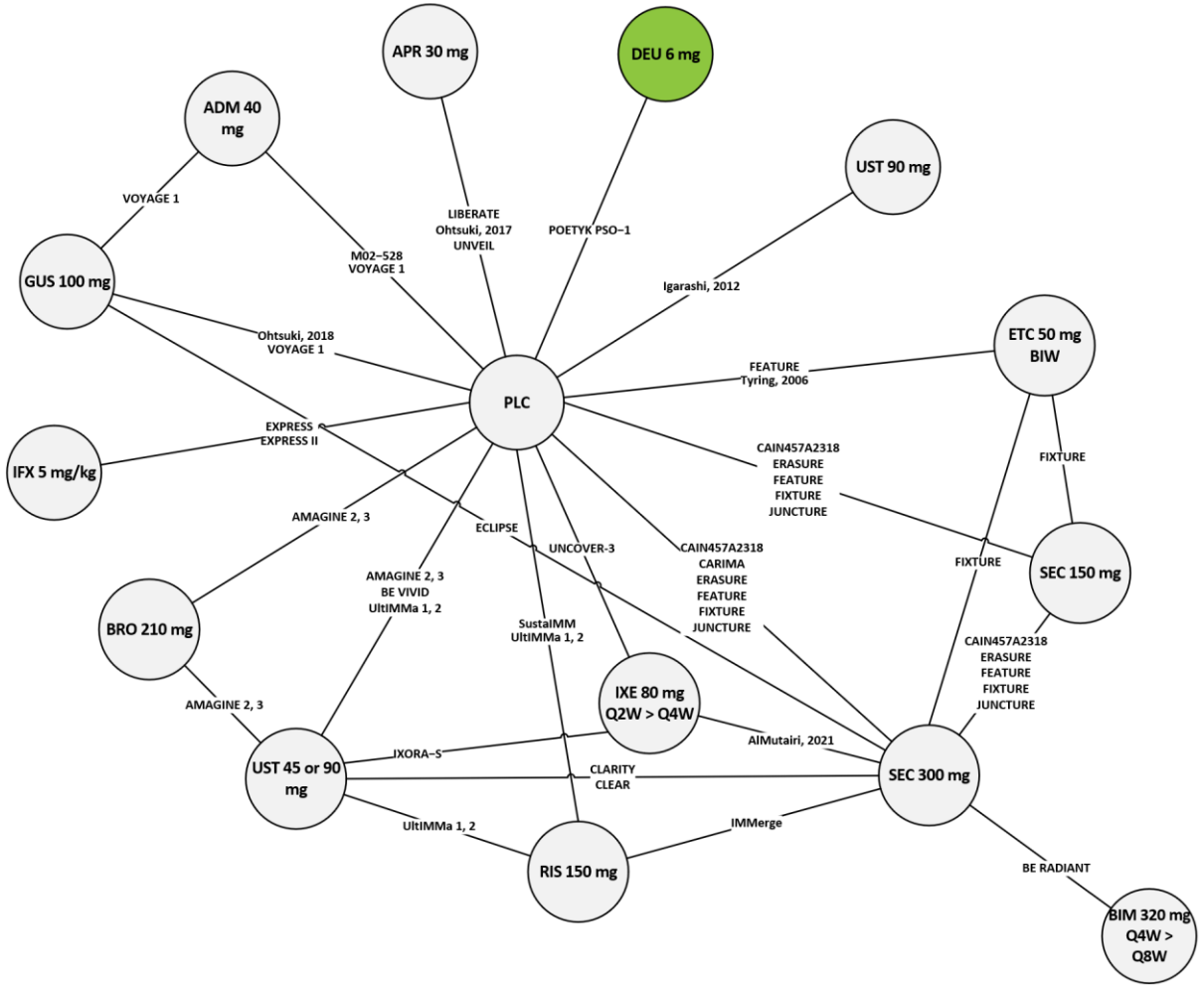
NMA/ITC network diagram(s) – 44-60 week time point



