Notices issued in accordance with Part 9, regulation 165, of The Human Medicines Regulations 2012 (SI 2012/1916).

The status of borderline medicinal products is mostly determined in accordance with statutory determination procedures laid down in Part 9 of the Human Medicines Regulations 2012. In some cases, the MHRA may deem it appropriate to issue a determination without following the statutory procedure. These determinations are made under Regulation 165 and will result in one of two notices being issued to companies. The grounds for issuing these determinations are not specified in the regulations but those most commonly used are set out below.

Urgent Notices

Urgent Notices are issued on one or more of the following grounds:

1. Where an unauthorised medicinal product poses an identifiable risk to public/patient safety by virtue of an ingredient or combination of ingredients that are known to be capable of exerting a significant modification to human physiology.

2. Where an unauthorised medicinal product poses an identifiable risk to public/patient safety by virtue of claims which may result in the avoidance of necessary professional medical advice or encouragement to self-medicate without seeking necessary professional medical advice.

3. Where an identical, or essentially similar product has already been determined to be a medicinal product in accordance with the procedures laid down in Part 9 of the Human Medicines Regulations 2012, subject to current medicines regulations or, via the UK courts.

4. Where a product is a copy of, or is identical in all material respects to, another relevant medicinal product that is already an authorised or registered medicine and which, in the opinion of the MHRA, could not be perceived as being used for a non-medicinal purpose.

Other notices

A notice under Regulation 165 will also be issued where advertising material for a product makes clear medical claims such that the product falls within Limb 1 of the definition of medicinal product and the company responsible has not voluntarily complied with a MHRA request to remove or reword the material within a set timescale (with effect from November 2018)

The MHRA will not disclose details of product names, retailers or manufacturers in this summary.

URGENT NOTICES ISSUED UNDER REGULATION 165

June 2016 : Total Urgent Notices issued:- 25

No of cases	Reason(s)
25	Assessment found that products contained Synephrine; Yohimbine; Picamilon; Phenibut; Hydroxycitric Acid; Hoodia; GABA

July 2016 : Total Urgent Notices issued:- 38

No of cases	Reason(s)
38	Assessment found that products contained Synephrine; Yohimbe; Picamilon; Ephedrine; Hydroxycitric Acid; Phenibut; GABA; Melatonin; Aspirin

August 2016 : Total Urgent Notices issued:- 6

No of cases	Reason(s)
5	Assessment found that products contained DMAA; Synephrine; Melatonin; Rhubarb Root; Lidocaine
1	Product presented for treatment/prevention of Hangovers

September 2016 : Total Urgent Notices issued:- 40

No of cases	Reason(s)
40	Assessment found that products contained Synephrine; Yohimbine; DMAA; Phenibut; Ephedra; Amygdalin; GABA; Agnus castus; Black cohosh

October 2016 : Total Urgent Notices issued:- 4

No of cases	Reason(s)
4	Assessment found that products contained Hoodia; GABA; Agnus castus; Black cohosh

November 2016 : Total Urgent Notices issued:- 13

No of cases	Reason(s)
13	Assessment found that products contained DMAA; Yohimbine; Synephrine; Picamilon; Phenibut; GABA; Melatonin; Pygeum Africanum

December 2016 : Total Urgent Notices issued:- 1

No of cases	Reason(s)
1	Assessment found that product contained Synephrine

January 2017 : Total Urgent Notices issued:- 1

No of cases	Reason(s)
1	Assessment found that product contained Hoodia

February 2017 : Total Urgent Notices issued:- 4

No of cases	Reason(s)
3	Assessment found that products contained Melatonin, GABA; Progesterone
1	Assessment found Saw palmetto in prostate product.

