Synthon, s.r.o.
Brnenska 32 / c.p.597
678 01 Blansko
Czech Republic
Tel: +420 516 427 322
Fax: +420 516 417 350
e-mail: synthon.cz@synthon.com
www.synthon.com



Certificate of Analysis

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Bicalutamide API

Lot Number : 19BL000456

Item Number : 125225 Date of Manufacture : 03-Jul-2019

Retest Date : 03-Jul-2022

Manufacturing Site : Synthon, s.r.o.

Appearance Complies White or almost white powder Identification IR spectrum Complies The same as Ref. Standard Identification HPLC retention time Complies The same as Ref. St. Prep. Clarity of solution Complies ≤ Ref. Susp. I Colour of solution Complies ≤ Reference Solution B7 Optical rotation 0.0 ° -0.1 - 0.1 ° Loss on drying 0.2 % ≤ 0.5 % Sulphated ash 0.1 % ≤ 0.1 % Residue of catalyst (for CF Pharma drug subst.) Not Performed ≤ 0.0005 % Heavy metals Complies ≤ 0.0005 % Residual solvents (GC) (for Synthon drug subst.) Complies ≤ 0.041 % Actonitrile 0.009 % ≤ 0.041 % Ethanol ≤ 0.05 % ≤ 0.5 % 2-Propanol ≤ 0.05 % ≤ 0.5 % Residual solvents (GC) (for CF Pharma drug subst.) Not Performed ≤ 0.088 % Dichloromethane Not Performed ≤ 0.088 % Dichloromethane Not Performed ≤ 0.089 % Dimethylacetamide Not Performed ≤ 0.089 % Impurities (HPLC) (for Synthon drug s	Tests	Results	Acceptance Criteria
Identification HPLC retention time Complies The same as Ref. St. Prep. Clarity of solution Complies ≤ Ref. Susp. I Colour of solution 0.0 ° -0.1 - 0.1 ° Optical rotation 0.0 ° -0.1 - 0.1 ° Loss on drying 0.2 % ≤ 0.5 % Sulphated ash 0.1 % ≤ 0.1 % Residue of catalyst (for CF Pharma drug subst.) Validation 20.0005 % Heavy metals Complies ≤ 0.0002 % Residual solvents (GC) (for Synthon drug subst.) Complies ≤ 0.041 % Ethanol ≤ 0.05 % ≤ 0.5 % 2-Propanol ≤ 0.05 % ≤ 0.5 % Residual solvents (GC) (for CF Pharma drug subst.) Not Performed ≤ 0.088 % N,N-dimethylformamide Not Performed ≤ 0.088 % Dichloromethane Not Performed ≤ 0.060 % Toluene Not Performed ≤ 0.089 % Dimethylacetamide Not Performed ≤ 0.109 % Impurities (HPLC) (for Synthon drug subst.) ≤ 0.05 % ≤ 0.1 % A/509 ≤ 0.05 % ≤ 0.1 % <	Appearance	Complies	White or almost white powder
Clarity of solution Complies ≤ Ref. Susp. 1 Colour of solution 0.0 ° -0.1 - 0.1 ° Optical rotation 0.0 ° -0.1 - 0.1 ° Loss on drying 0.2 % ≤ 0.5 % Sulphated ash 0.1 % ≤ 0.1 % Residue of catalyst (for CF Pharma drug subst.) Very Complies ≤ 0.0005 % Heavy metals Complies ≤ 0.0005 % Residual solvents (GC) (for Synthon drug subst.) Very Complies ≤ 0.002 % Acctonitrile 0.009 % ≤ 0.041 % ≤ 0.5 % 2-Propanol ≤ 0.05 % ≤ 0.5 % ≤ 0.5 % Residual solvents (GC) (for CF Pharma drug subst.) Not Performed ≤ 0.088 % ≤ 0.088 % Residual solvents (GC) (for CF Pharma drug subst.) Not Performed ≤ 0.088 % ≤ 0.089 % Dichloromethane Not Performed ≤ 0.089 % ≤ 0.099 % Impurities (HPLC) (for Synthon drug subst.) Not Performed ≤ 0.099 % Impurities (HPLC) (for Synthon drug subst.) ≤ 0.05 % ≤ 0.1 % Largest unidentified impurity ≤ 0.05 % ≤ 0.1 %	Identification IR spectrum	Complies	The same as Ref. Standard
Colour of solution	Identification HPLC retention time	Complies	The same as Ref. St. Prep.
Optical rotation 0.0 ° -0.1 - 0.1 ° Loss on drying 0.2 % ≤ 0.5 % Sulphated ash 0.1 % ≤ 0.1 % Residue of catalyst (for CF Pharma drug subst.) Very Completed ≤ 0.0005 % Palladium Not Performed ≤ 0.002 % Heavy metals Complies ≤ 0.002 % Residual solvents (GC) (for Synthon drug subst.) Very Completed ≤ 0.041 % Ethanol ≤ 0.05 % ≤ 0.5 % 2-Propanol ≤ 0.05 % ≤ 0.5 % Residual solvents (GC) (for CF Pharma drug subst.) Not Performed ≤ 0.088 % No-dimethylformamide Not Performed ≤ 0.060 % Dichloromethane Not Performed ≤ 0.069 % Toluene Not Performed ≤ 0.089 % Dimethylacetamide Not Performed ≤ 0.09 % Impurities (HPLC) (for Synthon drug subst.) ≤ 0.05 % ≤ 0.1 % Largest unidentified impurity ≤ 0.05 % ≤ 0.1 %	Clarity of solution	Complies	≤ Ref. Susp. I
