
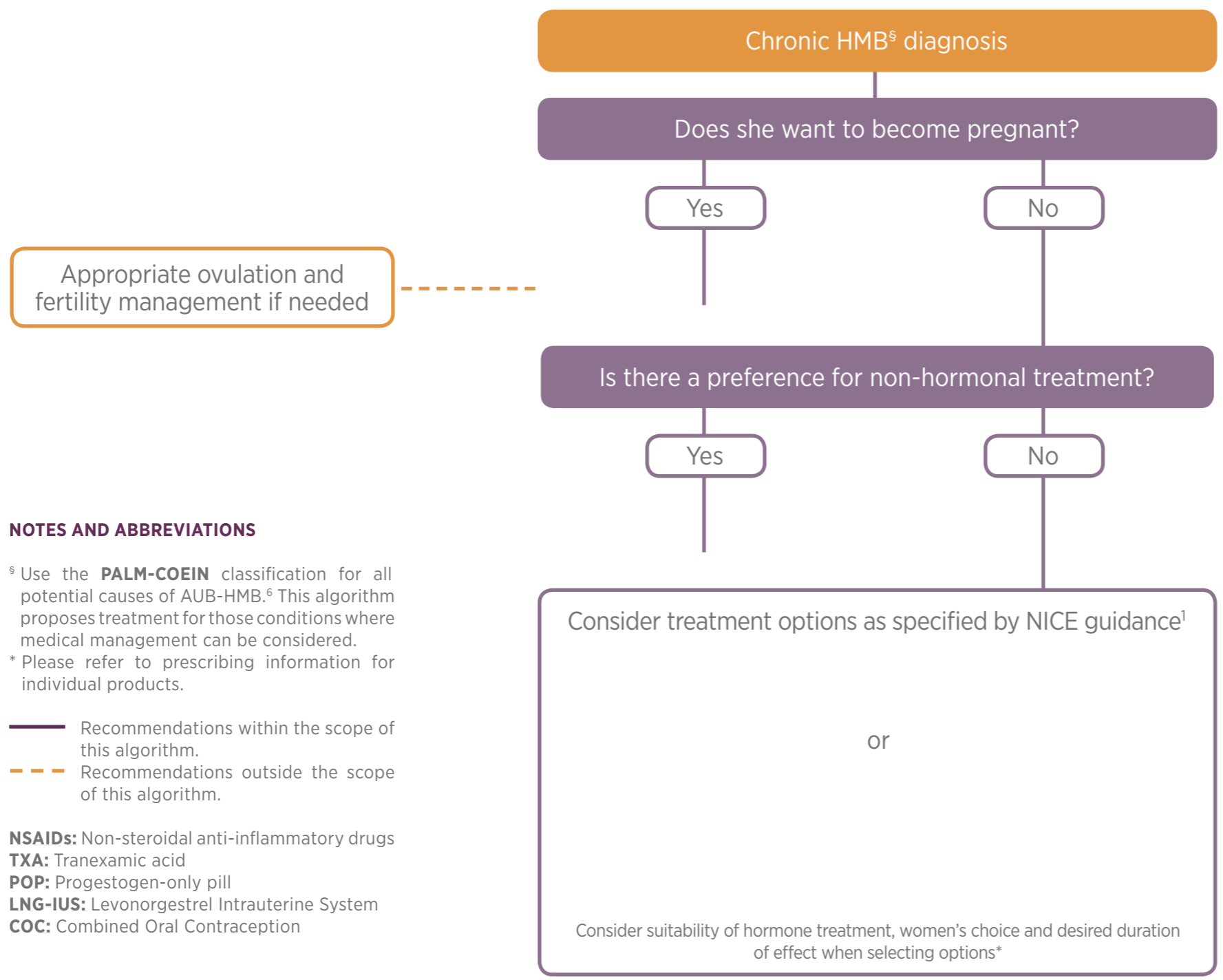


The **HELP** treatment algorithm for chronic HMB

 Click on each treatment option for further information



NOTES AND ABBREVIATIONS

[§] Use the **PALM-COEIN** classification for all potential causes of AUB-HMB.⁶ This algorithm proposes treatment for those conditions where medical management can be considered.
 * Please refer to prescribing information for individual products.

