Apremilast for moderate to severe plaque psoriasis

4th Appraisal Committee meeting, September 2016

Background & Clinical Effectiveness

Lead team: John Pounsford, Dani Preedy, Marta Soares

Committee B

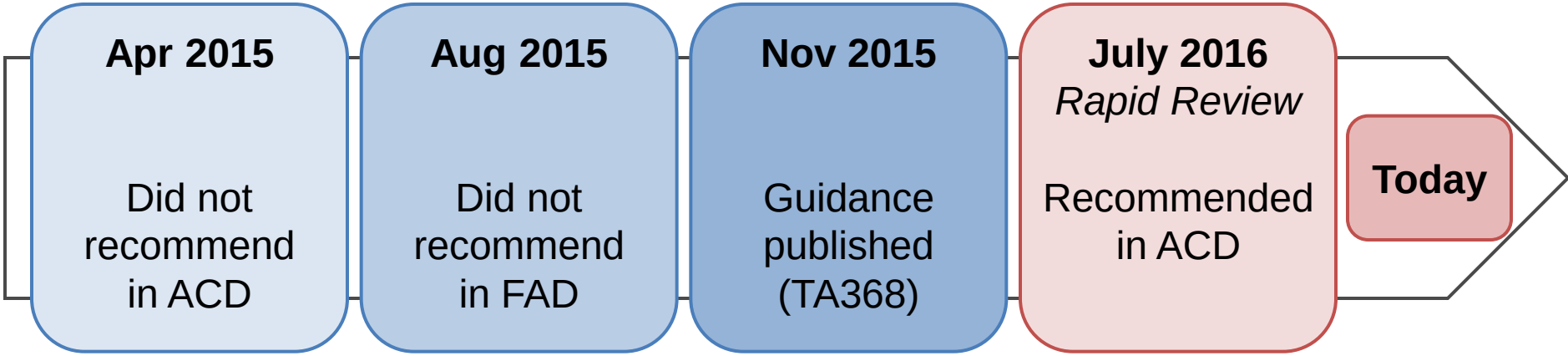
Company: Celgene

Evidence Review Group: University of York

Chair: Amanda Adler

NICE technical team: Helen Tucker, Sophie Laurenson, Raisa Sidhu, Zoe Garrett

History of apremilast appraisal at NICE

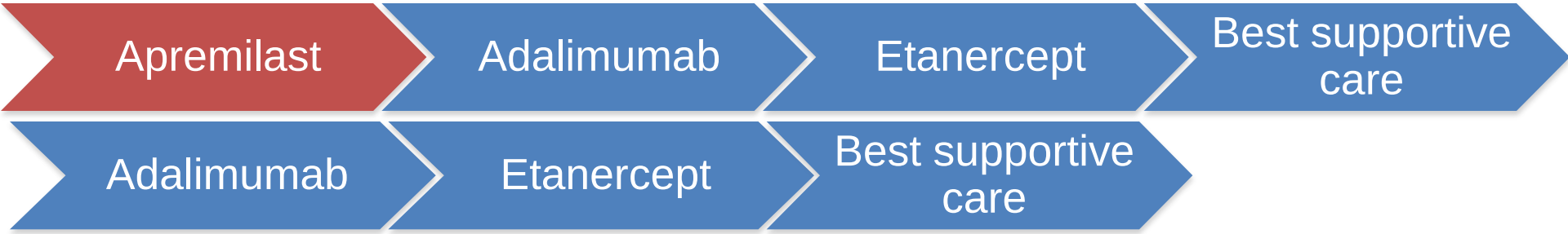


Recommendation 1.1

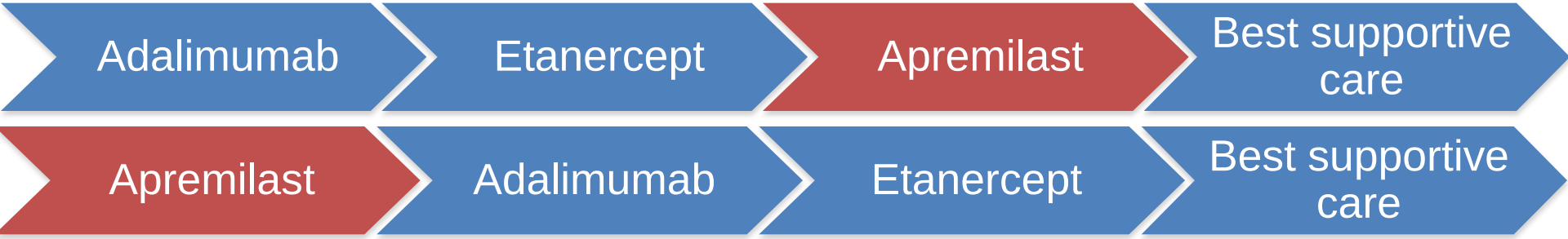
- Apremilast is recommended as an option for treating chronic plaque psoriasis in adults whose disease has not responded to other systemic therapies, for example, ciclosporin, methotrexate **or** PUVA (psoralen and ultraviolet-A light), or these treatments are contraindicated or the person cannot tolerate them, only when:
  - the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10
  - the company provides apremilast with the discount agreed in the patient access scheme.

