HPR154

Evaluation of the updated French Autorisation d'Accès Précoce (AAP) Early Access Authorization Pathway

Elise Evers[1], Sesh Rahim[2], Oliver Darlington[2] and Andrew Mumford[2]

[1] **Initiate Consultancy**, Zug, Switzerland [2] **Initiate Consultancy**, Northampton, UK

Background

In July 2021, the French Autorisation Temporaire d'Utilisation (ATU) underwent a reform aimed at improving the speed of Health Technology Assessment (HTA) reviews and enhancing access to innovative therapies:

- **Accès Compassionnel (AC)** replaced the Autorisation Temporaire d'Utilisation nominative (ATUn) and Recommandation Temporaire d'Utilisation (RTU).
- **Autorisation d'Accès Précoce (AAP)** replaced the ATU de cohorte (ATUc), ATU d'extension d'indication (ATUei), post-ATU and Prise En Charge Temporaire (PECT)

To be granted early access, a therapy or product must meet the following criteria:

1. Absence of appropriate treatment
2. Impossibility of delaying the treatment
3. Strong presumption of efficacy and safety of the medicine
4. Presumed innovative nature of the medicine

Objectives

Our goal is to assess the products reviewed by the Transparency Committee (TC) under the AAP pathway since its inception (up to March 2023) and identify trends in disease or treatment categories and predictors of a positive submission outcome. Additionally, we will propose recommendations for manufacturers to enhance their likelihood of a successful submission.

Methods

All 124 AAP submissions are publicly available from the Haute Autorité de Santé (HAS) website[1] and were reviewed as of 31 March 2023. The following information was collected and tabulated in Excel:

- Drug name, disease category and indication
- AAP status (approved, declined or renewed)
- Criteria met (**1**, **2**, **3** and **4**)

Descriptive statistics were produced to infer any trends in disease categories, therapy areas, and reasons for rejection.

Results

Figure 1. AAP decisions (March 2023)

Figure 2. Therapies submitted for AAP in France

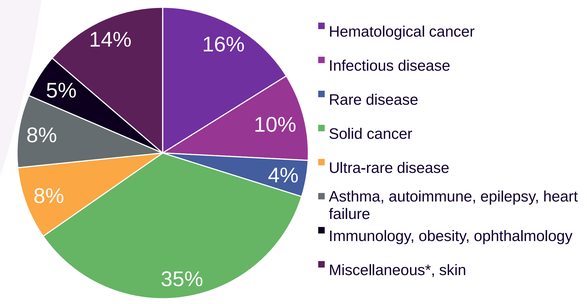
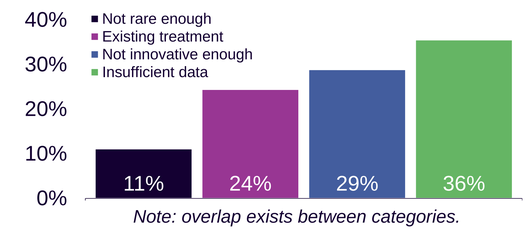


Figure 3. Reasons for AAP rejection



Note: overlap exists between categories.

Out of the 124 submissions that were evaluated, 104 (84%) were approved for AAP, which included renewals of previously granted authorization (15 out of 124), with the remaining 20 submissions being rejected (Figure 1).

The largest proportion of submissions were in oncology (46%), with 35% of treatments indicated for solid cancers, and 16% for hematological cancers (Figure 2). Rare and ultra-rare diseases accounted for 4% and 8% of submissions, respectively, and included conditions such as achondroplasia, Pompe disease, amyloidosis, and progeria. Additionally, nine submissions (7%) were for COVID-19 treatments.

All treatments for rare diseases were approved, whereas 10% of therapies for ultra-rare diseases were not, corresponding to an overall success rate in rare and ultra-rare diseases of 80% (Table 1). Submissions in oncology were also frequently successful, with 80% of treatments for hematological cancers and 73% of solid cancers treatments resulting in positive outcomes. Treatments for infectious diseases were only approved or renewed in 75% of cases, with three out of nine COVID-19 treatments being refused for AAP.

In many cases, multiple reasons were cited by the TC for refusing AAP (Figure 3). The main reasons cited for rejection were insufficient efficacy and safety data (36%), lack of innovation compared with existing treatment options (29%), the availability of existing treatment options (24%), and the disease not being rare enough to qualify for special consideration (11%).

Table 1. Decisions for main disease groups

Decision	Solid cancer	Hematological cancer	Infectious disease	Rare disease	Ultra-rare disease
No	14%	10%	25%	0%	10%
Yes	73%	80%	67%	80%	80%
Renewal	14%	10%	8%	20%	10%

**Miscellaneous category includes graft vs. host diseases, knee cartilage repair therapy, sickle cell disease, hydrocephaly, and methotrexate toxicity.*

Conclusion

In conclusion, the assessment of products reviewed by the TC under the AAP pathway since its inception up to March 2023 demonstrated that most submissions were approved, with solid and hematological cancers being the most common therapy areas. Treatments for rare and ultra-rare diseases, and oncology treatments had high submission success rates. The main reasons for rejection were insufficient efficacy and safety data, lack of innovation, the availability of existing treatment options, and the disease not being deemed rare enough. Manufacturers can use these findings to enhance their likelihood of a successful submission by focusing on providing robust efficacy and safety data and effectively demonstrating the innovative nature of new therapies. Overall, the findings highlight the importance of the AAP pathway in providing access to innovative treatments for patients.

References

1. Haute Autorité de Santé. (2023). Accueil. Haute Autorité de Santé. https://www.has-sante.fr/. Accessed April 21, 2023.