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Janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

12 July 2017

HALDOL DECANOATE AND HALDOL® ALL DOSAGE FORMS (TABLETS, ORAL SOLUTION, INJECTION)

Dear Healthcare Professional,

On behalf of Janssen, AM Mangion Ltd., would like to inform you that the European Medicines Agency (EMA) selected all dosage forms of Haldol® and Haldol Decanoate for an Article 30 referral, as part of an ongoing review of major and important compounds across the European Union (EU). The aim of the referral procedure was to harmonise the product information across the EU Member States. The review was carried out by the EMA's Committee for Medicinal Products for Human Use (CHMP) which adopted a harmonised Summary of Product Characteristics (SmPC), labeling and package leaflet for Haldol® tablets, oral solution, solution for injection, Haldol Decanoate®, which will become valid once the Maltese Health Authorities approve it. Haldol Decanoate® 50mg for Injection is being imported in Malta via Central Procurement Supplies Unit.

The SmPCs for each formulation are now consistent in all EU Member States.

Summary

- Indications have been harmonised across all EU Member States and have been updated to current medical terminology for both Haldol and Haldol Decanoate. This has resulted in some Member States now having indications that were previously not registered. (The harmonised indications are appended to this letter).
- Indications where evidence was considered as insufficient, or a risk-benefit ratio as negative, have been deleted: Hiccups.
- The maximal daily dosage for Haldol was reduced to:
    - 10 to 20 mg depending on the indication in adults
    - 5 mg in elderly

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- 3 to 5 mg depending on the indication in pediatrics
- To lower side effects always the lowest possible dose should be given

- Posology and method of administration section for Haldol Decanoate has been changed as follows:
  - Patients must be stabilized on oral Haldol before switching to Haldol Decanoate at 10-15 times the last 24 hour dose.
  - It is recommended Haldol Decanoate be given every 4 weeks by deep intramuscular injection.
  - The dose may be adjusted up or down to a maximum of 300 mg every 4 weeks in 50 mg increments.
  - Supplements with non-decanoate Haldol may be needed during initial transfer. The total dose must not exceed the equivalent of 20 mg/day of oral Haldol
  - For the elderly,
  - The recommended starting dose is 12.5 to 25 mg every 4-weeks even if the dose conversion suggests a larger dose.
  - Dose may be adjusted according to individual patient response every 4-weeks to a maximum of 75 mg.
  - A dose of greater than 75 mg every 4-weeks should only be considered if the patient previously tolerated a higher oral Haldol dose equivalent.
  - Supplements with non-decanoate Haldol may be needed during initial transfer. The total dose must not exceed the equivalent of 5mg/day or the previously tolerated dose of oral Haldol
- Contraindications related to QT prolongation have been added such as
  - Known QT prolongation
  - Ventricular arrhythmia or torsade de pointes
- Interaction with other medicinal products and other forms of interaction were updated
  - To include medications which may potentiate the risk of QT prolongation and cardiac arrhythmias
  - Or increase the Haloperidol plasma level.
- Other sections of the SmPC that were updated:

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- Fertility, pregnancy and lactation
- Undesirable effects

Please see following pages for further details on the harmonised indications and posology for each dosage form.

Call for reporting
Healthcare professionals are reminded to continue to report suspected adverse reactions associated with this product in accordance with the national spontaneous reporting system. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the ADR Reporting Website: www.medicines authority.gov.mt/adrportal

Alternatively kindly contact directly Mr Claude Vella Bonanno at A.M. Mangion Ltd, Mangion Building, New Street Off Valletta Road, Luqa LQA 6000, Malta or on phone number 00356 23976000 or email at rp@ammangion.com

Company contact points

If you have further questions or require additional information, please contact Ms Gaby Ganado on +356 2397 6000 or gganado@ITS.jnj.com

Yours faithfully,

Claude Vella Bonanno
Lead Responsible Person
AM Mangion Ltd.

HALDOL Decanoate

Therapeutic indications

HALDOL Decanoate is indicated for the maintenance treatment of schizophrenia and schizoaffective disorder in adult patients currently stabilised with oral haloperidol (see section 5.1).

Posology and method of administration

Treatment initiation and dose titration must be carried out under close clinical supervision.

Posology

The individual dose will depend on both the severity of the symptoms and the current oral haloperidol dose. Patients must always be maintained on the lowest effective dose.

As the initial dose of haloperidol decanoate is based on a multiple of the daily oral haloperidol dose, specific guidance on switching from other antipsychotics cannot be provided (see section 5.1).

