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Reimbursement Outcomes for Combination Therapies vs Monotherapies in Lung Cancer and Multiple Myeloma in the Top Five European Markets

Milena Izmirlieva, Director, Life Sciences Research
milena.izmirlieva@globaldata.com
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Combination therapies face greater market access challenges in theory



- Combination therapies face particular challenges with gaining market access
- Add-on therapy often unable to achieve cost effectiveness even if priced at zero
- Theoretically, cost-effectiveness challenges for combination therapies should be evident in both price-setting and price-taking healthcare systems, and regardless of whether QALYs or clinical effectiveness approaches are used
- But is this true in practice?

PharmOnline International (POLI) - Pharmaceutical Pricing & Reimbursement Database

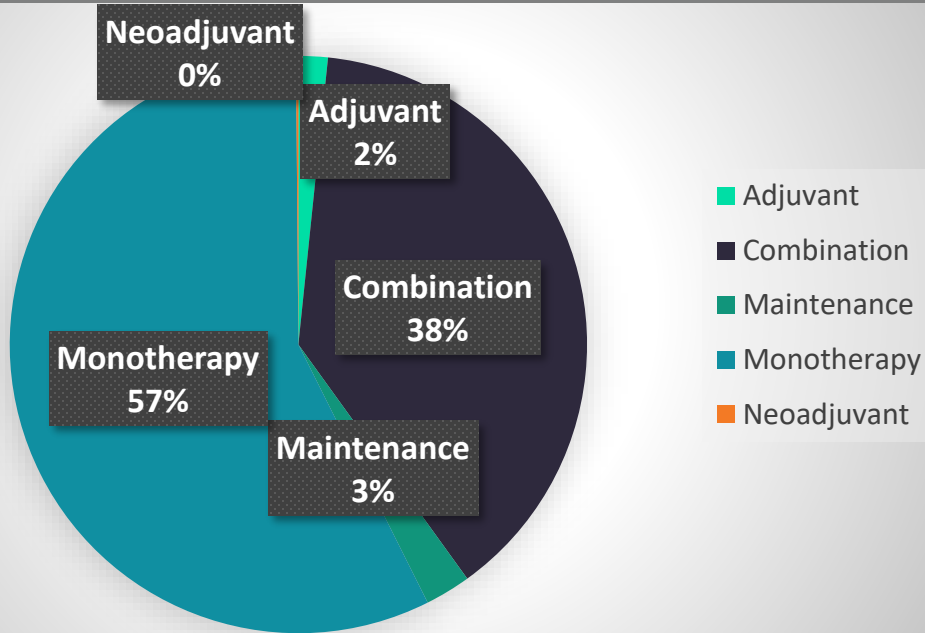
The POLI database helps users develop and manage ongoing global pricing and reimbursement strategies. It provides the price/cost, access timeline and regulatory status (reimbursement, orphan, parallel trade, etc.) of pharmaceuticals across 80 developed and emerging markets, based on an accurate, consistent pricing methodology.

- To assess this, we reviewed pricing and reimbursement outcomes for all originator drugs first priced between 1 January 2011 and 31 December 2020 in France, Germany, Italy, Spain and the United Kingdom, based on POLI data
 - POLI provides price level and reimbursement status for 80 countries
 - Reimbursement outcomes available by indication
 - Combination vs monotherapy status also available in POLI

Proportion of combination therapies in oncology



All oncology drugs first priced over the 10-year period in the top 5 European markets



Source: GlobalData

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- Combination therapies are particularly common in oncology
- Across cancer types, combination therapies accounted for 38% of treatments first priced over the 10-year period in the five countries

Number of products by type (combined for France, Germany, Italy, Spain and UK)

Type of therapy	All oncology	Lung cancer	Multiple myeloma
Adjuvant	61		
Combination	1429	113	314
Maintenance	95		43
Monotherapy	2130	271	42
Neoadjuvant	5		
Total	3720	384	399

Only products which were approved between 1 January 2011 and 31 December 2020 are included

Source: GlobalData POLI database

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- Combination therapies account for 29.4% of treatments in lung cancer, and 78.7% in multiple myeloma in France, Germany, Italy, Spain, and the United Kingdom combined.
- In comparison, across all cancer types in these countries, combination therapies account for 38.4% of all treatment types.

