RealEndpoints

Defining Value in Neurology Therapeutics

Institute of Medicine Seminar:
Financial Incentives to Support Unmet for Nervous System Disorders

January 21, 2015

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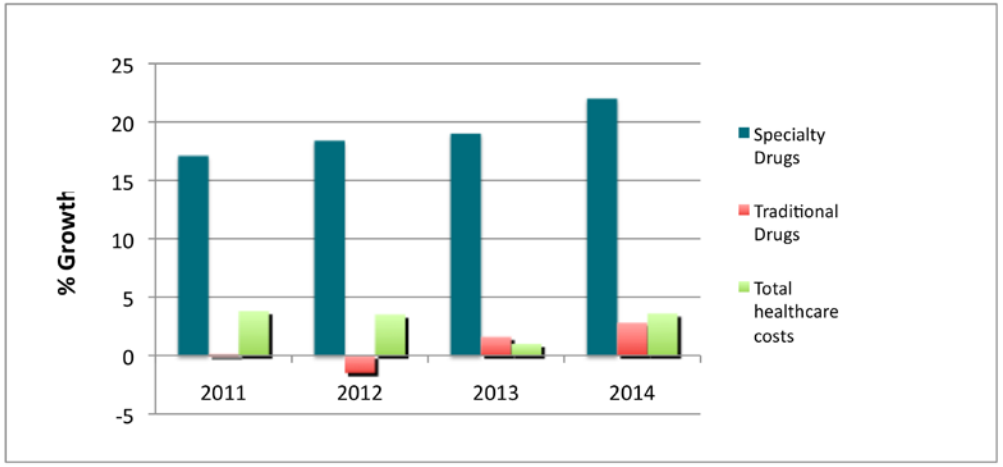
Specialty drugs driving growth in health costs

In 4-5 years, "50% of total drug spend will be for specialty drugs."
- -Albert Thigpen, SVP, Pharmacy Ops, Catamaran (Burrill Report 11/1/2013)

"If you'd asked me a year ago about medical pharmacy, it wasn't even on my radar. Today it's a top priority... a black hole destroying value."
- - Michael Sherman, CMO, Harvard Pilgrim

Growth in drug spending by type vs. total healthcare 2011-2014



SOURCE: Express Scripts 2012 Drug Trend Report; Health Affairs

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The next 12 months could see the entrance of new drugs potentially adding billions of dollars of new category spend

Therapeutic Category	Pipeline
MS	Lemtrada (Genzyme), laquinimod (Teva), ocrelizumab (Genentech), daclizumab (Biogen/AbbVie)
RA	secukinumab (Novartis), sirukumab (J&J/GSK), sarilumab (Sanofi/Regeneron)
Lipid	evolocumab (Amgen), alirocumab (Sanofi/Regeneron), bococizumab (Pfizer)
HCV	sofosbuvir/ledipasvir (Gilead), AbbVie triple (AbbVie), daclatasvir (BMS), asunaprevir/daclatasvir/791325 (BMS), MK-5172/MK-8742 (Merck), lambda/riba/daclatasvir (BMS)
Oncology	palbociclib (Pfizer), nivolumab (BMS) and PDL-1s (Merck, Roche)
Cystic fibrosis	VX-809 + ivacaftor (Vertex), ataluren (PTC Therapeutics)

