Repurposed Drugs Launched Under the AMNOG in Germany: Effects on Benefit Assessment and Price Development

Sake SM, Martyniszyn-Eiben A, Glüsen M, Berger I, Jürges L, Zavatta E, Schönermark MP[1,2]
[1]SKC Beratungsgesellschaft mbH, Hannover, Germany, [2]Medizinische Hochschule Hannover, Hannover, Germany

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Objectives

Drug repurposing, the use of established drugs in new, previously unrelated indications, offers many potential advantages, such as lower development costs and higher success probabilities in clinical trials, which is thought to be attractive especially for orphan indications. This analysis was conducted to assess the success of repurposed drugs in German HTA procedures and subsequent price negotiations based on AMNOG.

Methods

A drug was defined as repurposed if it was launched under the AMNOG in more than one therapeutic area as defined by the G-BA. Utilizing our MAIS database, containing information on dossier content, benefit assessment, G-BA resolution and negotiated rebate of all AMNOG procedures ever performed, we compared procedure outcomes of repurposed drugs to those active substances approved in more than one indication in a single therapeutic area (non-repurposed drugs).

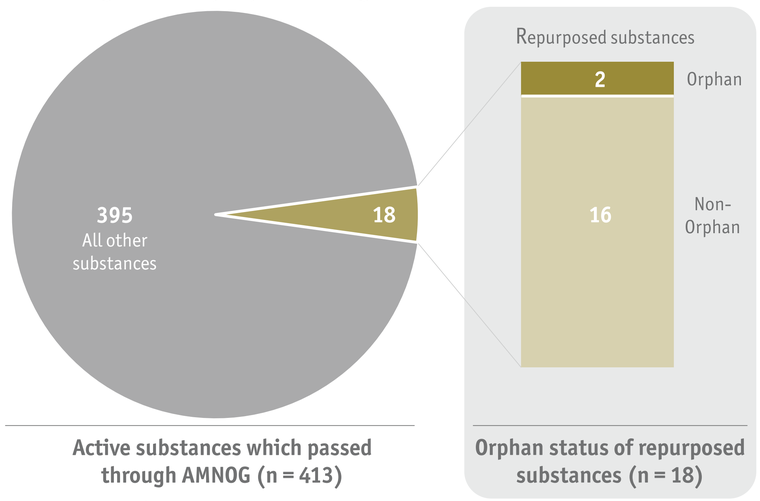
Results

The distribution of therapeutic areas of AMNOG procedures and orphan designations differs between repurposed and non-repurposed drugs

The **G-BA** assigns AMNOG procedures of individual active substances to 14 different **therapeutic areas**. These are derived from the respective approved indication to be evaluated. The following therapeutic areas exist:

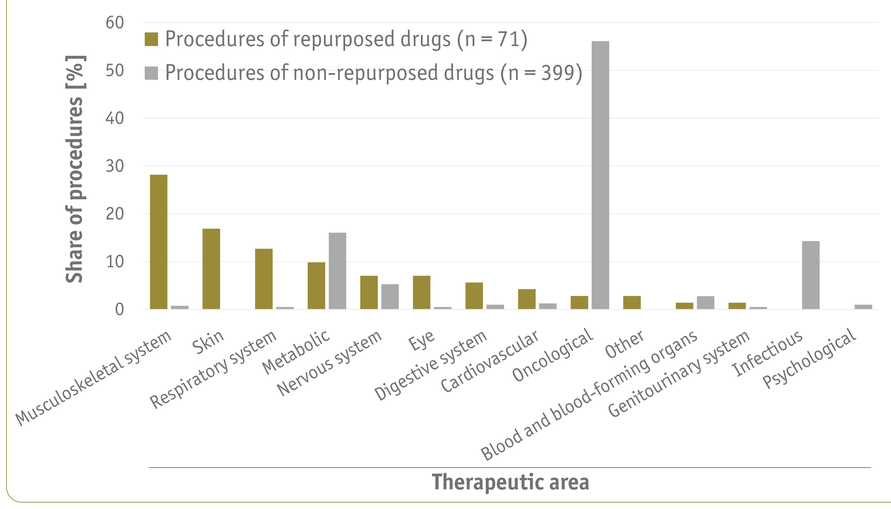
- Cardiovascular diseases
- Diseases of blood and blood-forming organs
- Diseases of the digestive system
- Diseases of the genitourinary system
- Diseases of the musculoskeletal system
- Diseases of the nervous system
- Diseases of the respiratory system
- Eye diseases
- Infectious diseases
- Metabolic diseases
- Oncological diseases
- Other
- Psychological diseases
- Skin diseases