- Recommendations within the scope of this algorithm.
- - - Recommendations outside the scope of this algorithm.

NSAIDs: Non-steroidal anti-inflammatory drugs
TXA: Tranexamic acid
POP: Progestogen-only pill
LNG-IUS: Levonorgestrel Intrauterine System
COC: Combined Oral Contraception

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018; 2. Bitzer J, et al. *Obstet Gynecol Surv* 2015;70(2):115-30; 3. Coulter A, et al. *Int J Technol Assess Health Care* 1995;11(3):456-471; 4. Kaunitz AM, Inki P. *Drugs* 2012;72 (2):193-215; 5. Endrikat J, et al. *Arch Gynecol Obstet* 2012;285:117-21; 6. Munro MG, et al. *Int J Gynecol Obstet* 2011;113(1):3-13.

Interim Treatment: Non-Hormonal

Non-steroidal anti-inflammatory drugs (NSAIDs)



- ✓ Addresses bleeding and pain
- ✓ Tablets are taken orally from day 1, or just before, until heavy blood loss has stopped¹
- ✓ Results show similar values for mefenamic acid, diclofenac and naproxen¹

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

Interim Treatment: Non-Hormonal

Non-steroidal anti-inflammatory drugs (NSAIDs)



How it works¹

NSAIDs reduce the production of prostaglandin and promote vasoconstriction

How it works

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

Interim Treatment: Non-Hormonal

Non-steroidal anti-inflammatory drugs (NSAIDs)



How well it works¹⁻⁴

- Efficacy in reducing Menstrual Blood Loss (MBL) varies widely according to type of NSAID, dosage used and duration of use
- A reduction of 16.2% to 29% in MBL is cited in the literature¹

How well it works (including effect of MBL)

Interim Treatment: Non-Hormonal

Non-steroidal anti-inflammatory drugs (NSAIDs)



Usefulness¹

Can be used:

- when further investigations or other treatment is being organised or considered as an interim measure
- where fertility preservation is required
- when hormonal treatments are not acceptable
- when pain is also a problem
- only at or around the time of a period

Will it be useful?

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

Interim Treatment: Non-Hormonal

Non-steroidal anti-inflammatory drugs (NSAIDs)



Side effects¹

Side effects include:

Indigestion, diarrhoea

Please refer to Summary of Product Characteristics for full list of side effects.

What other things
might it do?
(side effects)

Interim Treatment: Non-Hormonal

Non-steroidal anti-inflammatory drugs (NSAIDs)



Clinical considerations¹⁻³

- No contraceptive effect
- There is a risk of GI and cardiovascular events
- Treatment should be stopped if no symptomatic improvement is seen within 3 menstrual cycles

Background
clinical
considerations

Interim Treatment: Non-Hormonal

Tranexamic acid



- ✓ Slightly better effect on bleeding compared to NSAIDs but does not have an impact on pain^{1,2}
- ✓ 1g 3-4 times per day as long as needed for up to 4 days, a total dose of 4g daily should not be exceeded²

Interim Treatment: Non-Hormonal

Tranexamic acid



How it works¹

Tranexamic acid is a competitive inhibitor of plasminogen activator binding, therefore acting as an antifibrinolytic

How it works

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

Interim Treatment: Non-Hormonal

Tranexamic acid



How well it works^{1*}

Reduction in MBL of 46.7%

How well it works (including effect of MBL)

*Small clinical studies monitoring MBL over two to three cycles; studies vary according to inclusion criteria, comparator, dosing, duration of treatment, assessment of MBL
1. Coulter A et al. *International Journal of Technology Assessment in Health Care* 1995;11(3):456-71.

Interim Treatment: Non-Hormonal

Tranexamic acid



Usefulness¹

Can be used:

- when further investigations or other treatment is being organised or considered as an interim measure
- where fertility preservation is required
- when hormonal treatments are not acceptable

Will it be useful?

Interim Treatment: Non-Hormonal

Tranexamic acid



Side effects¹⁻³

Side effects include:

Nausea, vomiting, diarrhoea

Please refer to Summary of Product Characteristics for full list of side effects.