TA368 Apremilast position and comparators

- **Apremilast before biologics**



- **Apremilast after biologics** (not compared with no apremilast)



- **Apremilast in people who cannot take biologics**

Committee's considerations

STA (before rapid review)

Clinical	Apremilast more effective than placebo, but not as effective as biological therapies
	Clinicians would like to prescribe apremilast, either before or after biological therapies; decision driven partly by patient choice
Cost	Response rates remain relatively constant over time
	ICERs not be within the range considered to be a cost-effective

Rapid review

Population	Company proposal for severe population only. Appropriate as evidence only for severe group
New analysis	Takes into account Committees preferred assumptions
Sequencing	Lack external validity as biologics no longer cost effective
Vs. BSC	Valid comparison and used for decision making. • Company ICER: £***[CIC] /QALY gained • ERG ICER: £***[CIC] /QALY gained
Vs. biologics	Apremilast less effective and less expensive. Similar ICERs to biologics within their appraisals

Comments from:

Consultees:

- *The Psoriasis and Psoriatic Arthritis Alliance*
- *The Psoriasis Association*
- *Celegene*
- *British Association of Dermatologists*
- *Department of Health (no comments)*

Commentators:

- *AbbVie*
- *Janssen*
- *MSD (no comments)*
- *Novartis*

Support for recommendation

- ‘Celgene welcomes the draft positive recommendation’
- ‘The psoriasis Association welcomes the positive recommendation…’
- ‘The British Association of Dermatologists welcomes the decision by NICE to recommend apremilast’
- ‘I welcome the draft positive recommendation for apremilast, a significant step forward in patient choice.’ *NHS dermatologists*

Psoriasis and Psoriatic Arthritis Alliance

- '..from the data presented at the original appraisal meeting apremilast was less effective than biologics. With a PAS, that benefit does not improve….I fear that this may lead to those with the severest disease being offered a less effective treatment and therefore, not get optimal care.'

- 'I would like to see in 1.1 of the recommendation, clearer guidance where within the sequence of care apremilsat will be used.. so that....apremilast does not just displace or delay clinically more effective therapies in the severe psoriasis patient group'

Janssen

- **Stopping rule.**
  - Unlike the recommendations for biological therapies, the ACD recommendation for apremilast does not include a stopping rule. However, the apremilast cost-effectiveness model uses a trial period of 16 weeks for apremilast

- **Withdrawal rates**
  - ‘While it may be a necessary simplifying assumption to assume all therapies have the same withdrawal rate..” may not reflect actual adherence rates observed in real-world practice.

Janssen

- **Cost of best supportive care**
  - During the Appraisal Committee meeting, the Committee referred to two potential sources of length of stay data in relation to best supportive care –1) Fonia et al. 2010 and 2) NICE CG153 (2012) for psoriasis.
  - 'In summary, Janssen believes that Fonia reflects a less severe population than the population within the scope of this appraisal'
    - *N.b. Implication is that BSC costs are underestimated*
  - *N.b. Increasing BSc costs reduces the ICER*
  - *N.b. Scenario analysis:*
    - *Higher BSC and non-responder costs: £***[CIC]/QALY*
    - *Lower BSC and non-responder costs: £***[CIC]/QALY*

Abbie Vie

- ‘The guidance has not been developed in line with the NICE Methods and Process Guides’
  - Process is for new PAS
  - ACD discusses several unresolved issues – i.e. modelling and difficulty in assessing best position of apremilast
  - **Re before biologics:** the model should account for differences in efficacy at different lines of treatment
  - **Re same place as biologics**: An incremental analysis should be conducted

- Preliminary guidance lacks transparency
  - ‘We note that the company has censored all costs, QALYs, and ICERs. This makes it impossible for independent observers and members of the public to determine whether the NHS is in fact achieving value for money..’
  - Appears to ‘recommend a less effective product on the basis of its lower price - this appears to us to be potentially irrational.’

Abbie Vie

- Quality and representativeness of clinical practice and technical implementation
  - Model (available to Abbie Vie) had errors ‘several hundred pounds’ change to ICERs
  - External validation shows model doesn’t give same results as previous appraisals
  - BSC costs uncertain and a key driver

Novartis

- ‘the apremilast ACD states that apremilast is an option for “adults whose disease has not responded to other systemic therapies, for example, ciclosporin, methotrexate **or** PUVA”, ‘TA350 for secukinumab[1], TA180 for ustekinumab[2], TA146 for adalimumab[3] and TA103 for efalizumab and etanercept[4] all state that these therapies are options for patients when “the disease has failed to respond to standard systemic therapies, for example, ciclosporin, methotrexate **and** PUVA’
  - *n.b this reflects the wording of the marketing authorisation for Apremilast*

- Absence of stopping rule despite ‘initial 10 to 16 week period over which initial response to the treatment is assessed’
- Recommendation contradicts clinical advise in ACD – Apremilast wouldn’t be used instead of, or before biologics, as it is less effective

Issues for discussion

- Has the committee heard anything/seen new evidence to modify the guidance?
  - Should a stopping rule be added?
  - Not offering apremilast in the pre-biological setting?
  - Change ‘or’ or ‘and’ for PUVA?