Figure 1: Repurposed drugs launched under the AMNOG



- As of Oct 6th, 2022, 413 active substances have passed through AMNOG since it came into force in 2011.
- 18 of these 413 active substances (~4.4%) were identified to be approved in more than one therapeutic area as defined by the G-BA.
- 11.1% of repurposed (2/18) compared to 30.0% of all AMNOG substances (data not shown) have an active orphan drug status.

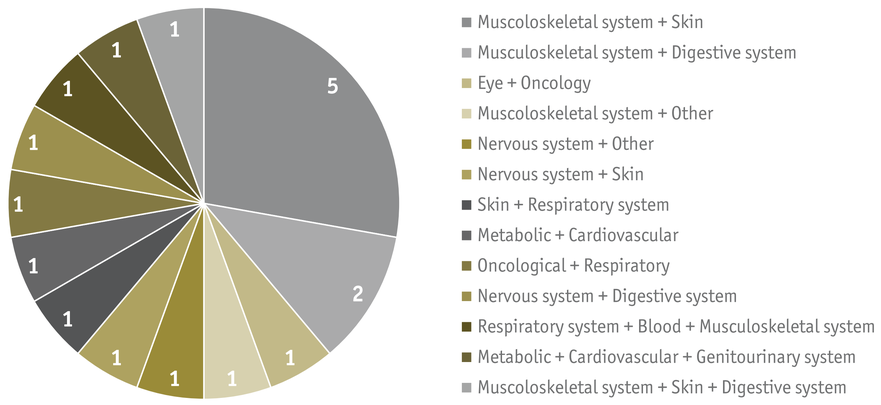
Figure 2: Share of procedures per therapeutic area



- AMNOG procedures for repurposed drugs were performed in 12 out of the 14 therapeutic areas – procedures for infectious and psychological diseases did not occur.
- The distribution of therapeutic areas differs significantly between procedures of repurposed and non-repurposed drugs:
  - The most common therapeutic areas of repurposed drugs were diseases of the musculoskeletal system followed by skin diseases and diseases of the respiratory system.
  - The most common therapeutic areas of non-repurposed drugs were oncological, metabolic and infectious diseases.

Method deep dive
For all shown analyses only initial submissions and procedures due to indication extension were considered. Other procedure initiators such as limitation expiry or loss of orphan status were not included.

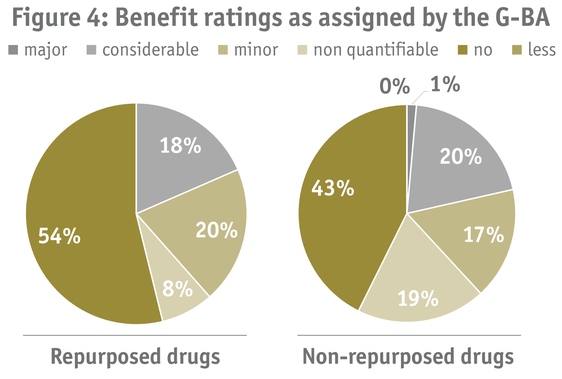
Figure 3: Frequency of therapeutic area combinations of repurposed drugs



- The most frequent combination of therapeutic areas is diseases of the musculoskeletal system together with skin diseases for 5 active substances.
  - All are immunosuppressive agents approved for the treatment of arthritis and dermatitis or psoriasis.
  - 4 of these 5 active substances are monoclonal antibodies.
- 2 active substances are approved for the treatment of diseases of the musculoskeletal and digestive system.
  - Both substances are approved for the treatment of arthritis and ulcerative colitis.
- 3 active substances passed through the AMNOG in three different therapeutic areas.
  - One substance is approved for the treatment of diabetes and heart and kidney failure, two are approved for the treatment of allergic and/or autoimmune diseases.

