**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

**ZAVEDOS** (idarubicin), anthracycline

**No clinical added value demonstrated in comparison with daunorubicin in induction therapy for newly diagnosed acute myeloid leukaemia in children**

**Main points**
- ZAVEDOS, in combination with cytarabine, now has marketing authorisation in the 1st-line setting for remission induction in previously untreated children with acute myeloid leukaemia (AML).
- As in adults, anthracyclines play a key role in chemotherapy regimens, particularly induction for AML.
- In the context of induction regimens, intravenous idarubicin is an alternative to daunorubicin in the treatment of previously untreated childhood AML.

**Pre-existing indications**
- ZAVEDOS already has marketing authorisation in adults in the treatment of acute myeloid leukaemia and relapsed acute lymphoblastic leukaemia.

**Therapeutic use**
- Therapy for AML consists of two treatment phases:
  - An induction phase: standard induction therapy generally consists of ARACYTINE (cytarabine) at conventional doses and anthracyclines (daunorubicin or idarubicin) or an anthracenedione (mitoxantrone) combined with a third cytotoxic agent, etoposide or 6-thioguanine. This obtains complete remission in about 80% of cases;
  - A consolidation phase: this phase generally involves three cycles of intensive chemotherapy, typically with high-dose ARACYTINE and, depending on the regimen, anthracyclines.
- To date, in France, two medicines have marketing authorisation specifically for paediatric AML:
  - CERUBIDINE (daunorubicin);
  - ZAVEDOS (idarubicin) in previously untreated childhood AML, in combination with cytarabine as 1st-line remission induction.

**Role of the medicinal product in the therapeutic strategy**
- In the context of induction regimens, intravenous ZAVEDOS is an alternative to CERUBIDINE in the treatment of previously untreated childhood AML.

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*This summary does not cover these indications.*

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Clinical data

- For decades, anthracyclines have played a key role in chemotherapy regimens for AML, in both adults and children.
- The data supporting idarubicin's extension of indication to AML induction therapy, in previously untreated children, are mainly from a study that compared idarubicin 12 mg/m²/day IV to daunorubicin (30 mg/m²/12h IV) as part of polychemotherapy regimens including cytarabine and etoposide. On D15, the proportion of early responders (≤ 5% blasts) was higher in children treated with idarubicin than in the daunorubicin group: 83% (119/144) versus 69% (103/149), p=0.01 (primary endpoint). No difference was observed between the two groups on the other criteria, including event-free survival and overall survival at 5 years.
- Like the other anthracyclines, idarubicin's profile is characterised by cardiotoxicity, myelosuppression and gastrointestinal toxicity.

Special prescribing conditions

- Medicine for hospital prescription.
- Prescription restricted to oncology or haematology specialists or doctors with cancer training.
- Medicinal product requiring special monitoring during treatment.

Benefit of the medicinal product

- The actual clinical benefit* of ZAVEDOS is substantial.
- ZAVEDOS does not provide any clinical added value** (CAV V) in comparison with daunorubicin as induction therapy for AML in previously untreated children, based on the results of the study that compared the efficacy of idarubicin to daunorubicin in an induction regimen.
- Recommends inclusion on the list of reimbursable products for hospital use in this indication.

* The actual clinical benefit (ACB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

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