March 2017 : Total Urgent Notices issued:- 3

No of cases	Reason(s)
3	Assessment found that products contained Synephrine; Hoodia; Lidocaine

April 2017 : Nil Urgent Notices issued

May 2017: Total Urgent Notices issued:- 5

No of cases	Reason(s)
4	Assessment found that products contained Hoodia; Benzocaine

June 2017: Total Urgent Notices issued:- 6

No of cases	Reason(s)
6	Assessment found that products contained Yohimbine, Amygdalin; Mistletoe; Lidocaine

July 2017: Total Urgent Notices issued:- 16

No of cases	Reason(s)
16	Assessment found that products contained Synephrine, Yohimbine; Phenibut; Melatonin; Lidocaine

August 2017: Total Urgent Notices issued:- 1

No of cases	Reason(s)
1	Assessment found that product contained Yohimbine

September 2017: Total Urgent Notices issued:- 7

No of cases	Reason(s)
7	Assessment found that products contained Yohimbine, Synephrine; Senna; GABA

October 2017: Total Urgent Notices issued:- 52

No of cases	Reason(s)
52	Assessment found that products contained Yohimbine, Synephrine, Ephedrine, DMAA; Aspirin; GABA; Melatonin; Hoodia; Lidocaine

November 2017: Total Urgent Notices issued:- 3

No of cases	Reason(s)
3	Products presented for treatment/prevention of Hangovers

December 2017: Total Urgent Notices issued:- 2

No of cases	Reason(s)
2	Products found to contain Clobetasol and presented for treatment of adverse skin conditions

January 2018: Total Urgent Notices issued:- 5

No of cases	Reason(s)
4	Assessment found that products contained Synephrine; Phenibut; Hoodia; Lidocaine
1	Product presented for treatment/prevention of Hangovers

February 2018: Nil Urgent Notices issued

March 2018: Total Urgent Notices issued:- 7

No of cases	Reason(s)
7	Assessment found that products contained Synephrine; DMAA; Yohimbine

April 2018: Total Urgent Notices issued:- 5

No of cases	Reason(s)
5	Assessment found that products contained Chlorphenamine, Piroxicam, Clobetasol, Lidocaine, Melatonin and GABA

May 2018: Total Urgent Notices issued:- 2

No of cases	Reason(s)
2	Assessment found that products contained Hoodia & CBD

June 2018: Nil Urgent Notices issued

July 2018: Nil Urgent Notices issued

August 2018: Nil Urgent Notices issued

September 2018: Total Urgent Notices issued:- 4

No of cases	Reason(s)
3	Assessment found that products contained Synephrine; Botulinum Toxin A
1	Assessment found product being sold with claims for treating hangovers

October 2018: Total Urgent Notices issued:- 7

No of cases	Reason(s)
6	Assessment found that products contained Synephrine; Yohimbine; Melatonin; GABA; Phenibut; Phosphatidylcholine
1	Assessment found product being sold with claims for treating hangovers

November 2018: Total Urgent Notices issued:- 6

No of cases	Reason(s)
6	Assessment found that products contained Synephrine; Yohimbine; Melatonin & Phenibut

December 2018: Nil Urgent Notices issued

January 2019: Total Urgent Notices issued:- 2

No of cases	Reason(s)
2	Assessment found product being sold with claims for treating hangovers

February 2019: Total Urgent Notices issued:- 4

No of cases	Reason(s)
4	Assessment found that products contained Synephrine &Yohimbine, Milk thistle & Saw Palmetto.

March 2019: Total Urgent Notices issued:- 8

No of cases	Reason(s)
8	Assessment found that 1 product contained Celandine and 7 CBD (with overt medicinal claims)

April 2019: Total Urgent Notices issued:- 8

No of cases	Reason(s)
8	Assessment found that products contained Melatonin, GABA, Lidocaine and 2 hangover prevention products

May 2019: Total Urgent Notices issued:- 2

No of cases	Reason(s)
2	Assessment found that 1 product contained Clobetasol and 1 hangover prevention product

June 2019: Total Urgent Notices issued:- 4

No of cases	Reason(s)
4	Assessment found that products contained Melatonin, DHEA, Yohimbine, Synephrine and Belladonna.

July 2019: Total Urgent Notices issued:- 5

No of cases	Reason(s)
5	Assessment found that products contained Yohimbine, Synephrine and DMAA.