Adults aged 18 years and above

Table 1: Haloperidol decanoate dose recommendations for adults aged 18 years and above

Transition from oral haloperidol • A haloperidol decanoate dose of 10 to 15 times the previous daily dose of oral haloperidol is recommended. • Based on this conversion, the haloperidol decanoate dose will be 25 to150 mg for most patients.
Continuation of treatment • It is recommended to adjust the haloperidol decanoate dose by up to 50 mg every 4 weeks (based on individual patient response) until an optimal therapeutic effect is obtained. • The most effective dose is expected to range between 50 and 200 mg. • It is recommended to assess the individual benefit-risk when considering doses above 200 mg every 4 weeks. • A maximum dose of 300 mg every 4 weeks must not be exceeded because the safety concerns outweigh the clinical benefits of treatment.
Dosing interval • Usually 4 weeks between injections. • Adjustment of the dosing interval may be required (based on individual patient response).

Supplementation with non-decanoate haloperidol • Supplementation with with non-decanoate haloperidol may be considered during transition to HALDOL decanoate, dose adjustment or episodes of exacerbation of psychotic symptoms (based on individual patient response). • The combined total dose of haloperidol from both formulations must not exceed the corresponding maximum oral haloperidol dose of 20 mg/day.

Elderly

Table 2: Haloperidol decanoate dose recommendations for elderly patients

Transition from oral haloperidol • A low haloperidol decanoate dose of 12.5 to 25 mg is recommended.
Continuation of treatment • It is recommended only to adjust the haloperidol decanoate dose if required (based on individual patient response) until an optimal therapeutic effect is obtained. • The most effective dose is expected to range between 25 and 75 mg. • Doses above 75 mg every 4 weeks should only be considered in patients who have tolerated higher doses and after reassessment of the patient's individual benefit-risk profile.

HALDOL solution for injection

Therapeutic indications

HALDOL solution for injection is indicated in adult patients for:

- Rapid control of severe acute psychomotor agitation associated with psychotic disorder or manic episodes of bipolar I disorder when oral therapy is not appropriate.
- Acute treatment of delirium when non-pharmacological treatments have failed.
- Treatment of mild to moderate chorea in Huntington's disease, when other medicinal products are ineffective or not tolerated, and oral therapy is not appropriate.
- Single or combination prophylaxis in patients at moderate to high risk of postoperative nausea and vomiting, when other medicinal products are ineffective or not tolerated.
- Combination treatment of postoperative nausea and vomiting when other medicinal products are ineffective or not tolerated.

Posology

Adults

A low initial dose is recommended, and this must be adjusted according to the patient's response in order to determine the minimal effective dose (see section 5.2).

Haloperidol dose recommendations for adults aged 18 years and above

Rapid control of severe acute psychomotor agitation associated with psychotic disorder or manic episodes of bipolar I disorder when oral therapy is not appropriate • 5 mg intramuscularly. • May be repeated hourly until sufficient symptom control is achieved. • In the majority of patients, doses of up to 15 mg/day are sufficient. The maximum dose is 20 mg/day. • The continued use of HALDOL should be evaluated early in treatment (see section 4.4). Treatment with HALDOL solution for injection must be discontinued as soon as clinically indicated and, if further treatment is needed, oral haloperidol should be initiated at a 1:1 dose conversion rate followed by dose adjustment according to clinical response.
Acute treatment of delirium when non-pharmacological treatments have failed • 1 to 10 mg intramuscularly. • Treatment should be started at the lowest possible dose, and the dose should be adjusted in increments at 2- to 4-hour intervals if agitation continues, up to a maximum of 10 mg/day.
Treatment of mild to moderate chorea in Huntington's disease, when other medicinal products are ineffective or not tolerated, and oral therapy is not appropriate • 2 to 5 mg intramuscularly. • May be repeated hourly until sufficient symptom control is achieved or up to a maximum of 10 mg/day.

Single or combination prophylaxis in patients at moderate to high risk of postoperative nausea and vomiting, when other medicinal products are ineffective or not tolerated • 1 to 2 mg intramuscularly, at induction or 30 minutes before the end of anaesthesia.
Combination treatment of postoperative nausea and vomiting when other medicinal products are ineffective or not tolerated • 1 to 2 mg intramuscularly.

Elderly

The recommended initial haloperidol dose in elderly patients is half the lowest adult dose.

Further doses may be administered and adjusted according to the patient's response. Careful and gradual dose up-titration in elderly patients is recommended.

The maximum dose is 5 mg/day.

Doses above 5 mg/day should only be considered in patients who have tolerated higher doses and after reassessment of the patient's individual benefit-risk profile

HALDOL tablets and oral solution

Therapeutic indications

Adult patients aged 18 years and above

- Treatment of schizophrenia and schizoaffective disorder.
- Acute treatment of delirium when non-pharmacological treatments have failed.
- Treatment of moderate to severe manic episodes associated with bipolar I disorder.
- Treatment of acute psychomotor agitation associated with psychotic disorder or manic episodes of bipolar I disorder.
- Treatment of persistent aggression and psychotic symptoms in patients with moderate to severe Alzheimer's dementia and vascular dementia when non-pharmacological treatments have failed and when there is a risk of harm to self or others.
- Treatment of tic disorders, including Tourette's syndrome, in patients with severe impairment after educational, psychological and other pharmacological treatments have failed.
- Treatment of mild to moderate chorea in Huntington's disease, when other medicinal products are ineffective or not tolerated.