Abbreviations: ADM = adalimumab; APR = apremilast; BIM = bimekizumab; BIW = twice weekly; BRO = brodalumab; DEU = deucravacitinib; ETC = etanercept; GUS = guselkumab; IFX = infliximab; IXE = ixekizumab; PLC = placebo; Q2W = every two weeks; Q4W = every four weeks; Q8W = every eight weeks; QW = once weekly; RIS = risankizumab; SEC = secukinumab; TIL = tildrakizumab; UST = ustekinumab

NMA/ITC results – Sensitivity Analysis 1

Comparator	PASI50, OR (95%CI)	PASI75, OR (95%CI)	PASI90, OR (95%CI)	PASI100, OR (95%CI)
Placebo	[redacted]	[redacted]	[redacted]	[redacted]
Dimethyl fumarate	[redacted]	[redacted]	[redacted]	[redacted]
Apremilast	[redacted]	[redacted]	[redacted]	[redacted]
Etanercept (50mg QW)	[redacted]	[redacted]	[redacted]	[redacted]
Adalimumab	[redacted]	[redacted]	[redacted]	[redacted]
Certolizumab pegol (200mg)	[redacted]	[redacted]	[redacted]	[redacted]
Infliximab	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab (45 or 90mg)	[redacted]	[redacted]	[redacted]	[redacted]
Tildrakizumab (200mg)	[redacted]	[redacted]	[redacted]	[redacted]
Guselkumab	[redacted]	[redacted]	[redacted]	[redacted]
Risankizumab	[redacted]	[redacted]	[redacted]	[redacted]
Secukinumab (300mg)	[redacted]	[redacted]	[redacted]	[redacted]
Brodalumab	[redacted]	[redacted]	[redacted]	[redacted]
Ixekizumab	[redacted]	[redacted]	[redacted]	[redacted]
Bimekizumab	[redacted]	[redacted]	[redacted]	[redacted]

NICE Abbreviations: PASI, psoriasis area and severity index; OR, odds ratio; CI, confidence intervals; NMA, network meta-analysis

NMA/ITC results – PASI50

Comparator	10-16 weeks, OR (95%CI)	24-28 weeks, OR (95%CI)	44-60 weeks, OR (95%CI)
Placebo	[redacted]	[redacted]	[redacted]
Dimethyl fumarate	[redacted]	No data	No data
Apremilast	[redacted]	[redacted]	[redacted]
Etanercept (50mg QW)	[redacted]	[redacted]	No data
Adalimumab	[redacted]	[redacted]	[redacted]
Certolizumab pegol (200mg)	[redacted]	No data	No data
Infliximab	[redacted]	[redacted]	[redacted]
Ustekinumab (45 or 90mg)	[redacted]	[redacted]	[redacted]
Tildrakizumab (200mg)	[redacted]	[redacted]	No data
Guselkumab	[redacted]	[redacted]	[redacted]
Risankizumab	[redacted]	[redacted]	[redacted]
Secukinumab (300mg)	[redacted]	[redacted]	[redacted]
Brodalumab	[redacted]	[redacted]	[redacted]
Ixekizumab	[redacted]	[redacted]	[redacted]
Bimekizumab	[redacted]	[redacted]	[redacted]

NICE Abbreviations: PASI, psoriasis area and severity index; OR, odds ratio; CI, confidence intervals; NMA, network meta-analysis

NMA/ITC results – PASI75

Comparator	10-16 weeks, OR (95%CI)	24-28 weeks, OR (95%CI)	44-60 weeks, OR (95%CI)
Placebo	[redacted]	[redacted]	[redacted]
Dimethyl fumarate	[redacted]	No data	No data
Apremilast	[redacted]	[redacted]	[redacted]
Etanercept (50mg QW)	[redacted]	[redacted]	No data
Adalimumab	[redacted]	[redacted]	[redacted]
Certolizumab pegol (200mg)	[redacted]	No data	No data
Infliximab	[redacted]	[redacted]	[redacted]
Ustekinumab (45 or 90mg)	[redacted]	[redacted]	[redacted]
Tildrakizumab (200mg)	[redacted]	[redacted]	No data
Guselkumab	[redacted]	[redacted]	[redacted]
Risankizumab	[redacted]	[redacted]	[redacted]
Secukinumab (300mg)	[redacted]	[redacted]	[redacted]
Brodalumab	[redacted]	[redacted]	[redacted]
Ixekizumab	[redacted]	[redacted]	[redacted]
Bimekizumab	[redacted]	[redacted]	[redacted]