August 2019: Total Urgent Notices issued:- 17

No of cases	Reason(s)
17	Assessment found that 16 products contained Melatonin, Senna, Milk thistle, Devils claw, St John's wort, Black cohosh or Lidocaine and 1 hangover prevention product.

September 2019: Total Urgent Notices issued:- 2

No of cases	Reason(s)
2	Assessment found that 1 product contained Clobetasol and 1 hangover prevention product.

OTHER NOTICES ISSUED UNDER REGULATION 165

November 2018 : Total "other" notices issued 4

No of cases	Reason(s)
3	CBD products made overt medicinal claims
1	Magnesium product made overt medicinal claims

December 2018: Nil Other Notices issued

January 2019 : Total "other" notices issued 4

No of cases	Reason(s)
1	Saw Palmetto product made overt medicinal claims
1	CBD product made overt medicinal claims
1	Glucosamine product made overt medicinal claims
1	Rhodiola Rosea product made overt medicinal claims

February 2019 : Total "other" notices issued 2

No of cases	Reason(s)
1	CBD products made overt medicinal claims
1	Milk thistle product made overt medicinal claims

March - May 2019 : Total "other" notices issued Nil

June 2019 : Total "other" notices issued

No of cases	Reason(s)
1	CBD products made overt medicinal claims

July 2019 : Total "other" notices issued Nil

August 2019 : Total "other" notices issued 1

No of cases	Reason(s)
1	CBD products made overt medicinal claims

September 2019 : Total "other" notices issued Nil

Explanatory Notes (Alphabetical)

Agnus castus	Agnus castus has well documented chemistry and established medicinal uses in both traditional and modern herbal medicine.. The EMA Committee on Herbal Medicinal Products (HMPC), has adopted a community herbal monograph for Vitex Agnus-castus as "well-established" and "traditional use" medicinal products with indications for the treatment of premenstrual syndrome and the relief of minor symptoms in the days before menstruation (premenstrual syndrome), respectively. This use is in line with the perception of the averagely well informed consumer. The classification of products containing Agnus castus has been confirmed by the Independent Review Panel for Borderline Products
Amygdalin	The sale, supply and advertising of preparations containing the cyanogenic substance Amygdalin (also known as B17 and Laetrile) has been subject to restriction in the UK since 1984. Part 1 of schedule 1 of The Human Medicines Regulations 2012 classifies cyanogenic substances other than preparations for external use, as prescription only medicines. In this Part "cyanogenic substances" means preparations which *are presented for sale or supply under the name of, or as containing, amygdalin, laetrile or vitamin B17; (et.seq)* In the UK it is an offence to sell, supply or advertise products containing Amygdalin without a marketing authorisation.
Aspirin	Aspirin is one of the oldest and most well-known and used medicines in the world. It is part of a group of medications called nonsteroidal anti-inflammatory drugs (NSAIDs) and cannot be sold or supplied in products that have not been authorised as medicines.
Benzocaine	Benzocaine is a topical/local anaesthetic. Its purpose is to prevent and treat localised pain by exerting a pharmacological action. Its purpose would be medicinal even where used in conjunction with a non-medical procedure (e.g. tattooing).
Black cohosh	Black cohosh, has well-documented chemistry and established medicinal uses in both traditional and modern herbal medicine The EMA Committee on Herbal Medicinal Products (HMPC), has adopted a community herbal monograph for black cohosh as "well-established medicinal products" with indications for the relief of menopausal complaints such as hot flushes and profuse sweating. This use is in line with the perception of the averagely well informed consumer. This use is in line with the perception of the averagely well informed consumer. The classification of products containing Black cohosh has been confirmed by the Independent Review Panel for Borderline Products.