Employers & insurers

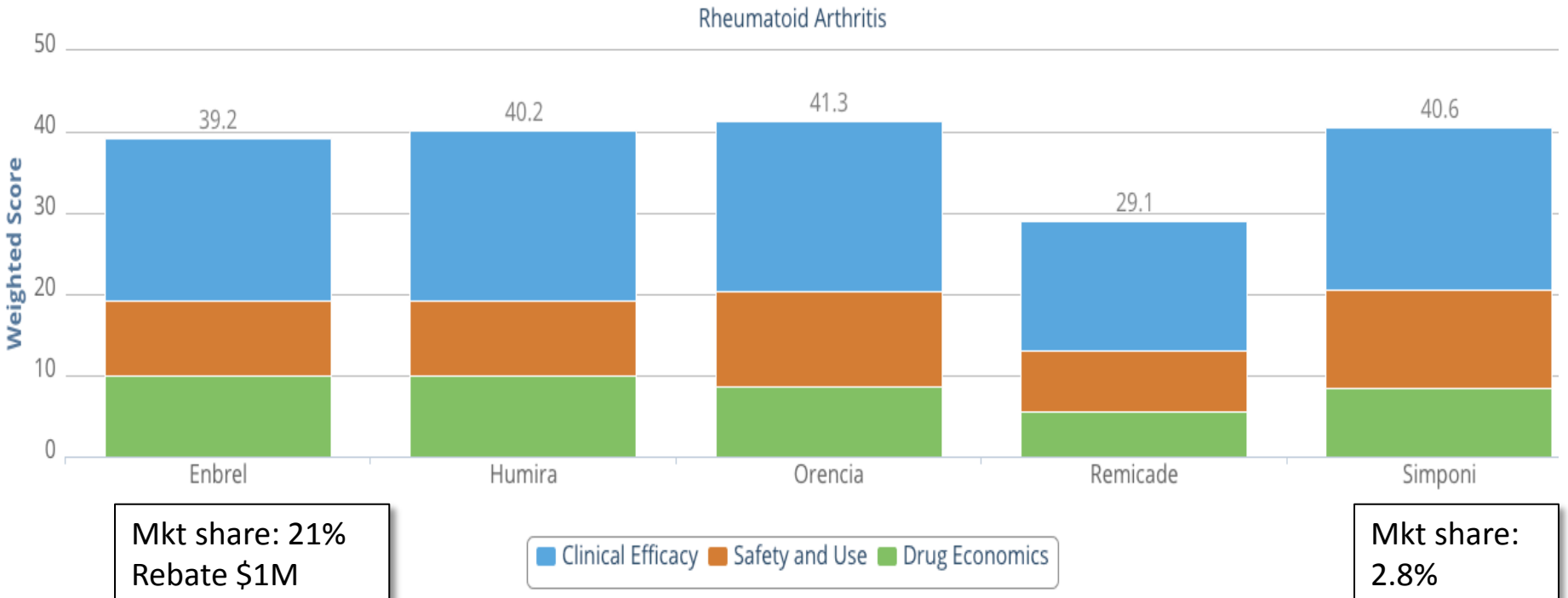
- "75% of my entire healthcare trend is driven by specialty drugs." -- Bob Galvin, CEO, Equity Healthcare"
- "We don't have a discussion with a client in which they're not asking us, at the start of the conversation, 'What are you going to do about specialty?" – VP, Nat'l Care Mgt, Top 3 Insurer
- Optum's dollar-for-dollar trend guarantee on specialty drugs

Providers are now taking on economic risk – moving away from fee-for-service

- ACA (and economics) encouraging the insurance-ization of provider networks
  - NorthShore LIJ on the NY state insurance exchange
  - Major private equity groups getting into the business of creating/supporting ACOs/integrated delivery systems
    - TPG and Evolent (via UPMC)
    - Oak and xG Solutions (via Geisinger)
- 75% of MDs in eastern MA now operating under at least partial risk-sharing structure
- Provider networks – unlike PBMs – see drugs within total cost of care…and will make decisions accordingly

Discounts/rebates now largest commercial cost in pharma* because plans demand them…differentiation hurdles *much* higher

Domain View (Click to view list) Selected value scores in RA and rebates from a 2M-beneficiary plan



Mkt share: 21%
Rebate $1M

Mkt share: 29%
Rebate $900k

Mkt share: 1.4%
Rebate $0

Mkt share: 44%
Rebate $5M

Mkt share: 2.8%
Rebate $0

*Avg. rebate: 29% in 2013 (up from 17% in '07); sales unit decline 2%; rebate increase 10% (Credit Suisse)

RxScorecard™ analysis of relative value of each product from payer point of view

In the absence of dramatic, provable differentiation, importance of cost increases

- The hurdles for “meaningful differentiation” have gotten higher…
  - In part because drugs that cost a lot more have to prove they’re worth more
  - In part because higher costs drive payers and providers to see advantages in older, cheaper therapies
    - The warfarin story
- Express Scripts & HCV
  - Willing to challenge head-on, for first time in a major, potentially fatal disease, the resistance of physicians and patients in order to provide their customers with a mechanism for bending the cost curve in specialty drugs.

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So how do we demonstrate and differentiate “value” – let alone “breakthrough value”?