Loss on drying 0.2 % ≤ 0.5 % Sulphated ash 0.1 % ≤ 0.1 % Residue of catalyst (for CF Pharma drug subst.) Palladium Not Performed ≤ 0.0005 % Heavy metals	Colour of solution	Complies	≤ Reference Solution B7
Sulphated ash 0.1% $\leq 0.1\%$ Residue of catalyst (for CF Pharma drug subst.) Palladium Not Performed $\leq 0.0005\%$ Heavy metals 0.009% $\leq 0.002\%$ Residual solvents (GC) (for Synthon drug subst.) Acctonitrile 0.009% $\leq 0.041\%$ Ethanol $\leq 0.05\%$ $\leq 0.5\%$ 2-Propanol $\leq 0.05\%$ $\leq 0.5\%$ Residual solvents (GC) (for CF Pharma drug subst.) N,N-dimethylformamide Not Performed $\leq 0.088\%$ Dichloromethane Not Performed $\leq 0.060\%$ Toluene Not Performed $\leq 0.089\%$ Dimethylacetamide Not Performed $\leq 0.089\%$ Dimethylacetamide Not Performed $\leq 0.099\%$ Impurities (HPLC) (for Synthon drug subst.) A/509 $\leq 0.05\%$ $\leq 0.1\%$ Largest unidentified impurity $\leq 0.05\%$ $\leq 0.1\%$	Optical rotation	0.0 °	-0.1 - 0.1 °
Residue of catalyst (for CF Pharma drug subst.) Palladium Not Performed $\leq 0.0005\%$ Heavy metals Complies $\leq 0.002\%$ Residual solvents (GC) (for Synthon drug subst.) Acetonitrile 0.009% $\leq 0.041\%$ Ethanol 2 -Propanol $\leq 0.05\%$ 2 -Propanol Residual solvents (GC) (for CF Pharma drug subst.) N,N-dimethylformamide Not Performed Dichloromethane Not Performed $\leq 0.088\%$ Dimethylacetamide Not Performed $\leq 0.089\%$ Dimethylacetamide Not Performed $\leq 0.099\%$ Impurities (HPLC) (for Synthon drug subst.) A/509 Largest unidentified impurity $\leq 0.05\%$ $\leq 0.1\%$	Loss on drying	0.2 %	≤ 0.5 %
PalladiumNot Performed $\leq 0.0005\%$ Heavy metalsComplies $\leq 0.002\%$ Residual solvents (GC) (for Synthon drug subst.) $= 0.009\%$ $\leq 0.041\%$ Acetonitrile 0.009% $\leq 0.041\%$ Ethanol $\leq 0.05\%$ $\leq 0.5\%$ 2-Propanol $\leq 0.05\%$ $\leq 0.5\%$ Residual solvents (GC) (for CF Pharma drug subst.)Not Performed $\leq 0.088\%$ N,N-dimethylformamideNot Performed $\leq 0.060\%$ DichloromethaneNot Performed $\leq 0.089\%$ DimethylacetamideNot Performed $\leq 0.089\%$ Impurities (HPLC) (for Synthon drug subst.) $\leq 0.05\%$ $\leq 0.1\%$ A/509 $\leq 0.05\%$ $\leq 0.1\%$ Largest unidentified impurity $\leq 0.05\%$ $\leq 0.1\%$	Sulphated ash	0.1 %	≤ 0.1 %
Heavy metals Complies $\leq 0.002 \%$ Residual solvents (GC) (for Synthon drug subst.) Acetonitrile 0.009% $\leq 0.041 \%$ Ethanol $\leq 0.05 \%$ $\leq 0.5 \%$ 2-Propanol $\leq 0.05 \%$ $\leq 0.5 \%$ Residual solvents (GC) (for CF Pharma drug subst.) N,N-dimethylformamide Not Performed $\leq 0.088 \%$ Dichloromethane Not Performed $\leq 0.060 \%$ Toluene Not Performed $\leq 0.089 \%$ Dimethylacetamide Not Performed $\leq 0.089 \%$ Dimethylacetamide Not Performed $\leq 0.099 \%$ Impurities (HPLC) (for Synthon drug subst.) A/509 $\leq 0.05 \%$ $\leq 0.1 \%$ Largest unidentified impurity $\leq 0.05 \%$ $\leq 0.1 \%$	Residue of catalyst (for CF Pharma drug subst.)		
Residual solvents (GC) (for Synthon drug subst.) Acetonitrile 0.009% $\leq 0.041\%$ Ethanol $\leq 0.05\%$ $\leq 0.5\%$ 2-Propanol Residual solvents (GC) (for CF Pharma drug subst.) N,N-dimethylformamide Not Performed $\leq 0.088\%$ Dichloromethane Not Performed $\leq 0.060\%$ Toluene Not Performed $\leq 0.089\%$ Dimethylacetamide Not Performed $\leq 0.089\%$ Impurities (HPLC) (for Synthon drug subst.) $A/509$ $\leq 0.05\%$ $\leq 0.1\%$	Palladium	Not Performed	≤ 0.0005 %