Botulinum Toxin A	Botulinum toxin is a neurotoxic protein produced by the bacterium Clostridium botulinum and related species. Botulinum toxin types A and B are used in medicine to treat various muscle spasms and diseases characterized by overactive muscle.
CBD	Cannabidiol (CBD) is a phytocannabinoid. CBD oil has been studied for its potential role in treating many common health issues, including anxiety, depression, acne and heart disease.
Chlorphenamine	Chlorpheniramine is an antihistamine that reduces the effects of natural chemical histamine in the body. Histamine can produce symptoms of sneezing, itching, watery eyes, and runny nose. Chlorpheniramine is used to treat runny nose, sneezing, itching, and watery eyes caused by allergies, the common cold, or the flu
Clobetasol propionate	Clobetasol propionate is a topical steroid used to treat the inflammation and itching caused by a number of skin conditions such as allergic reactions, eczema, and psoriasis
DMAA	This substance is regarded as being capable of significant modification to human physiology. Products containing DMAA have already been subject to regulatory controls in various countries around the world following a series of suspected links to serious adverse effects. It is the MHRA's view that the uncontrolled sale and supply of products containing DMAA poses potential risks to public safety. DMAA, is also known as 1,3-Dimethylamylamine methylhexanamine, dimethylamylamine, 4-methyl-2-hexanamine,4-methyl-2-hexylamine, 2-amino-4-methylhexane, 1,3-dimethylpentylamine, Geranmin, Geranium oil and Cranesbill. The classification of products containing DMAA has also been confirmed by the Independent Review Panel for Borderline Products.
GABA	GABA (gamma amino butyric acid) is an active neurotransmitter. It was originally developed in the United States as a pre-surgery anaesthetic. In small doses it has a euphoriant, stimulant effect and in larger doses can produce a sedative effect together with loss of memory; can cause cardiac arrest and can also cause nausea, vomiting, convulsions and coma. This substance therefore has the capacity to modify physiological function in human beings. The classification of products containing GABA has been confirmed by the Independent Review Panel for Borderline Products.
Hangover products	Products for the prevention or treatment of adverse symptoms of excess alcohol consumption are classed as medicines in the UK. Specific Guidance Notes have been in circulation for a number of years. Such products are also regarded as undesirable, as they may be used to encourage increased levels of alcohol consumption, which is already a major cause UK health and social behaviour concerns. The classification of such products has been confirmed by the Independent Review Panel for Borderline Products
Hoodia	Hoodia gordonii is a South African cactus, historically used by the bushmen of the Kalahari Desert to prevent hunger on long hunting trips. Various studies have established that the plant contains a chemical extract known as "P57", which has been shown to cause an artificial modification to the neurological functions responsible for controlling appetite. The classification of products containing Hoodia has been confirmed by the Independent Review Panel for Borderline Products.
Hydroxycitric Acid	HCA has been shown in studies as a potent competitive inhibitor of the extramitochondrial enzyme adenosine triphosphate-citrate (pro-3S)-lyase. This inhibitory action apparently suppresses de novo fatty synthesis, reduces food intake and decreases hepatic glycogen synthesis. Therefore, HCA may be administered to humans with a view to modifying physiological functions. The classification of products containing HCA has also been confirmed by the Independent Review Pane for Borderline Products
Lidocaine	Lidocaine is a topical/local anaesthetic. Its purpose is to prevent and treat localised pain by exerting a pharmacological action. Its purpose would be

