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Table 1: Data extraction of core model structures from the 14 original modelling studies

Study	Model type	Pain measurement	Pain outcomes modelled	AEs modelled	Titration considered?	Treatment lines modelled	Cycle length	Time horizon	Model replicated elsewhere
Annemans et al. ¹⁴	Markov	11-point NRS	3 categories of pain modelled as "mild" (NRS<4), "moderate" (NRS ≥4 and <7) or "severe" (NRS≥7)	Yes, modelled as discontinuation only	No	1 st and 2 nd line	4 weeks	1 year	Chevalier et al ³⁰
Armstrong et al. 15	Markov	Two categories of pain reduction: ≥30% reduction in pain, <30% reduction in pain (measurement instrument not clear)	Two categories of pain reduction: ≥30% pain or <30% pain reduction	Yes, cost and HRQL of managing headache, constipation, oedema, dizziness, somnolence, diarrhoea, vomiting, rash, urine retention, nausea, dry mouth	Yes	1 st and 2 nd line	Monthly	1 year	No
Beard et al. ¹⁶	Decision tree	Three categories of pain reduction: >50% pain reduction, 30-49% pain reduction and <30% pain reduction or reported a 11 point NRS	Three categories of pain reduction: >50% pain reduction, 30-49% pain reduction and <30% pain reduction	Yes, modelled as discontinuation only	No	1 st , 2 nd , 3 rd and 4 th line	NA	6 months	No
Bellows* et al. ¹⁷	Decision tree	Categorised as <50% pain reduction or ≥50% pain reduction	Two categories of pain relief: "Good" pain relief (≥50%	Yes, costs and HRQL relating to tolerable,	No	1 st line	NA	6 months	No

Study	Model type	Pain measurement	Pain outcomes modelled	AEs modelled	Titration considered?	Treatment lines modelled	Cycle length	Time horizon	Model replicated elsewhere
		based on daily numerical pain scores (measurement tool not clear)	reduction) and "poor" pain relief (<50% reduction)	intolerable and serious AEs					
Carlos et al.*18	Decision tree	Patient-reported subjective pain relief of 'moderate' or better, or (2) 'much improved' or better on the (PGIC) scale, or ≥50% reduction in pain reduced by factor of 1.193	Two categories of pain relief: "good" or "poor"	Yes, costs and HRQL relating to AEs and discontinuation from intolerable AEs included	No	1 st line	NA	12 weeks	No
Cepeda and Farrar ¹⁹	Decision tree	Two categories of pain relief: reduction of ≥50% or <50% (measurement method not clear)	Two categories of pain relief: "pain relief" or "no pain relief"	Yes, costs and HRQL included for major and minor AEs	No	1 st line	NA	1 month	No
Dakin et al. ²²	Markov	Proportion of patients experiencing "much" or "very much" improved on PGIC or CGIC, or "moderate" or "greater" improvement on PGASI or PGAI	Two categories of pain relief: "Responders" and "insufficient pain relief"	Yes, costs and HRQL relating to tolerable and intolerable AEs	Yes	1 st and 2 nd line	30 days	6 months	Ritchie, Liedgens & Nuijten ^{23,} Dakin et al.
De-Salas- Cansado et al. ²⁷	Decision tree	HRQL differences by treatment arm incorporated directly from analysis of EQ-5D data from	Change in EQ-5D score from baseline calculated in matched pairs	Not modelled	No	1 st line	NA	12 weeks	De-Salas- Cansado et al. ³

Study	Model type	Pain measurement	Pain outcomes modelled	AEs modelled	Titration considered?	Treatment lines modelled	Cycle length	Time horizon	Model replicated elsewhere
		matched analysis of paired samples from observational study	analysis						
Gordon et al. ⁴	Discrete individual simulation	11-point NRS	Level of pain (11 point scale)	Yes, costs and HRQL and withdrawal modelled in one arm of study	No	1 st and 2 nd line	Weekly	5 years	Prettyjohns et al ³¹
NICE 2013 ⁵	Decision tree	Three categories of pain reduction; >50% pain reduction, 30-49% pain reduction and <30% pain reduction†	Three categories of pain reduction; >50% pain reduction, 30-49% pain reduction and <30% pain reduction	Yes, costs and HRQL of nausea and dizziness modelled	No	1 st line	NA	20 weeks	No
O'Connor et al.*20	Decision tree	Binary definition of pain improvement; based on "much improved" or better in PGIC or patient-reported subjective pain relief defined as "moderate" or better	Two categories of pain relief: "good pain relief" and "poor pain relief"	Yes, HRQL incorporated with respect to minor, intolerable and serious AEs. Costs explored in SA	No	1 st line	NA	3 months	No
O'Connor et al.*21	Decision tree	Binary definition of pain improvement; based on "much improved" or better in PGIC or patient-reported subjective pain relief defined as "moderate" or better	Two categories of pain relief: "good pain relief" and "poor pain relief"	Yes, costs and HRQL were incorporated with respect to minor, intolerable and serious AEs	No	1 st line	NA	3 months	No

Study	Model type	Pain measurement	Pain outcomes modelled	AEs modelled	Titration considered?	Treatment lines modelled	Cycle length	Time horizon	Model replicated elsewhere
Smith and Roberts ²⁸	Markov	Two categories of pain reduction: ≥50% or <50%(measurement method not clear)	Two categories of pain reduction: ≥50% or <50%	Yes, costs and HRQL modelled with respect to severe side effects leading to discontinuation	No	1 st , 2 nd , 3 rd , 4 th and 5 th line	1 month	Lifetime	No
Tarride et al. ²⁵	Markov	11-point NRS	3 categories of pain modelled as "mild"/"none" (NRS<4), "moderate" (NRS ≥4 and <7) or "severe" (NRS≥7)	Not modelled	No	1 st line	1 day	12 weeks	Rodriguez et al. ²⁴ , Athanasakis et al. ²⁹

Key:

AE, adverse event; CGIC, Clinician Global Impression of Change; EQ-5D, European Quality of Life – 5 Dimensions; HRQL, health-related quality of life; NA, not applicable; NRS, numerical rating scale; PCIG, Patient Global Impression of Change; PGAI, Physician Global Assessment of Improvement; PGASI, Patient Global Assessment of Self-Improvement; SA, sensitivity analysis; Notes:

^{*} These studies were derived from Cepeda and Farrar¹⁹, but variations existed in the model structure; as such, they were included as original structures within the review.

[†] The systematic review used to inform the meta-analysis conducted by NICE to obtain efficacy estimates within their model included the following pain measurements: visual analogue scales, verbal rating scales, numerical rating scales, proportion of patients attaining particular level of global improvement of pain relief.