What other things
might it do?
(side effects)

Interim Treatment: Non-Hormonal

Tranexamic acid



Clinical considerations¹⁻³

- Rapid onset of action
- No contraceptive effect
- Treatment should be stopped if no symptomatic improvement is seen within 3 menstrual cycles
- Tranexamic acid does not treat painful periods
- Tranexamic acid is contraindicated in patients with a history of thrombosis

**Background
clinical
considerations**

Long-term Hormonal Treatment

Levonorgestrel intrauterine system (LNG-IUS)



- ✓ Intrauterine system initially releasing 20 µg of levonorgestrel directly into the endometrium every day¹
- ✓ Up to 96% blood reduction²⁻⁶
- ✓ Lasts for 5 years

1. Mirena - Bayer Ltd Mirena (52mg Intrauterine system levonorgestrel) SmPC www.medicines.ie.

2. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

3. Fox KE. *Curr Med Res Opin* 2012;28(9):1517-1525;

4. Kaunitz AM, Inki P. *Drugs* 2012;72 (2):193-215;

5. Endrikat J, et al. *Arch Gynecol Obstet.* 2012;285:117-21;

6. Hurskainen R, et al. *JAMA* 2004;291(12):1456-1463. The HELP group is a panel of physicians of 12 countries with expert interest in Heavy Menstrual Bleeding (HMB) supported by Bayer

Long-term Hormonal Treatment

Levonorgestrel intrauterine system (LNG-IUS)



How it works¹⁻³

Prevents endometrial proliferation which in turn reduces mean uterine vascular density

How it works

Long-term Hormonal Treatment

Levonorgestrel intrauterine system (LNG-IUS)



How well it works^{1,2}

Reduces MBL by up to 96% (range 71%–96%)*

How well it works (including effect of MBL)

*Studies vary according to inclusion criteria, comparator, dosing, duration of treatment, assessment of MBL

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018; 2. Fox KE. *Curr Med Res Opin* 2012;28(9):1517-1525;

Long-term Hormonal Treatment

Levonorgestrel intrauterine system (LNG-IUS)



Usefulness¹⁻⁵

Contraceptive effect

Associated with:

- a significant increase in levels of haemoglobin and ferritin
- a significant improvement in most Health Related Quality of Life (HR-QoL) over 5 years (at least comparable to those achieved with hysterectomy or endometrial ablation)

No impact on future fertility⁵

Will it be useful?

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;
2. Kaunitz AM, Inki P. *Drugs* 2012;72 (2):193-215;
3. Endrikat J, et al. *Arch Gynecol Obstet.* 2012;285:117-21;
4. Hurskainen R, et al. *JAMA* 2004;291(12):1456-1463.
5. Mirena- Bayer Ltd Mirena (52mg Intrauterine system levonorgestrel) SmPC www.medicines.ie

Long-term Hormonal Treatment

Levonorgestrel intrauterine system (LNG-IUS)



Side effects^{1,2}

Side effects include:

Uterine/vaginal bleeding including spotting, oligomenorrhoea, amenorrhoea

Please refer to Summary of Product Characteristics for full list of side effects.

What other things
might it do?
(side effects)

1. Mirena- Bayer Ltd Mirena (52mg Intrauterine system levonorgestrel) SmPC www.medicines.ie

2. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

Long-term Hormonal Treatment

Levonorgestrel intrauterine system (LNG-IUS)



Clinical considerations^{1,2}

Oligomenorrhea and Amenorrhea in 57% and 16% of women respectively at 12 months¹

- A uterine perforation rate of 0.14% was reported in the recent EURAS-IUD study
- Provides contraception

Background
clinical
considerations

Long-term Hormonal Treatment

Combined Oral Contraceptives (COCs)



- ✓ Combination of oestrogen and progestogen
- ✓ Possible dosing regimens include 21/7 and 26/2^{1,2}

1. Qlaria (estradiol valerate/dienogest) - Bayer Ltd. - Qlaria SmPC www.medicines.ie

2. Microlite - Bayer Ltd. Microlite 100/20mg tablets SmPC www.medicines.ie

Long-term Hormonal Treatment

Combined Oral Contraceptives (COCs)



How it works¹⁻³

Suppress ovulation and prevent endometrial proliferation

How it works

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

2. Fraser IS, et al. *Hum Reprod* 2011;26:2698-708.

3. Bitzer J, et al. *Medical management of heavy menstrual bleeding: a comprehensive review of the literature*. *Obstet Gynecol Surv.* 2015 Feb;70(2):115-30.