Pharmaceutical value can and should be quantitatively and transparently defined by identifying and weighting all key elements of medical and economic value

COPD

Show Scenario Notes

Clinical Efficacy

Max Possible Score: 40.0
Domain Weight: 40 %
Range: 2.7 - 10.7

Name	Low Score	High Score
Impact on Disease State (FEV1)	0.00	4.02
Impact on Disease State (Exacerbations)	2.66	7.98
Degree of Disease Modification	0.00	0.00

Safety & Use

Max Possible Score: 30.0
Domain Weight: 30 %
Range: 9.9 - 17.8

Name	Low Score	High Score
Targeting	0.00	0.00
Adherence (Convenience)	0.00	3.33
Adherence (Route of Administration)	2.50	5.00
Adherence (Side Effects & Symptomatology)	0.00	5.00
Severity of Side Effects	2.80	4.50
Monitoring	1.88	2.50

Drug Economics

Max Possible Score: 30.0
Domain Weight: 30 %
Range: 10.4 - 17.9

Name	Low Score	High Score
Health Outcome	0.00	2.50
Potential for Off-Label and Unproven Use	2.50	2.50
Class Price Leverage Opportunity (Forward Looking)	1.88	1.88
Switching Costs	0.30	4.00
Price per Average Course of Therapy	1.25	12.50

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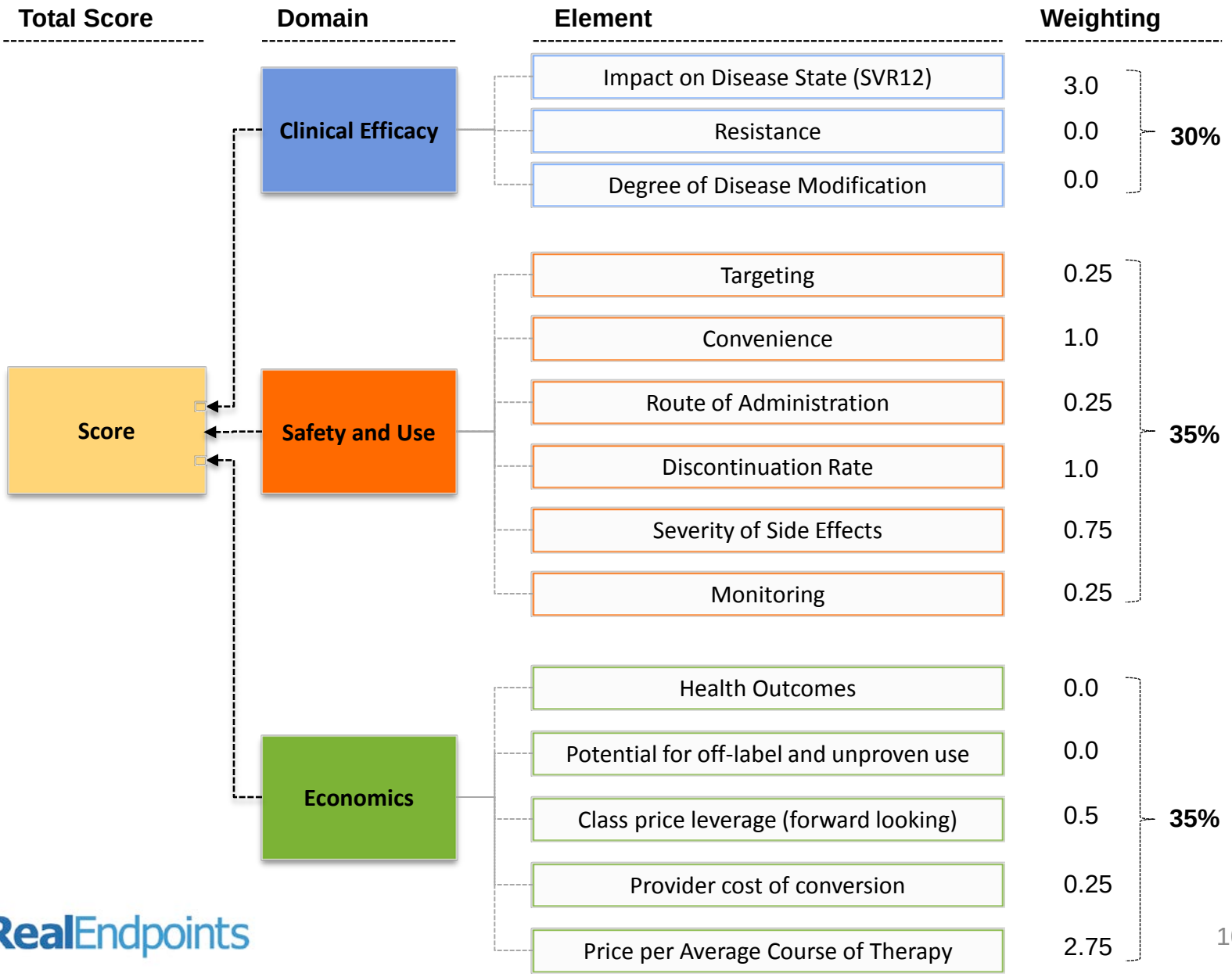
RxScorecard™ analysis of relative value of each product from payer point of view