Acetonitrile 0.009% $\leq 0.041\%$ Ethanol $\leq 0.05\%$ $\leq 0.5\%$ 2-Propanol $\leq 0.05\%$ $\leq 0.5\%$ Residual solvents (GC) (for CF Pharma drug subst.) \times N,N-dimethylformamideNot Performed $\leq 0.088\%$ DichloromethaneNot Performed $\leq 0.060\%$ TolueneNot Performed $\leq 0.089\%$ DimethylacetamideNot Performed $\leq 0.109\%$ Impurities (HPLC) (for Synthon drug subst.) \times \times A/509 \times \times \times Largest unidentified impurity \times \times \times	Heavy metals	Complies	≤ 0.002 %
Ethanol $\leq 0.05\%$ $\leq 0.5\%$ 2-Propanol $\leq 0.05\%$ $\leq 0.5\%$ Residual solvents (GC) (for CF Pharma drug subst.) N,N-dimethylformamide Not Performed $\leq 0.088\%$ Dichloromethane Not Performed $\leq 0.060\%$ Toluene Not Performed $\leq 0.089\%$ Dimethylacetamide Not Performed $\leq 0.089\%$ Dimethylacetamide Not Performed $\leq 0.109\%$ Impurities (HPLC) (for Synthon drug subst.) A/509 $\leq 0.05\%$ $\leq 0.1\%$ Largest unidentified impurity $\leq 0.05\%$ $\leq 0.1\%$	Residual solvents (GC) (for Synthon drug subst.)		
2-Propanol $\leq 0.05 \%$ $\leq 0.5 \%$ Residual solvents (GC) (for CF Pharma drug subst.)Not Performed $\leq 0.088 \%$ N,N-dimethylformamideNot Performed $\leq 0.060 \%$ DichloromethaneNot Performed $\leq 0.069 \%$ TolueneNot Performed $\leq 0.089 \%$ DimethylacetamideNot Performed $\leq 0.109 \%$ Impurities (HPLC) (for Synthon drug subst.) $\leq 0.05 \%$ $\leq 0.1 \%$ Largest unidentified impurity $\leq 0.05 \%$ $\leq 0.1 \%$	Acetonitrile	0.009 %	≤ 0.041 %
Residual solvents (GC) (for CF Pharma drug subst.) N,N-dimethylformamide Not Performed $\leq 0.088 \%$ Dichloromethane Not Performed $\leq 0.060 \%$ Toluene Not Performed $\leq 0.089 \%$ Dimethylacetamide Not Performed $\leq 0.109 \%$ Impurities (HPLC) (for Synthon drug subst.) $\Delta/509$ Largest unidentified impurity $\leq 0.05 \%$ $\leq 0.1 \%$	Ethanol	≤ 0.05 %	≤ 0.5 %
N,N-dimethylformamideNot Performed $\leq 0.088 \%$ DichloromethaneNot Performed $\leq 0.060 \%$ TolueneNot Performed $\leq 0.089 \%$ DimethylacetamideNot Performed $\leq 0.109 \%$ Impurities (HPLC) (for Synthon drug subst.) $\leq 0.05 \%$ $\leq 0.1 \%$ Largest unidentified impurity $\leq 0.05 \%$ $\leq 0.1 \%$	2-Propanol	≤ 0.05 %	≤ 0.5 %
Dichloromethane Not Performed $\leq 0.060 \%$ Toluene Not Performed $\leq 0.089 \%$ Dimethylacetamide Not Performed $\leq 0.109 \%$ Impurities (HPLC) (for Synthon drug subst.) $A/509 \qquad \leq 0.05 \% \qquad \leq 0.1 \%$ Largest unidentified impurity $\leq 0.05 \% \qquad \leq 0.1 \%$	Residual solvents (GC) (for CF Pharma drug subst.)		
Toluene Not Performed $\leq 0.089 \%$ Dimethylacetamide Not Performed $\leq 0.109 \%$ Impurities (HPLC) (for Synthon drug subst.) A/509 $\leq 0.05 \%$ $\leq 0.1 \%$ Largest unidentified impurity $\leq 0.05 \%$ $\leq 0.1 \%$	N,N-dimethylformamide	Not Performed	≤ 0.088 %
$\begin{array}{llllllllllllllllllllllllllllllllllll$	Dichloromethane	Not Performed	≤ 0.060 %
Impurities (HPLC) (for Synthon drug subst.) $ A/509 \hspace{1cm} \leq 0.05 \hspace{0.1cm} \% \hspace{1cm} \leq 0.1 \hspace{0.1cm} \% $ Largest unidentified impurity $ \leq 0.05 \hspace{0.1cm} \% \hspace{1cm} \leq 0.1 \hspace{0.1cm} \% $	Toluene	Not Performed	≤ 0.089 %
A/509 $\leq 0.05 \%$ $\leq 0.1 \%$ Largest unidentified impurity $\leq 0.05 \%$ $\leq 0.1 \%$	Dimethylacetamide	Not Performed	≤ 0.109 %
Largest unidentified impurity $\leq 0.05 \%$ $\leq 0.1 \%$	Impurities (HPLC) (for Synthon drug subst.)		
	A/509	≤ 0.05 %	≤ 0.1 %
Total impurities $\leq 0.05 \%$ $\leq 1.0 \%$	Largest unidentified impurity	≤ 0.05 %	≤ 0.1 %
	Total impurities	≤ 0.05 %	≤ 1.0 %