Long-term Hormonal Treatment

Combined Oral Contraceptives (COCs)



How well it works¹⁻⁴

There are a limited number of studies involving the use of COCs in HMB²

Reductions in MBL of up to 43% at three months are reported in small studies involving unlicensed COCs*

Reductions in median MBL of 88% are reported in studies of E2V/DNG in the treatment of HMB[†]

E2V/DNG - Estradiol Valerate & Dienogest
LNG/EE - Levonorgestrel & Ethinyl Estradiol

How well it works (including effect of MBL)

*Studies vary according to inclusion criteria, comparator, dosing, duration of treatment, assessment of MBL¹ †E2V/DNG is licensed for the treatment of HMB³

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

2. Fraser IS, et al. *Hum Reprod* 2011;26:2698-708.

3. Qlaria (estradiol valerate/dienogest) - Bayer Ltd. - Qlaria SmPC www.medicines.ie

4. Microlite - Bayer Ltd. Microlite 100/20mg tablets SmPC www.medicines.ie

Long-term Hormonal Treatment

Combined Oral Contraceptives (COCs)



Usefulness^{1,2}

- Contraceptive effect
- No impact on future fertility

Will it be useful?

Long-term Hormonal Treatment

Combined Oral Contraceptives (COCs)



Side effects¹⁻⁴

Side effects include:

Mood changes, headaches, nausea, fluid retention, breast tenderness

Please refer to Summary of Product Characteristics for full list of side effects.

What other things
might it do?
(side effects)

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;
2. Fraser IS, et al. *Hum Reprod* 2011;26:2698-708.
3. Qlaria (estradiol valerate/dienogest) - Bayer Ltd. - Qlaria SmPC www.medicines.ie
4. Microlite - Bayer Ltd. Microlite 100/20mg tablets SmPC www.medicines.ie

Long-term Hormonal Treatment

Combined Oral Contraceptives (COCs)



Clinical considerations¹⁻⁴

- 2 COCs (E2V/DNG, LNG/EE) are licensed for the treatment of HMB and are supported by clinical data in this indication

E2V/DNG - Estradiol Valerate & Dienogest
LNG/EE - Levonorgestrel & Ethinyl Estradiol

Background
clinical
considerations

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;
2. Fraser IS, et al. *Hum Reprod* 2011;26:2698-708.
3. Qlaria (estradiol valerate/dienogest) - Bayer Ltd. - Qlaria SmPC www.medicines.ie
4. Microlite - Bayer Ltd. Microlite 100/20mg tablets SmPC www.medicines.ie

Long-term Hormonal Treatment

Oral progestogens



- ✓ No oestrogen involved
- ✓ Oral progestogens, medroxyprogesterone acetate [2.5-10mg for 5 to 10 days]¹⁻²

Long-term Hormonal Treatment

Oral progestogens



How it works¹

Suppress ovulation and prevent endometrial proliferation

How it works

Long-term Hormonal Treatment

Oral progestogens



How well it works¹

One RCT (n = 44) reported an 83% reduction in MBL with long-course use of oral progestogens

Short-course oral progestogens (i.e. luteal phase only) have no effect on MBL and should not be used for the treatment of HMB

How well it works (including effect of MBL)

1. NICE *Heavy Menstrual Bleeding guideline 88*, 2018;

Long-term Hormonal Treatment

Oral progestogens



Usefulness¹

- Achievement of menstrual regularity in women with anovulatory bleeding
- When oestrogen-containing preparations are contraindicated

Will it be useful?

Long-term Hormonal Treatment

Oral progestogens



Side effects¹

Side effects include:

Weight gain, bloating, breast tenderness, headaches, acne

Please refer to Summary of Product Characteristics for full list of side effects.

What other things
might it do?
(side effects)

Long-term Hormonal Treatment

Oral progestogens



Clinical considerations¹

- No contraceptive effect

Background
clinical
considerations

1. Provera SmPC;