Elements Driving Value In HCV Today



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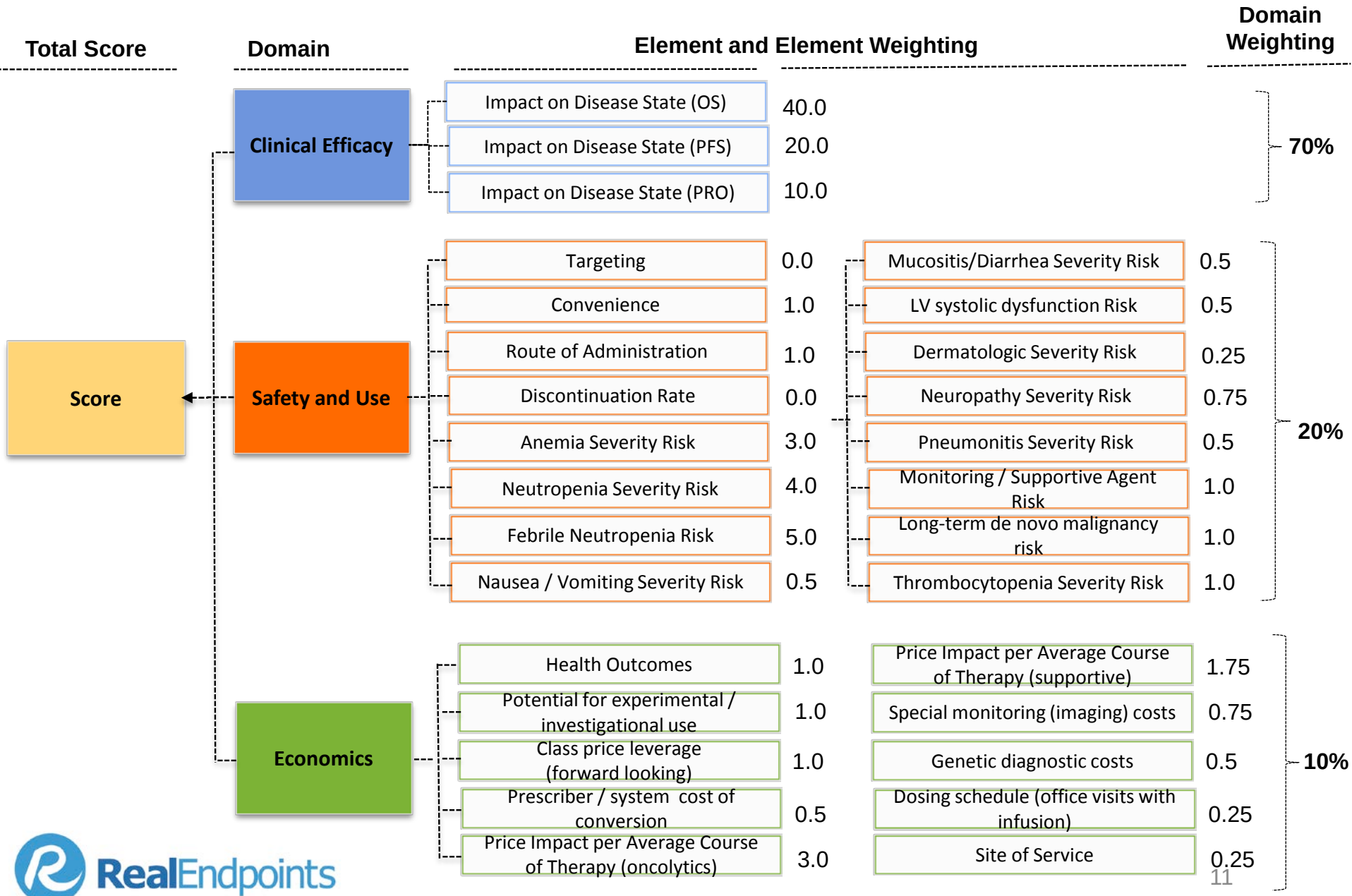
Elements Driving Value In Adjuvant Breast Cancer (ER-/PR-/HER2+)