While the additional benefit categories between repurposed and non-repurposed drugs does not differ profoundly, the current negotiated gross box rebate is lower for repurposed drugs

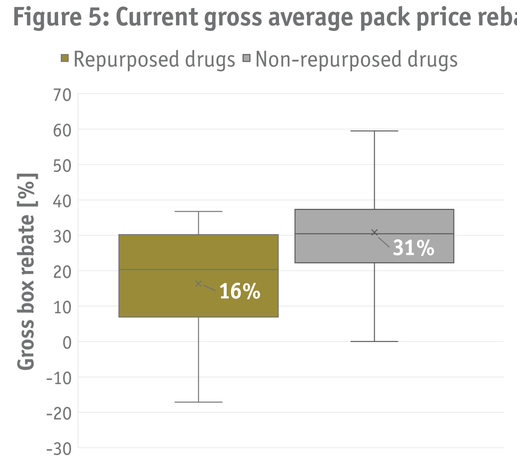
Figure 4: Benefit ratings as assigned by the G-BA



- The rate of non-quantifiable additional benefit ratings is more than twice as high for non-repurposed (19%) vs. repurposed (8%) drugs.
- With 54% the majority of procedures of repurposed drugs resulted in no additional benefit compared to 43% of procedures of non-repurposed drugs.
- Both repurposed and non-repurposed drugs are only very rarely granted the best or worst benefit categories major additional (0% vs. 1%) and less (0% vs. 0%) benefit.
- The shares of minor (20% vs. 17%) and considerable (18% vs 20%) additional benefits are similar for procedures of repurposed and non-repurposed drugs.

Method deep dive
The benefit rating per procedure is given. If there were several subpopulations within a procedure and the G-BA has decided on different benefit ratings per subpopulation, the highest additional benefit was included in the evaluation.

Figure 5: Current gross average pack price rebates



- The average negotiated gross box rebate is almost half as low for repurposed (16%) vs. non-repurposed drugs (31%), resulting in a reimbursement amount closer to the original launch price for repurposed drugs.
- The large whiskers of the box plots show that the negotiated discounts cover a wide range in both drug classes.

Method deep dive
After the benefit rating by the G-BA, the pharmaceutical companies negotiate the reimbursement amounts with the Sickness Funds. For this analysis the gross rebate was calculated by the reimbursement amount of the pack plus manufacturer's discount with value added tax divided by the launch price. For the repurposed drugs only rebates were considered, if price negotiations have already taken place in at least two therapeutic areas.

Conclusion

- The rate of orphan designations of repurposed active substances as defined in this analysis is three times lower than for their non-repurposed counterparts, contradicting the thought attractiveness of drug repurposing for orphan indications. The difference in the distribution of therapeutic areas of repurposed and non-repurposed drugs is possibly mainly due to the use of agents in etiologically related diseases, which, however, affect different organ systems (e.g., (auto)immune diseases or diabetes mellitus and cardiac and renal insufficiency).
- While benefit ratings of repurposed and non-repurposed drugs do not differ profoundly, the average negotiated rebate for repurposed drugs is almost half as low for non repurposed drugs.

The lower average negotiated rebate for repurposed drugs cannot solely be explained by the extent of the granted additional benefit. Hence, in addition to the launch sequence for repurposed drugs, the same applies as for other drugs: Besides the granted additional benefit, the result of the price negotiation also depends on a convincing value story, (sub-) population sizes, costs of the appropriate comparator therapy and a harmonized strategy for pricing throughout the complete AMNOG process.

schönermark kielhorn collegen

SKC Beratungsgesellschaft mbH | Hannover | Germany |
www.skc-consulting.de | Fon: +49 511 64 68 14-0
Email: sake@skc-beratung.de

All analyses have been conducted with our own comprehensive MAIS database that contains and links AMNOG information of all completed and ongoing benefit assessment procedures according to §35a SGB V of the German Federal Joint Committee (G-BA).