	medicinal even where used in conjunction with a non-medical procedure (e.g. tattooing).
Melatonin	Melatonin is a hormone produced by the pineal gland in the brain. Scientists believe it acts as a timing device to synchronise the human body clock with the light/dark cycle. The Agency determined that melatonin was a medicinal product on the basis of its known, significant pharmacological activity and its consequent effect on the human physiology. The agency's authority to make the determination was confirmed by the Court of Appeal (R. v. Medicines Control Agency ex parte Pharma Nord (UK) Limited 1998). The MHRA takes the view that a product with melatonin is a medicine requiring authorisation and there are licensed medicinal products available which can only be supplied by a registered pharmacist to fulfil a doctor's or dentist's prescription.
Phenibut	Phenibut is a central depressant and analogue of the inhibitory neurotransmitter y-aminobutyric acid (GABA) and is a GAB analogue The addition of a phenyl ring allows Phenibut to cross the blood-brain barrier. Phenibut was developed in Russia and has been used as a pharmaceutical drug to treat a wide range of ailments, including post traumatic stress disorder, anxiety, depression, asthenia, insomnia, alcoholism, stuttering and vestibular disorders, among other conditions. It is generally accepted that Phenibut has anxiolytic effects in both animal models and in humans.
Picamilon	Picamilon is a drug formed by the synthetic combination of Niacin and GABA. (see GABA above)
Piroxicam	Piroxicam belongs to a group of pain killers called Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and is used to relieve some symptoms caused by osteoarthritis (arthrosis, degenerative joint disease), rheumatoid arthritis and ankylosing spondylitis (rheumatism of the spine), such as swelling, stiffness and joint pain.
Progesterone	Progesterone is a naturally occurring progestin secreted by the corpus lutem. It is used in postmenopausal women receiving oestrogen replacement therapy to reduce the incidence of endometrial hyperplasia, for the management of secondary amenorrhea, to support embryo implantation and early pregnancy as part of assisted reproductive technology (ART) treatment of infertile women and for the treatment of amenorrhea and abnormal uterine bleeding caused by hormonal imbalance in patients without underlying organic pathology such as fibroids or uterine cancer.
Pygeum Africanum	Pygeum is a herb which has been licensed as a medicinal treatment for Benign Prostatic Hyperplasia (BHP)**.** It is known to have a slow elimination rate which means that prolonged used will result in elevated blood concentrations. The classification of products containing Pygeum has been confirmed by the Independent Panel for Borderline Products.
Rhubarb root	Rhubarb root has well-documented chemistry and established medicinal uses in both traditional and modern medicine. Rhubarb belongs to the stimulating laxatives containing hydroxyanthracene derivatives and is intended for short-term use in cases of occasional constipation. Rhubarb Root has well documented chemistry and established medicinal uses in both traditional and modern herbal medicine. The EMA Committee on Herbal Medicinal Products (HMPC), has adopted a community herbal monograph for Rhubarb Root as "well-established" medicinal products with indications for the treatment of occasional constipation The classification of products containing hydroxyanthracene derivatives has been confirmed by the Independent Review Panel for Borderline Products
Saw palmetto in Prostate product	Saw palmetto, has well-documented chemistry and established medicinal uses in both traditional and modern herbal medicine The EMA Committee on Herbal Medicinal Products (HMPC), has adopted a community herbal monograph for Saw palmetto as "well-established" and "traditional" medicinal products" with indications for the treatment of benign prostatic hyperplasia. This use is in line with the perception of the averagely well informed consumer. The classification of products containing Saw palmetto

	has been confirmed by the Independent Review Panel for Borderline Products
Synephrine	Synephrine is derived primarily from the herb *Citrus aurantium* (Bitter Orange). It is an alkaloid similar in structure to ephedrine and is frequently used as an alternative. It is used as a vasopressor and is an alpha-adrenergic agonist producing stimulation of adrenergic receptors. Synephrine works by stimulating the sympathic nervous system by reducing the tone of smooth muscle cells particularly in the lungs and uterus. Side-effects include anxiety, dyspnoea, hyperglycaemia and tachycardia; overdose can lead to cardiac arrhythmias and a rise in blood pressure. Synephrine is a drug product in Europe where it is known generically as "Oxedrine". It was originally produced as a synthetic derivative of amphetamine.
Yohimbine	Yohimbine is mainly obtained from the herbs *Pausinystalia yohimbe, Rauwolfia serpentina* and *Alchornia floribunda.* It is subject to the Prescription Only Order (POM). This means that products containing this substance may not be sold, supplied or advertised as retail products. Yohimbine is an alkaloid which blocks the release of adrenalin and, in the correct dose, acts as a sexual stimulant. Other properties of the substance include a stimulant effect on the heart, increase of heart rate and blood pressure and, locally, anaesthesia. Its actions are well documented.