Abbreviations: PASI, psoriasis area and severity index; OR, odds ratio; CI, confidence intervals; NMA, network meta-analysis

NMA/ITC results – PASI90

Comparator	10-16 weeks, OR (95%CI)	24-28 weeks, OR (95%CI)	44-60 weeks, OR (95%CI)
Placebo	[redacted]	[redacted]	[redacted]
Dimethyl fumarate	[redacted]	No data	No data
Apremilast	[redacted]	[redacted]	[redacted]
Etanercept (50mg QW)	[redacted]	[redacted]	No data
Adalimumab	[redacted]	[redacted]	[redacted]
Certolizumab pegol (200mg)	[redacted]	No data	No data
Infliximab	[redacted]	[redacted]	[redacted]
Ustekinumab (45 or 90mg)	[redacted]	[redacted]	[redacted]
Tildrakizumab (200mg)	[redacted]	[redacted]	No data
Guselkumab	[redacted]	[redacted]	[redacted]
Risankizumab	[redacted]	[redacted]	[redacted]
Secukinumab (300mg)	[redacted]	[redacted]	[redacted]
Brodalumab	[redacted]	[redacted]	[redacted]
Ixekizumab	[redacted]	[redacted]	[redacted]
Bimekizumab	[redacted]	[redacted]	[redacted]

Abbreviations: PASI, psoriasis area and severity index; OR, odds ratio; CI, confidence intervals; NMA, network meta-analysis

NMA/ITC results – PASI100

Comparator	10-16 weeks, OR (95%CI)	24-28 weeks, OR (95%CI)	44-60 weeks, OR (95%CI)
Placebo	[redacted]	[redacted]	[redacted]
Dimethyl fumarate	[redacted]	No data	No data
Apremilast	[redacted]	[redacted]	[redacted]
Etanercept (50mg QW)	[redacted]	[redacted]	No data
Adalimumab	[redacted]	[redacted]	[redacted]
Certolizumab pegol (200mg)	[redacted]	No data	No data
Infliximab	[redacted]	[redacted]	[redacted]
Ustekinumab (45 or 90mg)	[redacted]	[redacted]	[redacted]
Tildrakizumab (200mg)	[redacted]	[redacted]	No data
Guselkumab	[redacted]	[redacted]	[redacted]
Risankizumab	[redacted]	[redacted]	[redacted]
Secukinumab (300mg)	[redacted]	[redacted]	[redacted]
Brodalumab	[redacted]	[redacted]	[redacted]
Ixekizumab	[redacted]	[redacted]	[redacted]
Bimekizumab	[redacted]	[redacted]	[redacted]

NICE Abbreviations: PASI, psoriasis area and severity index; OR, odds ratio; CI, confidence intervals; NMA, network meta-analysis

NMA/ITC results – Tables

“deucravacitinib is..”

+	Statistically significantly superior
0	No significant differences detected
-	Statistically significantly inferior
	No data

NICE Abbreviations: PASI, psoriasis area severity index; QW, per week;

***Full results available on slides 34-38**

Plaque psoriasis 4th line treatment options in adults

Table - Treatment options and assessment of response

Treatment	Response assessed at	Treatment	Response assessed at
Etanercept	12 weeks	Dimethyl Fumarate	16 weeks
Infliximab	10 weeks	Brodalumab	12 weeks
Adalimumab	16 weeks	Guselkumab	16 weeks
Ustekinumab	16 weeks	Certolizumab pegol	12 weeks
Secukinumab	12 weeks	Tildrakizumab	28 weeks
Apremilast	16 weeks	Risankizumab	16 weeks
Ixekizumab	12 weeks	Bimekizumab	16 weeks
Deucravacitinib	[redacted]		

Adequate response is defined as attainment of PASI75 of PASI50 with a 5 point reduction in DLQI since starting treatment