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Elements of value can be different for patients, payers and providers

Patient-focused economics	• Patient drug cost-share (out-of-pocket) for oncolytics	4.5
	• Patient drug cost-share (out-of-pocket) for supportive agents	2
	• Patient other out-of-pocket costs (procedure, imaging, follow-up visits)	2
	• Patient burden on Quality of Life (based on performance status)	1.5
Payer-focused economics	• Health Outcomes	1
	• Potential for experimental/investigational use	1
	• Class price leverage (forward looking)	1
	• Prescriber or system cost of conversion	0.5
	• Price Impact per Average Course of Therapy (oncolytics)	3
	• Price Impact per Average Course of Therapy (supportive drugs)	1.75
	• Special monitoring (imaging) costs	0.75
	• Genetic diagnostic costs	0.5
	• Dosing schedule (office visits with infusion)	0.25
	• Site of Service	0.25

Once you've defined the list of elements, you need to define value for & within each element

Primary Evidence (Click to view secondary evidence)

Compared to the active comparator (LABA), Advair Diskus 250/50 mcg showed a 30.8% reduction in the mean annual rate of moderate to severe exacerbations. [10] (view all)

Endpoint used for scoring: Statistically Significant (%) Improvement in Rate or Risk of Severe/Moderate or Severe Exacerbations

Impact on Disease State (Exacerbations)	
Superior: ≥ 30% improvement in the rate or risk of severe exacerbations compared to placebo or active comparator (LABA).	10.00
High: ≥ 20% < 30% improvement in rate or risk of severe exacerbations compared to placebo or active comparator (LABA).	7.50
Moderate: ≥10% < 20% improvement in rate or risk of severe exacerbations compared to placebo or active comparator (LABA).	5.00
Low: ≥ 20% improvement in rate or risk of moderate and severe exacerbations compared to placebo or active comparator (LABA).	**2.50**
Negligible: No significant improvement in rate or risk of moderate and severe exacerbations compared to placebo or active comparator (LABA).	0.00

×

Strength of Evidence (Exacerbations)	
Head-to-Head Trial vs. SOC Powered for Superiority	1.00
Head-to-Head Trial vs. SOC Powered for Non-Inferiority	0.90
Head-to-Head Trial vs. Active Comparator (not SOC) Powered for Superiority	**0.80**
Head-to-Head Trial vs. PBO Powered for Superiority	0.70

=

Score Calculation	
Σ	**Element Score: 2.0**
*	Element Weight: 1.33 ×
Σ	**Weighted Score: 2.7**

* Element weight reflects the relative importance of this element vs. all other scoring elements in Rx Scorecard. Weights range from 0.25 to 2.0.

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But the relative value of drugs *can* and *should* be compared, transparently and quantitatively…ultimately creating a true definition of value

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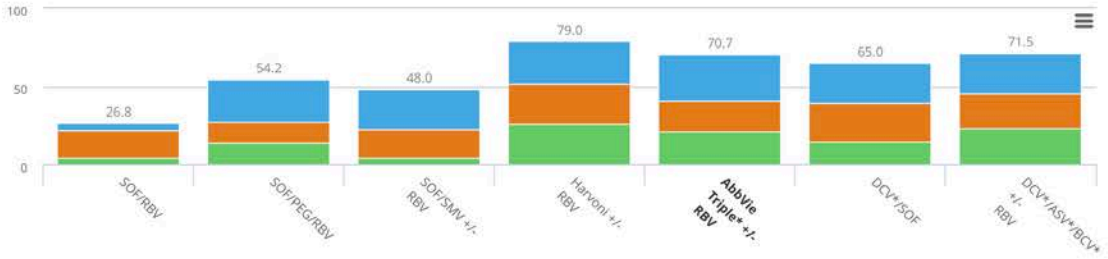
AbbVie Triple* +/- RBV (ABT-450/r/267/333 +/- ribavirin)