Paediatric patients

Treatment of:

- Schizophrenia in adolescents aged 13 to 17 years when other pharmacological treatments have failed or are not tolerated.
- Persistent, severe aggression in children and adolescents aged 6 to 17 years with autism or pervasive developmental disorders, when other treatments have failed or are not tolerated.
- Tic disorders, including Tourette's syndrome, in children and adolescents aged 10 to 17 years with severe impairment after educational, psychological and other pharmacological treatments have failed.

Posology

Adults

A low initial dose is recommended, which subsequently may be adjusted according to the patient's response. Patients must always be maintained on the minimal effective dose (see section 5.2).

Haloperidol dose recommendations for adults aged 18 years and above

Treatment of schizophrenia and schizoaffective disorder

- 2 to 10 mg/day orally, as a single dose or in 2 divided doses. Patients with first-episode schizophrenia generally respond to 2 to 4 mg/day, whereas patients with multiple-episode schizophrenia may need doses up to 10 mg /day.
- Adjustments to the dose may be made every 1 to 7 days.
- Doses above 10 mg/day have not demonstrated superior efficacy to lower doses in the majority of patients and may cause an increased incidence of extrapyramidal symptoms. The individual benefit-risk should be assessed when considering doses above 10 mg/day.
- The maximum dose is 20 mg/day because safety concerns outweigh the clinical benefits of treatment at higher doses.

Acute treatment of delirium when non-pharmacological treatments have failed

- 1 to 10 mg/day orally, as a single dose or in 2 to 3 divided doses.
- Treatment should be started at the lowest possible dose, and the dose should be adjusted in increments at 2- to 4-hour intervals if agitation continues, up to a maximum of 10 mg/day.

Treatment of moderate to severe manic episodes associated with bipolar I disorder

- 2 to 10 mg/day orally, as a single dose or in 2 divided doses.
- Adjustments to the dose may be made every 1 to 3 days.
- Doses above 10 mg/day have not demonstrated superior efficacy to lower doses in the majority of patients and may cause an increased incidence of extrapyramidal symptoms. The individual benefit-risk should be assessed when considering doses above 10 mg/day.
- The maximum dose is 15 mg/day because safety concerns outweigh the clinical benefits of treatment at higher doses.
- The continued use of HALDOL should be evaluated early in treatment (see section 4.4).

Treatment of acute psychomotor agitation associated with psychotic disorder or manic episodes of bipolar I disorder

- 5 to 10 mg orally, repeated after 12 hours if necessary to a maximum of 20 mg/day.
- The continued use of HALDOL should be evaluated early in treatment (see section 4.4).
- When switching from haloperidol intramuscular injection, HALDOL orally should be initiated at a 1:1 dose conversion rate followed by dose adjustment according to clinical response.

Treatment of persistent aggression and psychotic symptoms in patients with moderate to severe Alzheimer's dementia and vascular dementia when non-pharmacological treatments have failed and when there is a risk of harm to self or others

- 0.5 to 5 mg/day orally, as a single dose or in 2 divided doses.
- Adjustments to the dose may be made every 1 to 3 days.
- The need for continued treatment must be reassessed after no more than 6 weeks.

Treatment of tic disorders, including Tourette's syndrome, in patients with severe impairment after educational, psychological and other pharmacological treatments have failed

- 0.5 to 5 mg/day orally, as a single dose or in 2 divided doses.
- Adjustments to the dose may be made every 1 to 7 days.
- The need for continued treatment must be reassessed every 6 to 12 months.

Treatment of mild to moderate chorea in Huntington's disease, when other medicinal

products are ineffective or not tolerated

- 2 to 10 mg/day orally, as a single dose or in 2 divided doses.
- Adjustments to the dose may be made every 1 to 3 days.

Elderly

The following initial haloperidol doses are recommended in elderly patients:

- Treatment of persistent aggression and psychotic symptoms in patients with moderate to severe Alzheimer's dementia and vascular dementia when non-pharmacological treatments have failed and when there is a risk of harm to self or others – 0.5 mg/day.
- All other indications – half the lowest adult dose.

The haloperidol dose may be adjusted according to the patient's response. Careful and gradual dose up-titration in elderly patients is recommended.

The maximum dose in elderly patients is 5 mg/day.

Doses above 5 mg/day should only be considered in patients who have tolerated higher doses and after reassessment of the patient's individual benefit-risk profile.