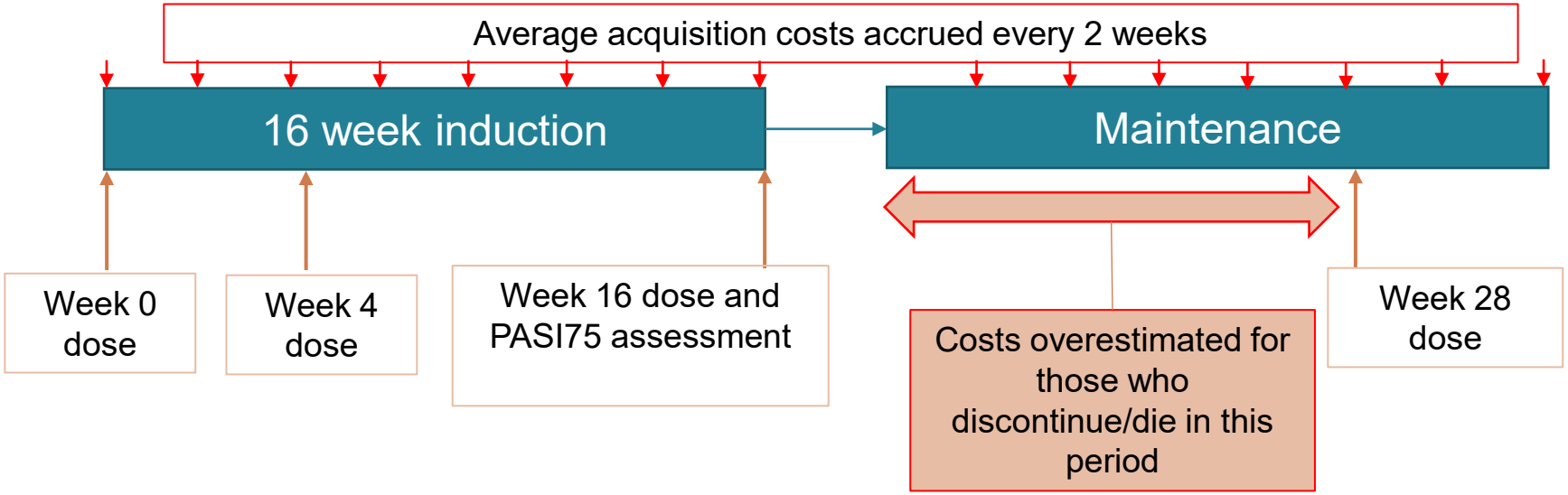
Key issue: Drug acquisition costs

Per cycle application of these costs may over or underestimate them

Background

- The dosing schedules do not always align with the length of the induction periods in the model
- This can cause overestimation of costs for drugs where the first scheduled maintenance dose is due several cycles into the maintenance phase or underestimation of costs where the first maintenance dose is due at the start of the maintenance period. (effect exaggerated with longer dosing intervals)

e.g risankizumab



Insert question for committee [present as simple dilemma as far as possible, e.g., The company says use Gompertz, the EAG says use lognormal – which is more plausible?]

Abbreviations: PASI, psoriasis activity severity index; EAG, external assessment group

Key issue: Drug acquisition costs

Per cycle application of these costs may over or underestimate them

Background

- The dosing schedules do not always align with the length of the induction periods in the model
- This can cause overestimation of costs for drugs where the first scheduled maintenance dose is due several cycles into the maintenance phase or underestimation of costs where the first maintenance dose is due at the start of the maintenance period (effect exaggerated with longer dosing intervals)

Company

- Acknowledges that costs modelled in this way do not fully reflect the exact cost of each dosing scheme
- However, this does not introduce a systematic bias in costs for any of the treatments
- Noted the EAG scenarios showed a varied impact on cost-effectiveness depending on the comparator sequence (e.g ICER for deucravacitinib decreased versus some comparators but increased versus others)

EAG comments

- Acknowledged that implementing exact dose based costing would require substantial changes to model
- "The EAG is generally satisfied with the company response"
- Noted that the EAG scenarios can be used to assess any potential impacts on ICERs and NHBs

Insert question for committee [present as simple dilemma as far as possible, e.g., The company says use Gompertz, the EAG says use lognormal – which is more plausible?]

NICE Abbreviations: EAG, external assessment group; ICER, incremental cost effectiveness ratio