Synthon, s.r.o.
Brnenska 32 / c.p.597
678 01 Blansko
Czech Republic
Tel: +420 516 427 322
Fax: +420 516 417 350
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Bicalutamide API		Lot Number: 19BL000456
Tests	Results	Acceptance Criteria
Impurities (HPLC) (for CF Pharma drug subst.)		
Diol (A/509)	Not Performed	≤ 0.1 %
Sulfinate (A/507)	Not Performed	≤ 0.1 %
Acid (A/510)	Not Performed	≤ 0.1 %
Anilide (A#520)	Not Performed	≤ 0.1 %
Aniline (A/502)	Not Performed	≤ 0.1 %
Sulfon (A#514)	Not Performed	≤ 0.1 %
2-F-Bica (A#518)	Not Performed	≤ 0.1 %
iso-Bica (A#519)	Not Performed	≤ 0.1 %
Largest unidentified impurity	Not Performed	≤ 0.1 %
Total impurities	Not Performed	≤ 1.0 %
Assay (HPLC, dry basis)	100.0 %	98.0 - 102.0 %
Microbial contamination		
Total aerobic microbial count (TAMC)	<10 CFU/g	$\leq 1000 \text{ CFU/g}$
Total combined yeasts/moulds count (TYMC)	<10 CFU/g	≤100 CFU/g
Escherichia coli	Complies	Not present/g
Particle size distribution		
d(0.9)	13 μm	< 50 μm

This batch complies with the specification set in CASS.NUS.BCM.002.01.

Issued by: Michaela Matejková Date of Issue: 06/Sep/2019

QA manager This is an electronic signature

Report: 127630 Date: 06 Sep 2019/10:42:56 From: LW7 Production