Reimbursement outcomes: lung cancer



Number of products by reimbursement level: lung cancer

	Monotherapy	Combination
France		
0%	6	5
100%	38	4
30%	6	
Non-T2A List	11	1
Germany		
90% (min copayment: EUR5, max copayment: EUR10)	58	13
Italy		
0%	17	7
100%	31	2
Spain		
0%	8	8
100%	17	3
Reimbursed in hospital only	19	
United Kingdom		
100%	60	13

Source: GlobalData POLI database

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- Combination therapies more likely to face reimbursement rejection compared to monotherapies
- Across the five countries, 20 out of the 56 combination therapy presentations (equivalent to 35.7%) were rejected for reimbursement compared to 11.4% (31 out of 271) for monotherapy presentations

Reimbursement outcomes: multiple myeloma



Number of products by reimbursement level: multiple myeloma

	Monotherapy	Combination
France		
100%	7	6
Non-T2A List	2	8
Germany		
90% (min copayment: EUR5, max copayment: EUR10)	10	50
Italy		
0%		1
100%	7	33
Spain		
0%		6
100%		7
100% (Notified private sector price, public price N/A)	3	
Reimbursed in hospital only	5	
United Kingdom		
100%	8	21

Source: GlobalData POLI database

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- Higher rate of reimbursement rejection decisions for combination therapies: 5.3% of combination therapy presentations (7 out of 132) were rejected for reimbursement, while every single monotherapy was approved for reimbursement.
- Considering that combination therapies outnumber monotherapies by more than threefold, the higher likelihood of denying reimbursement for combination therapies suggests a potential loss for patients.

What about impact on price?



- Italy: reimbursement eligibility assessed before price, but price set through negotiation; final reimbursement decision takes price into account and products deemed to be less cost-effective end up in lower reimbursement tier unless manufacturer offers risk sharing agreement to gain final reimbursement.
 - 78% received 0% reimbursement among combination therapies compared to 35% among monotherapies in lung cancer;
 - 3% received 0% reimbursement among combination therapies compared to 0% among monotherapies in multiple myeloma
- Spain: price is set only for reimbursable products, price negotiation with manufacturers, products assigned different reimbursement levels
 - 73% of combination therapies got 0% reimbursement compared to 18% of monotherapies in lung cancer
 - 46% of combination therapies got 0% reimbursement compared to 0% of monotherapies in multiple myeloma

Number of products by ASMR rating granted in France: lung cancer

	Monotherapy	Combination
ASMR III	11	
ASMR IV	30	1
ASMR V	14	
Insufficient SMR	1	1
Missing		6
Reimbursement not requested by manufacturer		2
Blank	5	6

Source: GlobalData POLI database

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Number of products by ASMR rating granted in France: multiple myeloma

	Monotherapy	Combination
ASMR III	2	
ASMR IV	7	4
ASMR V	2	4
Insufficient SMR		4
Blank		14

Source: GlobalData POLI database

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- ASMR affects price level: I, II and III subject to efficiency evaluation and given a European price guarantee, while IV and V enter price negotiations
- Combination therapies less likely to get favourable ASMR rating
- Combination therapies more likely to get insufficient SMR and missing ASMR and were the only ones with 'reimbursement not requested by manufacturer'



Number of products by G-BA rating granted in Germany: lung cancer

	Monotherapy	Combination
Considerable added benefit	22	
Low added benefit	3	
Major added benefit	3	
No added benefit	24	7
Blank	6	6

Source: GlobalData POLI database

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Number of products by G-BA rating granted in Germany: multiple myeloma

	Monotherapy	Combination
Considerable added benefit	4	6
No added benefit	3	8
Not quantifiable		3
Blank	3	33

Source: GlobalData POLI database

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- Benefit assessment affects price: products with major, considerable, low and non-quantifiable added benefit enter price negotiation, while others are subject to internal reference pricing.
- No combination therapies in lung cancer and only 18% of those in multiple myeloma qualified for price negotiation compared to 48% of monotherapies in lung cancer and 40% of monotherapies in multiple myeloma.

- All monotherapies and combination therapies recorded in POLI as reimbursable as reimbursement is possible at the local level
- Obscures the fact manufacturer may be required to provide a confidential discount under patient access scheme (PAS) to gain positive NICE guidance.
- NICE guidance was reviewed and, in fact, NICE had issued negative guidance for:
 - 5 monotherapies and 11 combination therapies in lung cancer
 - 4 monotherapies and 4 combination therapies in multiple myeloma
- Products with positive NICE guidance may have been required to enter a PAS to gain positive guidance.

- Empirical research confirms the theoretical expectations for lung cancer and multiple myeloma
- Combination therapies do have a more difficult time in gaining reimbursement
- Even when they gain reimbursement they are more likely to be placed in lower reimbursement tier
- They face higher pressure on prices than monotherapies, although that pricing pressure is not always obvious and may come in the form of risk sharing agreements and being subjected to internal price linkage or internal reference pricing



For any questions contact:
milena.izmirlieva@globaldata.com