Score: 70.7 out of 100.0
Range: 0.0 - 78.9
Genotype 1a Naive



(Indicates a drug that has not been FDA approved.)*

Clinical Efficacy

Score: 30.0 of 30.0
Range: 0.0 - 30.0

Element	Weighted Score
Impact on Disease State - SVR12	30.0
Impact on Disease State - Resistance	0.0
Degree of Disease Modification	0.0
Σ	30.0

Safety & Use

Score: 19.6 of 35.0
Range: 0.0 - 25.8

Element	Weighted Score
Targeting	1.3
Adherence (Convenience)	4.5
Adherence (Route of Administration)	2.5
Adherence (Side Effects & Symptomatology)	10.0
Severity of Side Effects	0.8
Monitoring	0.6

Drug Economics

Score: 21.1 of 35.0
Range: 0.0 - 26.2

Element	Weighted Score
Health Outcome	0.0
Potential for Off-Label and Unproven Use	0.0
Class Price Leverage Opportunity (Forward-Looking)	1.3
Cost of Conversion	0.0
Price per Average Course of Therapy	19.8
Σ	21.1

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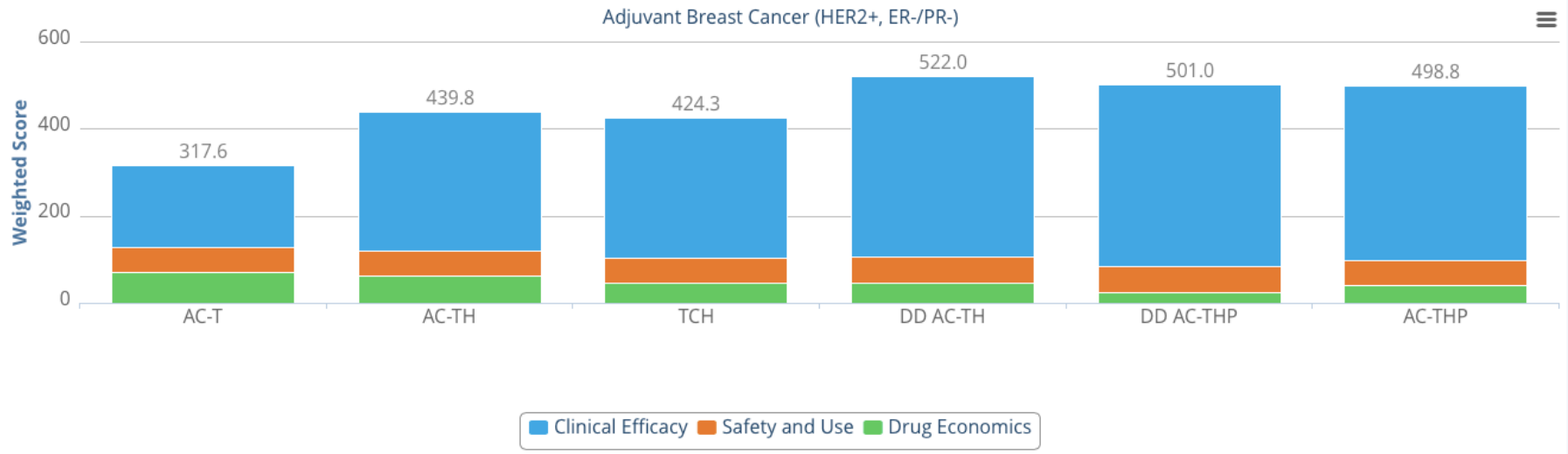
And relative value comparisons are possible – and necessary – in all therapeutic areas

Adjuvant Breast Cancer (HER2+, ER-/PR-)

Hide Scenario Notes

(Indicates a drug that has not been FDA approved.)*

Domain View (Click to view list)



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